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(54) Title: COMPOSITIONS AND METHODS FOR TREATING PERIPHERAL ARTERY DISEASE

(57) Abstract: The present disclosure provides compositions and methods for treating Peripheral Artery Diseases in a subject by administering an ectonucleotide pyrophosphatase phosphodiesterase-1 (ENPP1) agent or an ectonucleotide pyrophosphatase phosphodiesterase-3 (ENPP3).

COMPOSITIONS AND METHODS FOR TREATING PERIPHERAL ARTERY DISEASE

FIELD OF THE DISCLOSURE

The disclosure relates to compositions and methods of treating vascular diseases.

CROSS REFERENCE

This application claims priority to U.S. Application No. 63/030,840 filed on May 27, 2020, the content of which is herein incorporated by reference in its entirety.

SEQUENCE LISTING

This application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on May 27th, 2021, is named 4427-10202_sequence_ST25.txt and is 340 kilo bytes in size.

BACKGROUND

Peripheral Artery Disease (PAD) is a common disorder that occurs due to atherosclerosis characterized by stenosis and/or obstruction of lower limbs arteries leading to decreased muscle perfusion and oxygenation. Symptomatic PAD patients suffer symptoms of intermittent claudication (IC), defined as fatigue, discomfort, or pain occurring in limb muscles during effort, due to exercise-induced ischemia. PAD is progressive and can lead to necrosis, gangrene, and need for limb amputation. Due to the complexity and multifactorial origins of PAD, as well as the differences in muscular adaptive responses, precise PAD pathophysiological mechanisms are still largely unknown.

SUMMARY OF THE DISCLOSURE

The disclosure is based, at least in part, on the surprising discovery that an ENPP1 polypeptide inhibited the unwanted proliferation of vascular smooth muscle cells that occurs following trauma to peripheral arteries in mammals. As described in the working examples, the therapeutic effects of an ENPP1-Fc fusion protein were assessed with respect to the

ability to inhibit stenosis after angioplasty in previously injured and stented peripheral arteries of Yorkshire swine. Animals treated with the ENPP1-Fc protein exhibited markedly lower intimal thickening in stented profunda arteries relative to animals treated with a vehicle control, demonstrating that ENPP1 has therapeutic utility in inhibiting and/or preventing intimal thickening and/or proliferation in injured peripheral arteries.

Accordingly, in one aspect, the disclosure relates to a method for treating a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby treat said peripheral artery disease in said subject.

The disclosure includes a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

In some embodiments of any of the methods described herein, the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

The disclosure also includes a method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

In some embodiments of any of the methods described herein, the subject has common femoral artery disease.

In some embodiments of any of the methods described herein, the subject has femoral-popliteal disease.

In some embodiments of any of the methods described herein, the subject has tibial-peroneal disease.

The disclosure also relates to a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who undergoes surgery on said peripheral artery, the method comprising: administering to the subject an

effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

In some embodiments of any of the methods described herein, the agent is administered prior to, during and/or after said surgery.

In some embodiments of any of the methods described herein, the surgery comprises placement of a stent.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises ENPP1 variants that retain enzymatic activity.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises a nucleic acid encoding an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises a viral vector comprising a nucleic acid encoding an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises the extracellular domain of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises the catalytic domain of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises amino acids 99 to 925 of SEQ ID NO:1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises a heterologous protein.

In some embodiments of any of the methods described herein, the heterologous protein increases the circulating half-life of the ENPP1 polypeptide in mammal.

In some embodiments of any of the methods described herein, the heterologous protein is an Fc region of an immunoglobulin molecule.

In some embodiments of any of the methods described herein, the immunoglobulin molecule is an IgG1 molecule.

In some embodiments of any of the methods described herein, the heterologous protein is an albumin molecule.

In some embodiments of any of the methods described herein, the heterologous protein is carboxy-terminal to the ENPP1 polypeptide.

In some embodiments of any of the methods described herein, ENPP1 agent comprises a linker.

In some embodiments of any of the methods described herein, the linker separates the ENPP1 polypeptide and the heterologous protein.

In some embodiments of any of the methods described herein, the linker comprises the following amino acid sequence: (GGGGS)_n, wherein n is an integer from 1 to 10.

In some embodiments of any of the methods described herein, the ENPP1 agent is administered to the subject subcutaneously.

In some embodiments of any of the methods described herein, the ENPP1 agent is administered to the subject intravenously.

In some embodiments of any of the methods described herein, the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

In another aspect, the disclosure also includes a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery.

In another aspect, the disclosure features a method for reducing and/or preventing stenosis or restenosis in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent stenosis or restenosis in said peripheral artery.

In some embodiments of any of the methods described herein, the agent is administered prior to, during and/or after stent placement.

In another aspect, the disclosure features a method for treating a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby treat said peripheral artery disease in said subject.

In yet another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

In some embodiments of any of the methods described herein, the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

In another aspect, the disclosure features a method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

In some embodiments of any of the methods described herein, the subject has common femoral artery disease.

In some embodiments of any of the methods described herein, the subject has femoral-popliteal disease.

In some embodiments of any of the methods described herein, the subject has tibial-peroneal disease.

In another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who requires surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

In some embodiments of any of the methods described herein, the agent is administered prior to, during and/or after said surgery.

In some embodiments of any of the methods described herein, the surgery comprises placement of a stent.

In some embodiments of any of the methods described herein, the subject does not have a deficiency of ENPP1.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises an ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises ENPP3 variants that retain enzymatic activity.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a nucleic acid encoding an ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a viral vector comprising a nucleic acid encoding an ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises the extracellular domain of ENPP3.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises the catalytic domain of ENPP3.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises amino acids 49 to 875 of SEQ ID NO: 7.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises a heterologous protein.

In some embodiments of any of the methods described herein, the heterologous protein increases the circulating half-life of the ENPP3 polypeptide in mammal.

In some embodiments of any of the methods described herein, the heterologous protein is an Fc region of an immunoglobulin molecule.

In some embodiments of any of the methods described herein, the immunoglobulin molecule is an IgG1 molecule.

In some embodiments of any of the methods described herein, the heterologous protein is an albumin molecule.

In some embodiments of any of the methods described herein, the heterologous protein is carboxy-terminal to the ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a linker.

In some embodiments of any of the methods described herein, the linker separates the ENPP3 polypeptide and the heterologous protein.

In some embodiments of any of the methods described herein, the linker comprises the following amino acid sequence: (GGGGS)_n, wherein n is an integer from 1 to 10.

In some embodiments of any of the methods described herein, the ENPP3 agent is administered to the subject subcutaneously.

In some embodiments of any of the methods described herein, the ENPP3 agent is administered to the subject intravenously.

In some embodiments of any of the methods described herein, the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

In some embodiments of any of the methods described herein, the subject has occlusive peripheral artery disease.

In another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery.

In another aspect, the disclosure features a method for reducing and/or preventing stenosis or restenosis in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent stenosis or restenosis in said peripheral artery.

In some embodiments of any of the methods described herein, the ENPP3 agent is administered prior to, during and/or after stent placement.

In yet another aspect, the disclosure features a coated stent comprising a vascular stent; and a coating on the stent, the coating comprising an ENPP1 agent; and a carrier for said ENPP1 agent, wherein said coating is configured to release said ENPP1 agent from the stent at a rate of 1-10 $\mu\text{g/ml}$ per day.

In some embodiments of any of the stents described herein, the ENPP1 agent in an amount between 1 wt % and 50 wt %, based on a total weight of the coating.

In some embodiments of any of the stents described herein, the ENPP1 agent is selected from a group consisting of: ENPP1, ENPP1-Fc, ENPP1-Albumin, and ENPP1 mRNA.

In some embodiments of any of the stents described herein, the ENPP1 agent comprises ENPP1 variants that retain enzymatic activity.

In some embodiments of any of the stents described herein, the carrier is non-reactive with said ENPP1 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric carrier that is physically bound to said ENPP1 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric carrier that is chemically bound to said ENPP1 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric biodegradable carrier.

In some embodiments of any of the stents described herein, the carrier comprises a nonpolymeric carrier.

In some embodiments of any of the stents described herein, the nonpolymeric carrier is selected from a group consisting of: Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil.

In some embodiments of any of the stents described herein, the carrier is a liquid at body temperature.

In some embodiments of any of the stents described herein, the carrier is a solid at body temperature.

In yet another aspect, the disclosure features a coated stent comprising a vascular stent; and a coating on the stent, the coating comprising an ENPP3 agent; and a carrier for said ENPP3 agent, wherein said coating is configured to release said ENPP3 agent from the stent at a rate of 1-10 $\mu\text{g/ml}$ per day.

In some embodiments of any of the stents described herein, the ENPP3 agent in an amount between 1 wt % and 50 wt %, based on a total weight of the coating.

In some embodiments of any of the stents described herein, the ENPP3 agent is selected from a group consisting of: ENPP3, ENPP3-Fc, ENPP3-Albumin, and ENPP3 mRNA.

In some embodiments of any of the stents described herein, the ENPP3 agent comprises ENPP3 variants that retain enzymatic activity.

In some embodiments of any of the stents described herein, the carrier is non-reactive with said ENPP3 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric carrier that is physically bound to said ENPP3 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric carrier that is chemically bound to said ENPP3 agent.

In some embodiments of any of the stents described herein, the carrier comprises a polymeric biodegradable carrier.

In some embodiments of any of the stents described herein, the carrier comprises a nonpolymeric carrier.

In some embodiments of any of the stents described herein, the nonpolymeric carrier is selected from a group consisting of: Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil.

In some embodiments of any of the stents described herein, the carrier is liquid at body temperature.

In some embodiments of any of the stents described herein, the carrier is solid at body temperature.

In yet another aspect, the disclosure features a method for treating a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby treat said peripheral artery disease in said subject.

In yet another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

In some embodiments of any of the methods described herein, the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

In yet another aspect, the disclosure features a method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

In some embodiments of any of the methods described herein, the subject has common femoral artery disease.

In some embodiments of any of the methods described herein, the subject has femoral-popliteal disease.

In some embodiments of any of the methods described herein, the subject has tibial-peroneal disease.

In yet another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who has a condition requiring surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to

release said ENPP1 agent in an amount effective to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

In some embodiments of any of the methods described herein, the agent is administered prior to, during and/or after said surgery.

In some embodiments of any of the methods described herein, the condition requiring surgery is due to a prior placement of a non-eluting arterial stent in said artery.

In some embodiments of any of the methods described herein, the condition requiring is due to a prior placement of an eluting arterial stent in said artery which elutes therapeutic agents other than said ENPP1 agent.

In some embodiments of any of the methods described herein, the subject does not have a deficiency of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises a nucleic acid encoding an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises a viral vector comprising a nucleic acid encoding an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises the extracellular domain of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises the catalytic domain of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises amino acids 99 to 925 of SEQ ID NO:1.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide comprises a heterologous protein.

In some embodiments of any of the methods described herein, the heterologous protein increases the circulating half-life of the ENPP1 polypeptide in mammal.

In some embodiments of any of the methods described herein, the heterologous protein is an Fc region of an immunoglobulin molecule.

In some embodiments of any of the methods described herein, the immunoglobulin molecule is an IgG1 molecule.

In some embodiments of any of the methods described herein, the heterologous protein is an albumin molecule.

In some embodiments of any of the methods described herein, the heterologous protein is carboxy-terminal to the ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises a linker.

In some embodiments of any of the methods described herein, the ENPP1 polypeptide and the heterologous protein.

In some embodiments of any of the methods described herein, the linker comprises the following amino acid sequence: (GGGGS)_n, wherein n is an integer from 1 to 10.

In some embodiments of any of the methods described herein, the ENPP1 agent is administered to the subject subcutaneously.

In some embodiments of any of the methods described herein, wherein the ENPP1 agent is administered to the subject intravenously.

In some embodiments of any of the methods described herein, the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

In yet another aspect, the disclosure features a method for treating a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby treat said peripheral artery disease in said subject.

In yet another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated

with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

In some embodiments of any of the methods described herein, the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

In yet another aspect, the disclosure features a method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

In some embodiments of any of the methods described herein, the subject has common femoral artery disease.

In some embodiments of any of the methods described herein, the subject has femoral-popliteal disease.

In some embodiments of any of the methods described herein, the subject has tibial-peroneal disease.

In yet another aspect, the disclosure features a method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who has a condition requiring surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

In some embodiments of any of the methods described herein, the agent is administered prior to, during and/or after said surgery.

In some embodiments of any of the methods described herein, the condition requiring surgery is due to a prior placement of a non-eluting arterial stent in said artery.

In some embodiments of any of the methods described herein, the condition requiring is due to a prior placement of an eluting arterial stent in said artery which elutes therapeutic agents other than said ENPP3 agent.

In some embodiments of any of the methods described herein, the subject does not have a deficiency of ENPP1.

In some embodiments of any of the methods described herein, the ENPP1 agent comprises an ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a nucleic acid encoding an ENPP1 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a viral vector comprising a nucleic acid encoding an ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises the extracellular domain of ENPP3.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises the catalytic domain of ENPP3.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises amino acids 49-875 of SEQ ID NO:7.

In some embodiments of any of the methods described herein, the ENPP3 polypeptide comprises a heterologous protein.

In some embodiments of any of the methods described herein, the heterologous protein increases the circulating half-life of the ENPP3 polypeptide in mammal.

In some embodiments of any of the methods described herein, the heterologous protein is an Fc region of an immunoglobulin molecule.

In some embodiments of any of the methods described herein, the immunoglobulin molecule is an IgG1 molecule.

In some embodiments of any of the methods described herein, the heterologous protein is an albumin molecule.

In some embodiments of any of the methods described herein, the heterologous protein is carboxy-terminal to the ENPP3 polypeptide.

In some embodiments of any of the methods described herein, the ENPP3 agent comprises a linker.

In some embodiments of any of the methods described herein, the linker separates the ENPP3 polypeptide and the heterologous protein.

In some embodiments of any of the methods described herein, the linker comprises the following amino acid sequence: (GGGGS) n , wherein n is an integer from 1 to 10.

In some embodiments of any of the methods described herein, the ENPP3 agent is administered to the subject subcutaneously.

In some embodiments of any of the methods described herein, the ENPP3 agent is administered to the subject intravenously.

In some embodiments of any of the methods described herein, the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

Other features and advantages of the disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a series of photographs of representative profunda artery images captured by angiography at day 14 and day 42 post stent implantation. The two control images illustrate a narrowing of the profunda due to intimal proliferation at day 42 relative to the morphology of the vessel at day 14. By contrast, in animals treated with ENPP1-Fc little visible change in profunda morphology was observed between day 14 and day 42. The upper and lower boundary of the stent within the vessel is identified in each photograph by rectangles.

Figure 2 is a series of photographs of representative profunda artery images captured by Optical Coherence Tomography (OCT) at day 14 and day 42 post stent implantation. The two control images illustrate a pronounced intimal thickening within the profunda at day 42 relative to the morphology of the vessel at day 14. By contrast, in animals treated with ENPP1-Fc little visible intimal thickening was observed between day 14 and day 42. The extent of stenosis is highlighted in the day 42 photographs.

Figure 3 is a bar graph depicting the percent area of stenosis at day 14 and day 42 in the profunda of pigs treated with ENPP1-Fc (Treatment) or given vehicle control (Control), as measured by OCT.

Figure 4A is a cross-section of an artery experiencing restenosis in the presence of an uncoated stent. The endothelium **12** normally serves as a solid barrier between the layer of smooth muscle cells **14** and the arterial lumen **20**. Small tears **16** in the endothelium **12** can expose smooth muscle cells **14**, which can then migrate into the arterial lumen **20** and hyper proliferate into a mass **18** which can partially or completely occlude the lumen **20** even though an uncoated stent **21** is placed, during a procedure **60** such as angioplasty, in the artery **10** to keep the arterial lumen **20** open. Fig. 4B is a cross-section of an artery **10** containing a coated stent **22**. The stent has a coating **24** containing a carrier and a bioactive compound such as ENPP1 agent **65** that inhibits and or prevents restenosis. By using a stent having this coating **24**, the tears **16** shown in FIG. 4A in the endothelium **12** may be reduced or eliminated. Additionally, the mass **18** created by a proliferation of smooth muscle cells **14**, as shown in FIG. 4A, is eliminated or substantially reduced.

DETAILED DESCRIPTION

Definitions

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although any methods and materials similar or equivalent to those described herein can be used in practice or testing of the present disclosure, the preferred methods and materials are described.

For clarity, "*NPPI*" and "*ENPP1*" refer to the same protein and are used interchangeably herein. As used herein, the term "*ENPP1 protein*" or "*ENPP1 polypeptide*" refers to ectonucleotide pyrophosphatase/phosphodiesterase-1 protein encoded by the ENPP1 gene that is capable of cleaving ATP to generate PPi and also reduces ectopic calcification in soft tissue.

ENPP1 protein is a type II transmembrane glycoprotein and cleaves a variety of substrates, including phosphodiester bonds of nucleotides and nucleotide sugars and pyrophosphate bonds of nucleotides and nucleotide sugars. ENPP1 protein has a transmembrane domain and soluble extracellular domain. The extracellular domain is further

subdivided into somatomedin B domain, catalytic domain and the nuclease domain. The sequence and structure of wild-type ENPP1 is described in detail in PCT Application Publication No. WO 2014/126965 to Braddock, et al., which is incorporated herein in its entirety by reference.

ENPP1 polypeptides as used herein encompasses polypeptides that exhibit ENPP1 enzymatic activity, mutants of ENPP1 that retain ENPP1 enzymatic activity, fragments of ENPP1 or variants of ENPP1 including deletion variants that exhibit ENPP1 enzymatic activity. ENPP1 enzymatic activity refers to the ability of the ENPP1 polypeptide to cleave Adenosine Triphosphate (ATP) into plasma pyrophosphate (PPi), as noted below.

ENPP3 polypeptides as used herein encompasses polypeptides that exhibit ATP cleavage enzymatic activity, mutants of ENPP3 that retain ATP cleavage enzymatic activity, fragments of ENPP3 or variants of ENPP3 including deletion variants that exhibit ATP cleavage enzymatic activity. ATP cleavage enzymatic activity refers to the ability of the ENPP3 polypeptide to cleave Adenosine Triphosphate (ATP) into plasma pyrophosphate (PPi), as noted below.

Some examples of ENPP1 and ENPP3 polypeptides, mutants, or mutant fragments thereof, have been previously disclosed in International PCT Application Publications No. WO/2014/126965- Braddock et al., WO/2016/187408-Braddock et al., WO/2017/087936- Braddock et al., and WO2018/027024-Braddock et al., all of which are incorporated by reference in their entireties herein.

Enzymatically active” with respect to an ENPP1 polypeptide or an ENPP3 polypeptide is defined as possessing ATP hydrolytic activity into AMP and PPi and/or AP3a hydrolysis to ADP and AMP. NPP1 and NPP3 readily hydrolyze ATP into AMP and PPi. The steady-state Michaelis-Menten enzymatic constants of NPP1 are determined using ATP as a substrate. NPP1 can be demonstrated to cleave ATP by HPLC analysis of the enzymatic reaction, and the identity of the substrates and products of the reaction are confirmed by using ATP, AMP, and ADP standards. The ATP substrate degrades over time in the presence of NPP1, with the accumulation of the enzymatic product AMP. Using varying concentrations of ATP substrate, the initial rate velocities for NPP1 are derived in the presence of ATP, and the data is fit to a curve to derive the enzymatic rate constants. At physiologic pH, the kinetic rate constants of NPP1 are $K_m=144 \mu\text{M}$ and $k_{cat}=7.8 \text{ s}^{-1}$.

As used herein the term “*plasma pyrophosphate (PPi) levels*” refers to the amount of pyrophosphate present in plasma of animals. In certain embodiments, animals include rat, mouse, cat, dog, human, cow and horse. There are several ways to measure PPi, one of which is by enzymatic assay using uridine-diphosphoglucose (UDPG) pyrophosphorylase (*Lust & Seegmiller, 1976, Clin. Chim. Acta 66:241-249; Cheung & Suhadolnik, 1977, Anal. Biochem. 83:61-63*) with modifications.

Typically, plasma PPi levels in healthy human subjects range from about 1 μM to about 3 μM , in some cases between 1-2 μM . Subjects who have defective ENPP1 expression tend to exhibit low ppi levels which range from at least 10% below normal levels, at least 20% below normal levels, at least 30% below normal levels, at least 40% below normal levels, at least 50% below normal levels, at least 60% below normal levels, at least 70% below normal levels, at least 80% below normal levels and combinations thereof. In patients afflicted with Generalized Arterial Calcification of Infancy (GACI), the ppi levels are found to be less than 1 μM and in some cases are below the level of detection. In patients afflicted with Pseudoxanthoma Elasticum (PXE), the ppi levels are below 0.5 μM . (*Arterioscler Thromb Vasc Biol. 2014 Sep;34(9):1985-9; Braddock et al., Nat Commun. 2015; 6: 10006.*)

As used herein, the term “PPi” refers to inorganic pyrophosphate.

As used herein the terms “*alteration*,” “*defect*,” “*variation*” or “*mutation*” refer to a mutation in a gene in a cell that affects the function, activity, expression (transcription or translation) or conformation of the polypeptide it encodes, including missense and nonsense mutations, insertions, deletions, frameshifts and premature terminations.

As used herein, the term “*ENPP1 precursor protein*” refers to ENPP1 with its signal peptide sequence at the ENPP1 N-terminus. Upon proteolysis, the signal sequence is cleaved from ENPP1 to provide the ENPP1 protein. Signal peptide sequences useful within the disclosure include, but are not limited to, Albumin signal sequence, Azurocidin signal sequence, ENPP1 signal peptide sequence, ENPP2 signal peptide sequence, ENPP7 signal peptide sequence, and/or ENPP5 signal peptide sequence.

As used herein, the term “*ENPP3 precursor protein*” refers to ENPP3 with its signal peptide sequence at the ENPP3 N-terminus. Upon proteolysis, the signal sequence is cleaved from ENPP3 to provide the ENPP3 protein. Signal peptide sequences useful within the disclosure include, but are not limited to, Albumin signal peptide sequence, Azurocidin signal

peptide sequence, ENPP1 signal peptide sequence, ENPP2 signal peptide sequence, ENPP7 signal peptide sequence, and/or ENPP5 signal peptide sequence.

As used herein, the term “*Azurocidin signal peptide sequence*” refers to the signal peptide derived from human azurocidin. Azurocidin, also known as cationic antimicrobial protein CAP37 or heparin-binding protein (HBP), is a protein that in humans is encoded by the AZU1 gene. The nucleotide sequence encoding Azurocin signal peptide MTRLTVLALLAGLLASSRA (SEQ ID NO: 42) is fused with the nucleotide sequence of NPP1 or NPP3 gene which when encoded generates ENPP1 precursor protein or ENPP3 precursor protein. (*Optimized signal peptides for the development of high expressing CHO cell lines*, Kober et al., *Biotechnol Bioeng.* 2013 Apr; 110(4):1164-73)

As used herein, the term “*ENPP1-Fc construct*” refers to ENPP1 (e.g., the extracellular domain of ENPP1) recombinantly fused and/or chemically conjugated (including both covalent and non-covalent conjugations) to an FcR binding domain of an IgG molecule (preferably, a human IgG). In certain embodiments, the C-terminus of ENPP1 is fused or conjugated to the N-terminus of the FcR binding domain.

As used herein, the term “*ENPP3-Fc construct*” refers to ENPP3 recombinantly fused and/or chemically conjugated (including both covalent and non-covalent conjugations) to an FcR binding domain of an IgG molecule (preferably, a human IgG). In certain embodiments, the C-terminus of ENPP1 is fused or conjugated to the N-terminus of the FcR binding domain.

As used herein, the term “*Fc*” refers to a human IgG (immunoglobulin) Fc domain. Subtypes of IgG such as IgG1, IgG2, IgG3, and IgG4 are contemplated for use as Fc domains. The “*Fc region or Fc polypeptide*” is the portion of an IgG molecule that correlates to a crystallizable fragment obtained by papain digestion of an IgG molecule. The Fc region comprises the C-terminal half of the two heavy chains of an IgG molecule that are linked by disulfide bonds. It has no antigen binding activity but contains the carbohydrate moiety and the binding sites for complement and Fc receptors, including the FcRn receptor. The Fc fragment contains the entire second constant domain CH2 (residues 231-340 of human IgG1, according to the Kabat numbering system) and the third constant domain CH3 (residues 341-447). The term “IgG hinge-Fc region” or “hinge-Fc fragment” refers to a region of an IgG molecule consisting of the Fc region (residues 231-447) and a hinge region (residues 216-230) extending from the N-terminus of the Fc region. The term “constant domain” refers to

the portion of an immunoglobulin molecule having a more conserved amino acid sequence relative to the other portion of the immunoglobulin, the variable domain, which contains the antigen binding site. The constant domain contains the CH1, CH2 and CH3 domains of the heavy chain and the CHL domain of the light chain.

As used herein the term “*functional equivalent variant*”, as used herein, relates to a polypeptide substantially homologous to the sequences of ENPP1 or ENPP3 (defined above) and that preserves the enzymatic and biological activities of ENPP1 or ENPP3, respectively. Methods for determining whether a variant preserves the biological activity of the native ENPP1 or ENPP3 are widely known to the skilled person and include any of the assays used in the experimental part of said application. Particularly, functionally equivalent variants of ENPP1 or ENPP3 delivered by viral vectors is encompassed by the present disclosure.

The functionally equivalent variants of ENPP1 or ENPP3 are polypeptides substantially homologous to the native ENPP1 or ENPP3 respectively. The expression “substantially homologous”, relates to a protein sequence when said protein sequence has a degree of identity with respect to the ENPP1 or ENPP3 sequences described above of at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% respectively and still retaining at least 50%, 55%, 60%, 70%, 80% or 90% activity of wild type ENPP1 or ENPP3 protein with respect to ATP cleavage.

The degree of identity between two polypeptides is determined using computer algorithms and methods that are widely known for the persons skilled in the art. The identity between two amino acid sequences is preferably determined by using the BLASTP algorithm (*BLAST Manual*, Altschul, S., et al., NCBI NLM NIH Bethesda, Md. 20894, Altschul, S., et al., *J. Mol. Biol.* 215: 403-410 (1990)), though other similar algorithms can also be used. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information.

“*Functionally equivalent variants*” of ENPP1 or ENPP3 may be obtained by replacing nucleotides within the polynucleotide accounting for codon preference in the host cell that is to be used to produce the ENPP1 or ENPP3 respectively. Such “codon optimization” can be determined via computer algorithms which incorporate codon frequency tables such as “Human high.cod” for codon preference as provided by the University of Wisconsin Package Version 9.0, Genetics Computer Group, Madison, Wis. The variants of ENPP1 or ENPP3 polypeptides are expected to retain at least 50%, 55%, 60%, 70%, 80% or 90% activity of wild type ENPP1 or ENPP3 protein with respect to ATP cleavage.

As used herein, the term “*wild-type*” refers to a gene or gene product isolated from a naturally occurring source. A wild-type gene is most frequently observed in a population and is thus arbitrarily designed the “normal” or “wild-type” form of the human NPP1 or NPP3 genes. In contrast, the term “functionally equivalent” refers to a NPP1 or NPP3 gene or gene product that displays modifications in sequence and/or functional properties (i.e., altered characteristics) when compared to the wild-type gene or gene product. Naturally occurring mutants can be isolated; these are identified by the fact that they have altered characteristics (including altered nucleic acid sequences) when compared to the wild-type gene or gene product.

“About” as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of + 20% or + 10%, more preferably + 5%, even more preferably + 1%, and still more preferably + 0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

As defined herein, the term “*moiety*” refers to a chemical component or biological molecule that can be covalently or non-covalently linked to ENPP1 or ENPP3 polypeptide and has the ability to confer a desired property to the protein to which it is attached. For example, the term moiety can refer to a bone targeting peptide such as polyaspartic acid or polyglutamic acid (of 4-20 consecutive asp or glu residues) or a molecule that extends the half-life of ENPP1 or ENPP3 polypeptide. Some other examples of moieties include Fc, albumin, transferrin, polyethylene glycol (PEG), homo-amino acid polymer (HAP), proline-alanine-serine polymer (PAS), elastin-like peptide (ELP), and gelatin-like protein (GLK).

As defined herein, the term “*subject*”, “*individual*” or “*patient*” refers to mammal preferably a human who does not possess a loss of function mutation in the NPP1 gene, such as those loss of function mutations that result in pathological calcification and pathological ossification diseases such as Generalized Arterial Calcification of Infancy (GACI), Autosomal Recessive Hypophosphatemic Rickets Type 2 (ARHR2), Infantile idiopathic arterial calcification (IIAC), Ossification of the Posterior Longitudinal Ligament (OPLL), hypophosphatemic rickets, osteoarthritis, calcification of atherosclerotic plaques, hereditary and non-hereditary forms of osteoarthritis, ankylosing spondylitis, hardening of the arteries occurring with aging, calciphylaxis resulting from end stage renal disease and progeria. Such a patient will have a normal level of NPP1 in serum which refers to the amount of NPP1 required to maintain a normal level of plasma pyrophosphate (PPi) in a healthy subject. A normal level of PPi corresponds to 2-3 μM .

As defined herein, the phrase “*medial area*” is the area between lamina elastica externa and lamina elastica interna of an artery.

As defined herein, the phrase “*intimal area*” and said intimal area is the area between said lamina elastica interna and lumen of an artery.

As defined herein, the phrase “*lamina elastica externa*” refers to a layer of elastic connective tissue lying immediately outside the smooth muscle of the tunica media of an artery.

As defined herein, the phrase “*lamina elastica interna*” refers to a layer of elastic tissue that forms the outermost part of the tunica intima of blood vessels.

As defined herein, the phrase “*lumen*” refers to the interior of a vessel, such as the central space in an artery, vein or capillary through which blood flow occurs.

As defined herein, the phrase “*surgery*” refers to an invasive medical procedure that involves vascular interventions which result in tissue injury by scalpel incision or radiofrequency ablation or cryoablation or laser ablation.

As defined herein, the phrase “*tissue injury*” refers to proliferation or onset of proliferation and migration of vascular smooth muscle eventually resulting in the thickening of arterial walls and decreased arterial lumen space resulting restenosis after percutaneous vascular interventions such as stenting or angioplasty.

As defined herein, the phrase “*deficient for NPP1*” or “*ENPP1 deficiency*” refers to a reduction in an amount of NPP1 protein or in NPP1 activity relative to a normal serum level of NPP1 protein or normal activity of NPP1, wherein such a reduction results in a disease or disorder of pathological calcification and/or pathological ossification. Such pathological diseases include but are not limited to GACI and ARHR2. ENPP1 deficiency, as used herein, does not refer to small reductions in an amount of NPP1 protein and/or NPP1 activity that do not result in a disease or disorder of pathological calcification and/or pathological ossification.

As defined herein, the phrase “*vascular trauma*” refers to injury to a blood vessel—an artery, which carries blood to an extremity or an organ, or a vein, which returns blood to the heart. Vascular injuries may also be caused by invasive procedures, such as vascular bypass surgery.

As defined herein the phrase “*accidental trauma*” refers to a blood vessel such as artery by a blunt injury which occurs when a blood vessel is crushed or stretched due to exertion of physical force or penetrating injury which occurs when a blood vessel is punctured, torn or severed. Blunt injury occurs during physical alterations such as boxing and penetrating injury occurs due to sharp objects such as knife or bullet wounds. The trauma or injury can be caused by different factors, such as radiation, viral infections, development of immune complexes, and hyperlipidemia.

As defined herein the phrase “*restenosis*” refers to recurrence of stenosis. Stenosis refers to the narrowing of a blood vessel, leading to restricted blood flow. Restenosis usually pertains to an artery or other large blood vessel that has become narrowed, received treatment to clear the blockage and subsequently become re-narrowed. Restenosis is commonly detected by using one or more of ultrasound, X-ray computed tomography (CT), nuclear imaging, optical imaging or contrast enhanced image or immunohistochemical detection.

As defined herein the phrase “*myointimal proliferation*” refers to the proliferation of vascular smooth muscle cells that occurs at the tunica intima of an arterial wall of an individual.

As used herein the term “*ENPP1 fragment*” refers to a fragment or a portion of ENPP1 protein or an active subsequence of the full-length NPP1 having at least an ENPP1 catalytic domain administered in protein form or in the form of a nucleic acid encoding the same.

As used herein, the term “*ENPP1 agent*” refers to ENPP1 polypeptide or fusion protein or ENPP1 fragment comprising at least catalytic domain capable of producing plasma pyrophosphate (Ppi) by cleavage of adenosine triphosphate (ATP) or a polynucleotide such as cDNA or RNA encoding ENPP1 fusion protein or ENPP1 fragment comprising at least catalytic domain capable of producing Ppi by enzymatic cleavage of ATP or a vector such as a viral vector containing a polynucleotide encoding the same.

As used herein the term “*ablation*” refers to the removal or destruction of a body part or tissue or its function. Ablation may be performed by surgery, hormones, drugs, radiofrequency, heat.

As used herein, the phrase “*reduce or prevent myointimal proliferation*” refers to the ability of soluble NPP1 upon administration to reduce the level of proliferation vascular smooth muscle cells at the site of tissue injury thereby reducing the thickening of arterial walls and prevent the occurrence of or reduce the level of restenosis of the artery.

As used herein the term “*non-surgical tissue injury*” refers to injuries sustained to a tissue or blood vessel during a traumatic event including but not limited to physical altercations involving use of blunt force or sharp objects such as knife, mechanical injury such fall from elevation, workplace injury due to heavy machinery or vehicular injury such as car accidents.

As used herein, the term “*stent*” refers to a tubular support placed inside a blood vessel, canal, or duct to aid healing or relieve an obstruction or prevent narrowing of the passage. Stents generally comprise an expandable mesh coil which is made of metal (ex: stainless steel, Cobalt alloy, Nickel-titanium alloy, manganese alloy, molybdenum alloy, platinum alloy, tungsten alloy) or polymers (ex: Silicone).

As used herein, the term “*vascular stent*” refers to a tubular support placed inside an artery or vein of a mammal to aid healing or relieve an obstruction or prevent narrowing of the arterial passage.

As used herein, the term “*coated stent*” or “*eluting stent*” refers to a stent that is coated with a therapeutic molecule such as protein, chemical compound or nucleic acid that gradually elutes from the stent surface (interior or exterior) at the site of implantation thereby providing therapeutic relief. Therapeutic molecules such as ENPP1 agent or ENPP3 agent can be bonded directly to a metal stent, and some are bonded to a matrix polymer, which acts as a drug reservoir to ensure drug retention during deployment and a uniform distribution on

the stent. The types, compositions, and designs of the polymers coated on the stent dictate the eluting kinetic of the sustain time release of the drug over a period of weeks or months following the implantation in situ. The coating materials can be categorized as organic vs inorganic, bioerodable vs nonbioerodable, and synthetic vs naturally occurring substances.

As used herein, the term “*coating*” refers to composition comprising a polymeric carrier that is used in conjunction with an ENPP1 agent or ENPP3 agent to coat the stents. The coating may be applied in the form a spray or dried film comprising the ENPP1 agent or ENPP3 agent suspended in a polymeric matrix. The polymeric carrier is in an amount sufficient to provide a polymer matrix or support for the ENPP1 agent or ENPP3 agent. The polymer is preferably non-reactive with the ENPP1 agent or ENPP3 agent, i.e., no chemical reaction occurs when the two are mixed.

As used herein, the term “*solvent*” is defined according to its broadest recognized definition and includes any material into which the carrier (polymer) and the ENPP1 agent or ENPP3 agent can dissolve, fully or partially, at room temperature or from 20° C. to 40° C to form the coating composition. Sterile, double distilled water is a preferred solvent.

As used herein, the term “*site of injury*” refers to a region in the vasculature where the flow of blood or spinal fluid is constricted due to accumulation of one or more of lipids, cholesterol, calcium, and various types of cells, such as smooth muscle cells and platelets. The site of injury is commonly identified by using Cardiac catheterization. During a cardiac catheterization, a long, narrow tube called a catheter is inserted through a plastic introducer sheath (a short, hollow tube that is inserted into a blood vessel in your arm or leg). The catheter is guided through the blood vessel to the coronary arteries with the aid of an x-ray machine. Contrast material is injected through the catheter and x-ray images (Coronary angiogram) are created as the contrast material moves through the heart’s chambers, valves and major vessels. The digital photographs of the contrast material are used to identify the site of the narrowing or blockage in the coronary artery. Additional imaging procedures, called intra-vascular ultrasound (IVUS) and fractional flow reserve (FFR), may be performed along with cardiac catheterization in some cases to obtain detailed images of the walls of the blood vessels.

As used herein “*site of implant*” refers to the region at which the ENPP1 or ENPP3 coated stent is implanted in the vasculature. The coated stents of the invention can be placed

at the center of the to the site of tissue injury, immediately adjacent the site of tissue injury or within 200 μm on either side from the center of the site of tissue injury.

As used herein, the term “*myocardial infarction*” refers to a permanent damage to the heart muscle that occurs due to the formation of plaques in the interior walls of the arteries resulting in reduced blood flow to the heart and injuring heart muscles because of lack of oxygen supply. The symptoms of MI include chest pain, which travels from left arm to neck, shortness of breath, sweating, nausea, vomiting, abnormal heart beating, anxiety, fatigue, weakness, stress, depression, and other factors.

As used herein the term “*blunt force trauma*” refers to a physical trauma to a body part, either by impact, injury or physical attack or high-velocity impact. Blunt trauma can lead to contusions, abrasions, lacerations, and/or bone fractures.

As used herein the term “*non-surgical tissue injury*” or “*penetrating trauma*” refers to trauma to a body part which occurs when an object such as a projectile or knife enters a tissue of the body, creating an open wound.

As used herein the term “*scalpel incision*” refers to incision made in a tissue using a sharp object such as a scalpel during surgical procedure. An incision is a cut made into the tissues of the body to expose the underlying tissue, bone, or organ so that a surgical procedure can be performed.

As used herein the term “*Peripheral artery disease*” (PAD) refers to the narrowing of the peripheral arteries serving the legs, stomach, arms and head. (“Peripheral” in this case means away from the heart, in the outer regions of the body.) PAD most commonly affects arteries in the legs. PAD generally occurs due to atherosclerosis, a buildup of cholesterol and fatty deposits (plaque) which narrows or blocks blood flow to the arteries leading to the arms, legs and feet. The supply of oxygen to cells is also limited due to the plaque buildup in the artery walls. The most common symptoms of PAD involving the lower extremities are cramping, pain or tiredness in the leg or hip muscles while walking or climbing stairs. Patients with peripheral arterial disease have a higher risk of coronary artery disease, heart attack or stroke. Left untreated, PAD can lead to gangrene and amputation. The American College of Cardiology/American Heart Association Practice Guidelines defines the presentation of PAD by four categories: asymptomatic, claudication, critical limb ischemia, and acute limb ischemia (ALI). There are at least two major classification criterion that are routine used in art to classify the level of severity of PAD, Fontaine Classification system and

Rutherford Classification system (*Overview of Classification Systems in Peripheral Artery Disease, Rulon L. Hardman, Semin Intervent Radiol 2014;31:378–388*)

As used herein the term “*Claudication*” refers to fatigue, discomfort, or pain in the lower extremities, typically the calves, which is reproducibly brought on by exercise and relieved by rest.

As used herein the term “*Critical Limb Ischemia (CLI)*” refers to a condition wherein the patient experiences chronic ischemic rest pain, nocturnal recumbent pain, or ischemic skin lesions that may include ulcers or gangrene.

As used herein the term “*Acute Limb Ischemia (ALI)*” refers to patients with a sudden decrease in limb perfusion causing an immediate threat to limb viability.

As used herein the term “*Fontaine Classification System*” refers to classification system developed by Fontaine et al. (*Fontaine R, Kim M, Kieny R. Surgical treatment of peripheral circulation disorders [in German]. Helv Chir Acta 1954;21(5–6):499–533*). This classification system grades the clinical presentation of patients to four stages. The system is solely based on clinical symptoms, without other diagnostic tests and is as shown in table below.

GRADE	SYMPTOMS
Stage I PAD	Asymptomatic, incomplete blood vessel obstruction
Stage II PAD	Mild claudication pain in limb
Stage IIA PAD	Claudication at a distance > 200 m
Stage IIB PAD	Claudication at a distance < 200 m
Stage III PAD	Rest pain, mostly in the feet
Stage IV PAD	Necrosis and/or gangrene of the limb

As used herein the term “*Rutherford Classification System*” refers to classification system developed by Rutherford et al. (*Rutherford RB, Flanigan DP, Gupta SK, et al.*

Suggested standards for reports dealing with lower extremity ischemia. J Vasc Surg 1986;4(1):80–94 . The Rutherford system classifies PAD into acute and chronic limb ischemia, emphasizing that each presentation requires different treatment algorithms. The Rutherford classification also associates patient clinical symptoms with objective findings, including Doppler, arterial brachial indices (ABI), and pulse volume recordings.

Rutherford's chronic limb ischemia classification most resembles Fontaine's classification, with the addition of objective noninvasive data such as treadmill test. Treadmill protocols are well described in other publications. (*Hoyer C, Sandermann J, Petersen LJ. The toe-brachial index in the diagnosis of peripheral arterial disease. J Vasc Surg 2013;58(1): 231–238*). Treadmill exercise testing with and without preexercise and postexercise ABIs helps differentiate claudication from pseudoclaudication in patients with exertional leg symptoms. Patients who cannot perform treadmill testing can undergo similar stress testing using plantar flexion or thigh blood pressure cuff compression to cause reactive hyperemia. Rutherford's classification for chronic limb ischemia is shown in table below.

GRADE	CATEGORY	CLINICAL DESCRIPTION	OBJECTIVE CRITERIA
0	0	Asymptomatic—no hemodynamically significant occlusive disease	Normal treadmill or reactive hyperemia test
	1	Mild Claudication	Completes treadmill exercise; AP after exercise > 50 mm Hg but at least 20 mm Hg lower than resting value
I	2	Moderate Claudication	Between categories 1 and 3
	3	Severe Claudication	Cannot complete standard treadmill exercise, and AP after exercise < 50 mm Hg
II	4	Ischemic Rest Pain	Resting AP < 40 mm Hg, flat or barely pulsatile ankle or metatarsal PVR; TP < 30 mm Hg
III	5	Minor tissue loss—nonhealing ulcer, focal	Resting AP < 60 mm Hg, ankle or metatarsal PVR

		gangrene with diffuse pedal ischemia	flat or barely pulsatile; TP < 40 mm Hg
	6	Major tissue loss—extending above TM level, functional foot no longer salvageable	Same as category 5

Abbreviations: AP, ankle pressure; PVR, pulse volume recording; TM, transmetatarsal; TP, toe pressure.

As used herein the term “*toe pressure*” refers to the measurement of the blood pressure in the toe compared to the blood pressure in the arm

As used herein the term “*ankle pressure*” refers to the measurement of the blood pressure in the lower leg compared to the blood pressure in the arm

As used herein the term “*pulse volume recording*” refers to a noninvasive vascular test in which blood pressure cuffs and a hand-held ultrasound device (such as a Doppler or transducer) are used to obtain information about arterial blood flow in the arms and legs. As used herein, the term “*stage III peripheral artery disease*” refers to the PAD disease stage as indicated by the Fontaine classification system

As used herein, the term “*stage IV peripheral artery disease*” refers to a PAD disease stage as classified by the Fontaine classification system

As used herein, the term “*stage IV, grade III peripheral artery disease*” refers to a PAD disease stage as classified by the Rutherford classification system

As used herein, the term “*common femoral artery disease*” refers to a disease state wherein occlusion due to PAD occurs in the femoral artery of the patient.

As used herein, the term “*femoral-popliteal disease*” refers to a disease state wherein patients have obstructive occlusions due to PAD in the femoropopliteal artery.

As used herein, the term “*tibial-peroneal disease*” refers to a disease state wherein patients have obstructive occlusions due to PAD in a segment of the artery, referred to as tibial-peroneal trunk, below the knee, distal to the origin of the anterior tibial artery off the popliteal artery, and proximal to the branch point of the posterior tibial artery and the fibular artery.

As used herein, the term “*subject who requires surgery*” refers to a patient who is not ENPP1 deficient and has arterial occlusion in the peripheral arteries such as femoral, femoropopliteal or tibial-peroneal arteries.

As used herein, the term “*site of surgery*” refers to the region of the artery upon which a tissue injury has occurred either due to vascular trauma or accidental trauma.

As used herein the term “*angioplasty*” refers to a medical procedure that opens up a blocked or narrowed artery around the heart. It is a standard treatment for narrowed or blocked arteries

A “*low level of PPI*” refers to a condition in which the subject has at least 0.1% - 0.99% less than 2%-5% of normal levels of plasma pyrophosphate (PPI). Normal levels of Plasma PPI in healthy human subjects are in the range of 1.8 to 2.6 μM . $\pm$ 0.1 μM (*Arthritis and Rheumatism, Vol. 22, No. 8 (August 1979)*)

As used herein, the term “*treatment*” or “*treating*” is defined as the application or administration of soluble NPP1 (alone or in combination with another pharmaceutical agent), to a patient, or application or administration of a therapeutic agent to an isolated tissue or cell line from a patient (e.g., for diagnosis or ex vivo applications), who has a disease or disorder, a symptom of a disease or disorder or the potential to develop a disease or disorder, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect the disease or disorder, the symptoms of the disease or disorder, or the potential to develop the disease or disorder. Such treatments may be specifically tailored or modified, based on knowledge obtained from the field of pharmacogenomics.

As used herein, the term “*prevent*” or “*prevention*” or “*reduce*” means no disorder or disease development if none had occurred, or no further disorder or disease development if there had already been development of the disorder or disease. Also considered is the ability of one to prevent some or all of the symptoms associated with the disorder or disease.

As used herein, the term “*effective amount*” refers to an amount of an agent (e.g., NPP1 fusion or NPP3 fusion polypeptides) which, as compared to a corresponding subject who has not received such an amount, sufficient to provide improvement of a condition, disorder, disease, or to provide a decrease in progression or advancement of a condition, disorder, or disease. An effective amount also may result in treating, healing, preventing or ameliorating a condition, disease, or disorder. The term also includes within its scope

amounts effective to enhance normal physiological function. As used herein, the term “*polypeptide*” refers to a polymer composed of amino acid residues, related naturally occurring structural variants, and synthetic non-naturally occurring analogs thereof linked via peptide bonds.

As used here the term “*Isolated*” means altered or removed from the natural state. For example, a nucleic acid or a polypeptide naturally present in a living animal is not “isolated,” but the same nucleic acid or polypeptide partially or completely separated from the coexisting materials of its natural state is “isolated.” An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

As used herein, “*substantially purified*” refers to being essentially free of other components. For example, a substantially purified polypeptide is a polypeptide that has been separated from other components with which it is normally associated in its naturally occurring state. Non-limiting embodiments include 95% purity, 99% purity, 99.5% purity, 99.9% purity and 100% purity.

As used herein the term “*oligonucleotide*” or “*polynucleotide*” is a nucleic acid ranging from at least 2, in certain embodiments at least 8, 15 or 25 nucleotides in length, but may be up to 50, 100, 1000, or 5000 nucleotides long or a compound that specifically hybridizes to a polynucleotide.

As used herein, the term “*pharmaceutical composition*” or “composition” refers to a mixture of at least one compound useful within the disclosure with a pharmaceutically acceptable carrier. The pharmaceutical composition facilitates administration of the compound to a patient. Multiple techniques of administering a compound exist in the art including, but not limited to, subcutaneous, intravenous, oral, aerosol, inhalational, rectal, vaginal, transdermal, intranasal, buccal, sublingual, parenteral, intrathecal, intragastrical, ophthalmic, pulmonary, and topical administration.

As used herein, the term “*pharmaceutically acceptable*” refers to a material, such as a carrier or diluent, which does not abrogate the biological activity or properties of the compound, and is relatively non-toxic, i.e., the material may be administered to an individual without causing undesirable biological effects or interacting in a deleterious manner with any of the components of the composition in which it is contained; for example, phosphate-buffered saline (PBS)

As used herein, the term “*pathological calcification*” refers to the abnormal deposition of calcium salts in blood vessels, soft tissues, secretory and excretory passages of the body causing it to harden. There are two types, dystrophic calcification which occurs in dying and dead tissue and metastatic calcification which elevated extracellular levels of calcium (hypercalcemia), exceeding the homeostatic capacity of cells and tissues. Calcification can involve cells as well as extracellular matrix components such as collagen in basement membranes and elastic fibers in arterial walls. Some examples of tissues prone to calcification include: Gastric mucosa – the inner epithelial lining of the stomach, Kidneys and lungs, Cornea, heart valves, Systemic arteries and Pulmonary veins.

As used herein, the term “*pathological ossification*” refers to a pathological condition in which bone arises in tissues not in the osseous system and in connective tissues usually not manifesting osteogenic properties. Ossification is classified into three types depending on the nature of the tissue or organ being affected, endochondral ossification is ossification that occurs in and replaces cartilage. Intramembranous ossification is ossification of bone that occurs in and replaces connective tissue. Metaplastic ossification the development of bony substance in normally soft body structures; called also heterotrophic ossification.

As used herein, “*reduction of calcification*” is observed by using non-invasive methods like X-rays, micro CT and MRI. Reduction of calcification is also inferred by using radio imaging with 99mTc-pyrophosphate (99mPYP) uptake. The presence of calcifications in mice are evaluated via post-mortem by micro-computed tomography (CT) scans and histologic sections taken from the heart, aorta and kidneys with the use of dyes such as Hematoxylin and Eosin (H&E) and Alizarin red by following protocols established by Braddock et al. (Nature Communications volume 6, Article number: 10006 (2015))

As used herein the term “*Ectopic calcification*” refers to a condition characterized by a pathologic deposition of calcium salts in tissues or bone growth in soft tissues.

As used herein the term “*Ectopic calcification of soft tissue*” refers to inappropriate biomineralization, typically composed of calcium phosphate, hydroxyapatite, calcium oxalates and ocatacalcium phosphates occurring in soft tissues leading to loss of hardening of soft tissues. “*Arterial calcification*” refers to ectopic calcification that occurs in arteries and heart valves leading to hardening and or narrowing of arteries. Calcification in arteries is correlated with atherosclerotic plaque burden and increased risk of myocardial infarction,

increased ischemic episodes in peripheral vascular disease, and increased risk of dissection following angioplasty.

As used herein, the term “*Venous calcification*” refers to ectopic calcification that occurs in veins that reduces the elasticity of the veins and restricts blood flow which can then lead to increase in blood pressure and coronary defects.

As used herein, the term “*Vascular calcification*” refers to the pathological deposition of mineral in the vascular system. It has a variety of forms, including intimal calcification and medial calcification, but can also be found in the valves of the heart. Vascular calcification is associated with atherosclerosis, diabetes, certain heredity conditions, and kidney disease, especially CKD. Patients with vascular calcification are at higher risk for adverse cardiovascular events. Vascular calcification affects a wide variety of patients. Idiopathic infantile arterial calcification is a rare form of vascular calcification where the arteries of neonates calcify.

As used herein, the term “*Brain calcification*” (BC) refers to a nonspecific neuropathology wherein deposition of calcium and other mineral in blood vessel walls and tissue parenchyma occurs leading to neuronal death and gliosis. Brain calcification is” often associated with various chronic and acute brain disorders including Down’s syndrome, Lewy body disease, Alzheimer’s disease, Parkinson’s disease, vascular dementia, brain tumors, and various endocrinologic conditions. Calcification of heart tissue refers to accumulation of deposits of calcium (possibly including other minerals) in tissues of the heart, such as aorta tissue and coronary tissue.

The terms “*adeno-associated viral vector*”, “*AAV vector*”, “*adeno-associated virus*”, “*AAV virus*”, “*AAV virion*”, “*AAV viral particle*” and “*AAV particle*”, as used interchangeably herein, refer to a viral particle composed of at least one AAV capsid protein (preferably by all of the capsid proteins of a particular AAV serotype) and an encapsidated recombinant viral genome. The particle comprises a recombinant viral genome having a heterologous polynucleotide comprising a sequence encoding human ENPP1 or human ENPP3 or a functionally equivalent variant thereof,) and a transcriptional regulatory region that at least comprises a promoter flanked by the AAV inverted terminal repeats. The particle is typically referred to as an “*AAV vector particle*” or “*AAV vector*”.

As used herein, the term “*vector*” means a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. In some embodiments, the

vector is a plasmid, i.e., a circular double stranded DNA loop into which additional DNA segments may be ligated. In some embodiments, the vector is a viral vector, wherein additional nucleotide sequences may be ligated into the viral genome. In some embodiments, the vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). In other embodiments, the vectors (e.g., non-episomal mammalian vectors) is integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors (expression vectors) are capable of directing the expression of genes to which they are operatively linked.

As used herein, the term "*recombinant host cell*" (or simply "host cell"), as used herein, means a cell into which an exogenous nucleic acid and/or recombinant vector has been introduced. It should be understood that "recombinant host cell" and "host cell" mean not only the particular subject cell but also the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term "host cell" as used herein.

The term "*recombinant viral genome*", as used herein, refers to an AAV genome in which at least one extraneous expression cassette polynucleotide is inserted into the naturally occurring AAV genome. The genome of the AAV according to the disclosure typically comprises the cis-acting 5' and 3' inverted terminal repeat sequences (ITRs) and an expression cassette.

The term "*expression cassette*", as used herein, refers to a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements, which permit transcription of a particular nucleic acid in a target cell. The expression cassette of the recombinant viral genome of the AAV vector according to the disclosure comprises a transcriptional regulatory region operatively linked to a nucleotide sequence encoding ENPP1 or ENPP3 or a functionally equivalent variant thereof.

The term "*transcriptional regulatory region*", as used herein, refers to a nucleic acid fragment capable of regulating the expression of one or more genes. The transcriptional regulatory region according to the disclosure includes a promoter and, optionally, an enhancer.

The term “*promoter*”, as used herein, refers to a nucleic acid fragment that functions to control the transcription of one or more polynucleotides, located upstream the polynucleotide sequence(s), and which is structurally identified by the presence of a binding site for DNA-dependent RNA polymerase, transcription initiation sites, and any other DNA sequences including, but not limited to, transcription factor binding sites, repressor, and activator protein binding sites, and any other sequences of nucleotides known in the art to act directly or indirectly to regulate the amount of transcription from the promoter. Any kind of promoters may be used in the disclosure including inducible promoters, constitutive promoters and tissue-specific promoters.

The term “*enhancer*”, as used herein, refers to a DNA sequence element to which transcription factors bind to increase gene transcription. Examples of enhancers may be, without limitation, RSV enhancer, CMV enhancer, HCR enhancer, etc. In another embodiment, the enhancer is a liver-specific enhancer, more preferably a hepatic control region enhancer (HCR).

The term “*operatively linked*”, as used herein, refers to the functional relation and location of a promoter sequence with respect to a polynucleotide of interest (e.g. a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence). Generally, a promoter operatively linked is contiguous to the sequence of interest. However, an enhancer does not have to be contiguous to the sequence of interest to control its expression. In another embodiment, the promoter and the nucleotide sequence encoding ENPP1 or ENPP3 or a functionally equivalent variant thereof.

The term “*effective amount*” refers to a nontoxic but sufficient amount of a viral vector encoding ENPP1 or ENPP3 to provide the desired biological result. That result may be reduction and/or alleviation of the signs, symptoms, or causes of a disease, or any other desired alteration of a biological system.

The term “*Cap protein*”, as used herein, refers to a polypeptide having at least one functional activity of a native AAV Cap protein (e.g. VP1, VP2, VP3). Examples of functional activities of Cap proteins include the ability to induce formation of a capsid, facilitate accumulation of single-stranded DNA, facilitate AAV DNA packaging into capsids (i.e. encapsidation), bind to cellular receptors, and facilitate entry of the virion into host cells. In principle, any Cap protein can be used in the context of the present disclosure.

The term “*capsid*”, as used herein, refers to the structure in which the viral genome is packaged. A capsid consists of several oligomeric structural subunits made of proteins. For instance, AAV have an icosahedral capsid formed by the interaction of three capsid proteins: VP1, VP2 and VP3.

The term “*Rep protein*”, as used herein, refers to a polypeptide having at least one functional activity of a native AAV Rep protein (e.g. Rep 40, 52, 68, 78). A “functional activity” of a Rep protein is any activity associated with the physiological function of the protein, including facilitating replication of DNA through recognition, binding and nicking of the AAV origin of DNA replication as well as DNA helicase activity.

The term “*adeno-associated virus ITRs*” or “*AAV ITRs*”, as used herein, refers to the inverted terminal repeats present at both ends of the DNA strand of the genome of an adeno-associated virus. The ITR sequences are required for efficient multiplication of the AAV genome. Another property of these sequences is their ability to form a hairpin. This characteristic contributes to its self-priming which allows the primase-independent synthesis of the second DNA strand. Procedures for modifying these ITR sequences are known in the art (*Brown T, “Gene Cloning”, Chapman & Hall, London, GB, 1995; Watson R, et al., “Recombinant DNA”, 2nd Ed. Scientific American Books, New York, N.Y., US, 1992; Alberts B, et al., “Molecular Biology of the Cell”, Garland Publishing Inc., New York, N.Y., US, 2008; Innis M, et al., Eds., “PCR Protocols. A Guide to Methods and Applications”, Academic Press Inc., San Diego, Calif., US, 1990; and Schleef M, Ed., “Plasmid for Therapy and Vaccination”, Wiley-VCH Verlag GmbH, Weinheim, Del., 2001*).

The term “*tissue-specific*” promoter is only active in specific types of differentiated cells or tissues. Typically, the downstream gene in a tissue-specific promoter is one which is active to a much higher degree in the tissue(s) for which it is specific than in any other. In this case there may be little or substantially no activity of the promoter in any tissue other than the one(s) for which it is specific.

The term “*inducible promoter*”, as used herein, refers to a promoter that is physiologically or developmentally regulated, e.g. by the application of a chemical inducer. For example, it can be a tetracycline-inducible promoter, a mifepristone (RU-486)-inducible promoter and the like.

The term “*constitutive promoter*”, as used herein, refers to a promoter whose activity is maintained at a relatively constant level in all cells of an organism, or during most

developmental stages, with little or no regard to cell environmental conditions. In another embodiment, the transcriptional regulatory region allows constitutive expression of ENPP1. Examples of constitutive promoters include, without limitation, the retroviral Rous sarcoma virus (RSV) LTR promoter (optionally with the RSV enhancer), the cytomegalovirus (CMV) promoter (optionally with the CMV enhancer), the SV40 promoter, the dihydrofolate reductase promoter, the β -actin promoter, the phosphoglycerol kinase (PGK) promoter, and the EF1a promoter (*Boshart M, et al., Cell 1985; 41:521-530*).

The term “*polyadenylation signal*”, as used herein, relates to a nucleic acid sequence that mediates the attachment of a polyadenine stretch to the 3' terminus of the mRNA. Suitable polyadenylation signals include, without limitation, the SV40 early polyadenylation signal, the SV40 late polyadenylation signal, the HSV thymidine kinase polyadenylation signal, the protamine gene polyadenylation signal, the adenovirus 5 E1b polyadenylation signal, the bovine growth hormone polyadenylation signal, the human variant growth hormone polyadenylation signal and the like.

The term “*signal peptide*”, as used herein, refers to a sequence of amino acid residues (ranging in length from 10-30 residues) bound at the amino terminus of a nascent protein of interest during protein translation. The signal peptide is recognized by the signal recognition particle (SRP) and cleaved by the signal peptidase following transport at the endoplasmic reticulum. (*Lodish et al., 2000, Molecular Cell Biology, 4th edition*).

As used herein, the term “*immune response*” or “*immune reaction*” refers to the host's immune system to antigen in an invading (infecting) pathogenic organism, or to introduction or expression of foreign protein. The immune response is generally humoral and local; antibodies produced by B cells combine with antigen in an antigen-antibody complex to inactivate or neutralize antigen. Immune response is often observed when human proteins are injected into mouse model systems. Generally, the mouse model system is made immune tolerant by injecting immune suppressors prior to the introduction of a foreign antigen to ensure better viability.

As used herein, the term “*immunesuppression*” is a deliberate reduction of the activation or efficacy of the host immune system using immunesuppressant drugs to facilitate immune tolerance towards foreign antigens such as foreign proteins, organ transplants, bone marrow and tissue transplantation. Non limiting examples of immunosuppressant drugs include anti-CD4(GK1.5) antibody, Cyclophosphamide, Azathioprine (Imuran),

Mycophenolate mofetil (Cellcept), Cyclosporine (Neoral, Sandimmune, Gengraf), Methotrexate (Rheumatrex), Leflunomide (Arava), Cyclophosphamide (Cytosan) and Chlorambucil (Leukeran).

Ranges: throughout this disclosure, various aspects of the disclosure can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the disclosure. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range.

METHODS OF TREATMENT

The present disclosure relates to administration of an ENPP1 or ENPP3 agent to treat PAD, which includes administering sNPP1 and sNPP3 polypeptides and fusion proteins thereof to a subject, and to administration of nucleic acids encoding such polypeptides. Sequences of such polypeptides include the following, without limitation.

Sequences

SEQ ID NO: 1 - ENPP1 Amino Acid Sequence - Wild Type

	Met	Glu	Arg	Asp	Gly	Cys	Ala	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Glu
Gly	1				5					10					15
	Gly	Arg	Ala	Pro	Arg	Glu	Gly	Pro	Ala	Gly	Asn	Gly	Arg	Asp	Arg
Gly					20					25					30
	Arg	Ser	His	Ala	Ala	Glu	Ala	Pro	Gly	Asp	Pro	Gln	Ala	Ala	Ala
Ser					35					40					45
	Leu	Leu	Ala	Pro	Met	Asp	Val	Gly	Glu	Glu	Pro	Leu	Glu	Lys	Ala
Ala					50					55					60
	Arg	Ala	Arg	Thr	Ala	Lys	Asp	Pro	Asn	Thr	Tyr	Lys	Val	Leu	Ser
Leu															
	65				70					75					80
	Val	Leu	Ser	Val	Cys	Val	Leu	Thr	Thr	Ile	Leu	Gly	Cys	Ile	Phe
Gly															
					85					90					95

Cys Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg
 100 105 110
 Glu Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val
 115 120 125
 Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro
 130 135 140
 Thr His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu
 145 150 155
 160 Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp
 Cys 165 170 175
 Glu Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val
 180 185 190
 Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe
 195 200 205
 Tyr Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu
 210 215 220
 Lys Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys
 225 230 235
 240 Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys
 Thr 245 250 255
 His Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser
 260 265 270
 Phe Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser
 275 280 285
 Glu Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly
 290 295 300
 Phe Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr
 305 310 315
 320 Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp
 Ile 325 330 335
 Ala Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu
 340 345 350
 Tyr Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe
 355 360 365
 Pro Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly

	370		375		380
	Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met				
Val					
	385		390		395
400	Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys				
Leu					
		405		410	415
	Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys				
Lys					
		420		425	430
	Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile				
Lys					
		435		440	445
	Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro				
Asp					
		450		455	460
	Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser				
Cys					
	465		470		475
480	Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu				
Pro					
		485		490	495
	Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu Thr				
Phe					
		500		505	510
	Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg				
Lys					
		515		520	525
	Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn				
Met					
		530		535	540
	Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile				
Glu					
	545		550		555
560	Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp				
Leu					
		565		570	575
	Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu				
Asn					
		580		585	590
	His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu				
Val					
		595		600	605
	His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn				
Leu					
		610		615	620
	Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln				
Thr					
	625		630		635
640	Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu				
Thr					
		645		650	655

	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Glu	Asn	Thr	Ile
Cys															
				660					665					670	
	Leu	Leu	Ser	Gln	His	Gln	Phe	Met	Ser	Gly	Tyr	Ser	Gln	Asp	Ile
Leu															
			675					680					685		
	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr	Val	Asp	Arg	Asn	Asp	Ser	Phe
Ser															
		690					695					700			
	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln	Asp	Phe	Arg	Ile	Pro
Leu															
	705					710					715				
720															
	Ser	Pro	Val	His	Lys	Cys	Ser	Phe	Tyr	Lys	Asn	Asn	Thr	Lys	Val
Ser															
				725					730					735	
	Tyr	Gly	Phe	Leu	Ser	Pro	Pro	Gln	Leu	Asn	Lys	Asn	Ser	Ser	Gly
Ile															
			740					745					750		
	Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Thr	Asn	Ile	Val	Pro	Met	Tyr	Gln
Ser															
		755					760				765				
	Phe	Gln	Val	Ile	Trp	Arg	Tyr	Phe	His	Asp	Thr	Leu	Leu	Arg	Lys
Tyr															
		770				775				780					
	Ala	Glu	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro	Val	Phe
Asp															
	785				790				795						
800															
	Phe	Asp	Tyr	Asp	Gly	Arg	Cys	Asp	Ser	Leu	Glu	Asn	Leu	Arg	Gln
Lys															
				805				810					815		
	Arg	Arg	Val	Ile	Arg	Asn	Gln	Glu	Ile	Leu	Ile	Pro	Thr	His	Phe
Phe															
			820					825					830		
	Ile	Val	Leu	Thr	Ser	Cys	Lys	Asp	Thr	Ser	Gln	Thr	Pro	Leu	His
Cys															
		835					840				845				
	Glu	Asn	Leu	Asp	Thr	Leu	Ala	Phe	Ile	Leu	Pro	His	Arg	Thr	Asp
Asn															
		850				855				860					
	Ser	Glu	Ser	Cys	Val	His	Gly	Lys	His	Asp	Ser	Ser	Trp	Val	Glu
Glu															
	865				870				875						
880															
	Leu	Leu	Met	Leu	His	Arg	Ala	Arg	Ile	Thr	Asp	Val	Glu	His	Ile
Thr															
				885				890					895		
	Gly	Leu	Ser	Phe	Tyr	Gln	Gln	Arg	Lys	Glu	Pro	Val	Ser	Asp	Ile
Leu															
		900					905					910			
	Lys	Leu	Lys	Thr	His	Leu	Pro	Thr	Phe	Ser	Gln	Glu	Asp		
		915					920					925			

SEQ ID No: 2 - Azurocidin-ENPP1-FC

MTRLTVLALLAGLLASSRA**APSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPE
 HIWTCNKFRGCEKRLTRSLCACSDDCCKDKGDCCINYSVCQGEKSWVEEPCESESINEPQCPAGFETPPT
 LLFSLDGFRAEYLHTWGGLLPVISKLKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIIDNKMY
 DPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEE
 RILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLHRCL
 NLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPN
 QHFKEPYLKHFLPKRLHFAKSDRIEPLTFYLDLPQWQLALNPSEKRYCGSGFHGSDNVFSNMQALFVGYG
 PGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLKPNVYTPKHPKEVHPLVQCPFTRNP
 RDNLGCSNPSILPIEDFQTQFNLTVAEEKI IKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDIL
 MPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEA
 LLTTNIVPMYQSFQVIWRYFHDTLRLKYAEERNGVNVVSGPVDFDFDYDGRCDLENLRQKRRVIRNQE
 ILIPTHFFIVLTSCKDTSQTPHLCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDV
 EHITGLSFYQQRKEPVSDILKLKTHLPTFSQEDLIN**DKTHTCPPCPAPELLGGPSVFLFPKPKD**TLM
ISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQOGNVSFCSVMHEALHNHYTQKSLSLSPGK

Single underline - Azurocidin signal sequence, Double underline - Beginning and end of ENPP1 sequence, Bold residues- Fc sequence, ** indicates the cleavage point of the signal sequence.

SEQ ID No: 3 - Azurocidin-ENPP1-Alb

MTRLTVLALLAGLLASSRA**APSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPE
 HIWTCNKFRGCEKRLTRSLCACSDDCCKDKGDCCINYSVCQGEKSWVEEPCESESINEPQCPAGFETPPT
 LLFSLDGFRAEYLHTWGGLLPVISKLKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIIDNKMY
 DPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEE
 RILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLHRCL
 NLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPN
 QHFKEPYLKHFLPKRLHFAKSDRIEPLTFYLDLPQWQLALNPSEKRYCGSGFHGSDNVFSNMQALFVGYG
 PGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLKPNVYTPKHPKEVHPLVQCPFTRNP
 RDNLGCSNPSILPIEDFQTQFNLTVAEEKI IKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDIL
 MPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEA
 LLTTNIVPMYQSFQVIWRYFHDTLRLKYAEERNGVNVVSGPVDFDFDYDGRCDLENLRQKRRVIRNQE
 ILIPTHFFIVLTSCKDTSQTPHLCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDV
 EHITGLSFYQQRKEPVSDILKLKTHLPTFSQEDLIN**MKWVTFLLLLFVSGSAFSGVFRREAHKSEIA**
HRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANDCKSLHTLFGDKLCA
IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSPFERPEAEAMCTSFKENPTTFMGHYLHEVAR
RHPYFYAPELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFAK
AWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDILLECADDRAELAKYMCENQATISSKLQTCCD
KPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLR
LAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAP
QVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVER
RPCFSALTVDETYVPKEFKAETFTFHSDICTLPEKEKQIKKQTALAEVLVKKPKATAEQCLKTVMDDFA
QFLDTCKKAADKDTCFSTEGPNLVTRCKDALARSWSHPQFEK

Single underline - Azurocidin signal sequence, Double underline - Beginning and end of ENPP1 sequence, Bold residues- Albumin sequence, ** indicates the cleavage point of the signal sequence.

SEQ ID No: 4 - Azurocidin-ENPP1

MTRLTVLALLAGLLASSRA**APSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPE
 HIWTCNKFRGCEKRLTRSLCACSDDCCKDKGDCCINYSVCQGEKSWVEEPCESESINEPQCPAGFETPPT
 LLFSLDGFRAEYLHTWGGLLPVISKLKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIIDNKMY
 DPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEE

RILAVLQWLQLPKDERPHFYTLTYLEEDSSGHSYGPVSSEVIKALQVRDGMVGMMLMDGLKELNLHRCL
 NLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPN
 QHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDLPQWLALNPSERKYCGSGFHGSDNVFNSMQALFVGYG
 PGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLKPNVYTPKHPKEVHPLVQCPFTRNP
 RDNLGCSNPSILPIEDFQTQFNLTVAEEKI IKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDIL
 MPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEA
 LLTTNIVPMYQSFQVIWRYFHDTLRLKYAEERNGVNVVSGPVDFDFDYDGRCDLENLRQKRRVIRNQE
 ILIPTHFFIVLTSCKDTSQTAPSCAKEVKSCKGRCFERTFGNCRDAACVELGNCCLDYQETCIEPEH
 IWTCKNFKRCGEKRLTRSLCACSDCKDKGDCCINYSSVCQGEKSWVEEPCESINEPQCPAGFETPPTL
 LFSLDGFRAEYLHTWGGLLPVISKLKCKGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGII DNKMYD
 PKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDYKMYNGSVPFEEER
 ILAVLQWLQLPKDERPHFYTLTYLEEDSSGHSYGPVSSEVIKALQVRDGMVGMMLMDGLKELNLHRCLN
 LILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQ
 HFKPYLKHFLPKRLHFAKSDRIEPLTFYLDLPQWLALNPSERKYCGSGFHGSDNVFNSMQALFVGYG
 PGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLKPNVYTPKHPKEVHPLVQCPFTRNPR
 DNLGCSNPSILPIEDFQTQFNLTVAEEKI IKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDILM
 PLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEAL
 LLTTNIVPMYQSFQVIWRYFHDTLRLKYAEERNGVNVVSGPVDFDFDYDGRCDLENLRQKRRVIRNQE
 ILIPTHFFIVLTSCKDTSQTPLHCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDVE
 HITGLSFYQQRKEPVSDILKLKTHLPTFSQED

Single underline - Azurocidin signal sequence, Double underline -
 Beginning and end of ENPP1 sequence, ** indicates the cleavage point
 of the signal sequence.

SEQ ID NO: 5 - ENPP2 Amino Acid Sequence - Wild Type

Met	Ala	Arg	Arg	Ser	Ser	Phe	Gln	Ser	Cys	Gln	Ile	Ile	Ser	Leu	Phe	1	5	10	15
Thr	Phe	Ala	Val	Gly	Val	Asn	Ile	Cys	Leu	Gly	Phe	Thr	Ala	His	Arg	20	25	30	
Ile	Lys	Arg	Ala	Glu	Gly	Trp	Glu	Glu	Gly	Pro	Pro	Thr	Val	Leu	Ser	35	40	45	
Asp	Ser	Pro	Trp	Thr	Asn	Ile	Ser	Gly	Ser	Cys	Lys	Gly	Arg	Cys	Phe	50	55	60	
Glu	Leu	Gln	Glu	Ala	Gly	Pro	Pro	Asp	Cys	Arg	Cys	Asp	Asn	Leu	Cys	65	70	75	80
Lys	Ser	Tyr	Thr	Ser	Cys	Cys	His	Asp	Phe	Asp	Glu	Leu	Cys	Leu	Lys	85	90	95	
Thr	Ala	Arg	Gly	Trp	Glu	Cys	Thr	Lys	Asp	Arg	Cys	Gly	Glu	Val	Arg	100	105	110	
Asn	Glu	Glu	Asn	Ala	Cys	His	Cys	Ser	Glu	Asp	Cys	Leu	Ala	Arg	Gly	115	120	125	
Asp	Cys	Cys	Thr	Asn	Tyr	Gln	Val	Val	Cys	Lys	Gly	Glu	Ser	His	Trp	130	135	140	
Val	Asp	Asp	Asp	Cys	Glu	Glu	Ile	Lys	Ala	Ala	Glu	Cys	Pro	Ala	Gly	145	150	155	160
Phe	Val	Arg	Pro	Pro	Leu	Ile	Ile	Phe	Ser	Val	Asp	Gly	Phe	Arg	Ala	165	170	175	
Ser	Tyr	Met	Lys	Lys	Gly	Ser	Lys	Val	Met	Pro	Asn	Ile	Glu	Lys	Leu	180	185	190	
Arg	Ser	Cys	Gly	Thr	His	Ser	Pro	Tyr	Met	Arg	Pro	Val	Tyr	Pro	Thr	195	200	205	
Lys	Thr	Phe	Pro	Asn	Leu	Tyr	Thr	Leu	Ala	Thr	Gly	Leu	Tyr	Pro	Glu	210	215	220	
Ser	His	Gly	Ile	Val	Gly	Asn	Ser	Met	Tyr	Asp	Pro	Val	Phe	Asp	Ala				

225					230					235					240
Thr	Phe	His	Leu	Arg	Gly	Arg	Glu	Lys	Phe	Asn	His	Arg	Trp	Trp	Gly
				245					250					255	
Gly	Gln	Pro	Leu	Trp	Ile	Thr	Ala	Thr	Lys	Gln	Gly	Val	Lys	Ala	Gly
			260					265					270		
Thr	Phe	Phe	Trp	Ser	Val	Val	Ile	Pro	His	Glu	Arg	Arg	Ile	Leu	Thr
		275					280					285			
Ile	Leu	Gln	Trp	Leu	Thr	Leu	Pro	Asp	His	Glu	Arg	Pro	Ser	Val	Tyr
	290					295					300				
Ala	Phe	Tyr	Ser	Glu	Gln	Pro	Asp	Phe	Ser	Gly	His	Lys	Tyr	Gly	Pro
305					310					315					320
Phe	Gly	Pro	Glu	Met	Thr	Asn	Pro	Leu	Arg	Glu	Ile	Asp	Lys	Ile	Val
				325					330					335	
Gly	Gln	Leu	Met	Asp	Gly	Leu	Lys	Gln	Leu	Lys	Leu	His	Arg	Cys	Val
		340					345						350		
Asn	Val	Ile	Phe	Val	Gly	Asp	His	Gly	Met	Glu	Asp	Val	Thr	Cys	Asp
	355					360						365			
Arg	Thr	Glu	Phe	Leu	Ser	Asn	Tyr	Leu	Thr	Asn	Val	Asp	Asp	Ile	Thr
	370					375					380				
Leu	Val	Pro	Gly	Thr	Leu	Gly	Arg	Ile	Arg	Ser	Lys	Phe	Ser	Asn	Asn
385					390					395					400
Ala	Lys	Tyr	Asp	Pro	Lys	Ala	Ile	Ile	Ala	Asn	Leu	Thr	Cys	Lys	Lys
				405					410					415	
Pro	Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Lys	Gln	His	Leu	Pro	Lys	Arg
		420					425					430			
Leu	His	Tyr	Ala	Asn	Asn	Arg	Arg	Ile	Glu	Asp	Ile	His	Leu	Leu	Val
	435					440					445				
Glu	Arg	Arg	Trp	His	Val	Ala	Arg	Lys	Pro	Leu	Asp	Val	Tyr	Lys	Lys
	450					455					460				
Pro	Ser	Gly	Lys	Cys	Phe	Phe	Gln	Gly	Asp	His	Gly	Phe	Asp	Asn	Lys
465					470				475						480
Val	Asn	Ser	Met	Gln	Thr	Val	Phe	Val	Gly	Tyr	Gly	Ser	Thr	Phe	Lys
				485					490					495	
Tyr	Lys	Thr	Lys	Val	Pro	Pro	Phe	Glu	Asn	Ile	Glu	Leu	Tyr	Asn	Val
		500						505					510		
Met	Cys	Asp	Leu	Leu	Gly	Leu	Lys	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His
	515					520					525				
Gly	Ser	Leu	Asn	His	Leu	Leu	Arg	Thr	Asn	Thr	Phe	Arg	Pro	Thr	Met
	530					535				540					
Pro	Glu	Glu	Val	Thr	Arg	Pro	Asn	Tyr	Pro	Gly	Ile	Met	Tyr	Leu	Gln
545					550				555						560
Ser	Asp	Phe	Asp	Leu	Gly	Cys	Thr	Cys	Asp	Asp	Lys	Val	Glu	Pro	Lys
			565						570					575	
Asn	Lys	Leu	Asp	Glu	Leu	Asn	Lys	Arg	Leu	His	Thr	Lys	Gly	Ser	Thr
		580					585						590		
Glu	Ala	Glu	Thr	Arg	Lys	Phe	Arg	Gly	Ser	Arg	Asn	Glu	Asn	Lys	Glu
	595						600					605			
Asn	Ile	Asn	Gly	Asn	Phe	Glu	Pro	Arg	Lys	Glu	Arg	His	Leu	Leu	Tyr
	610					615					620				
Gly	Arg	Pro	Ala	Val	Leu	Tyr	Arg	Thr	Arg	Tyr	Asp	Ile	Leu	Tyr	His
625					630					635					640
Thr	Asp	Phe	Glu	Ser	Gly	Tyr	Ser	Glu	Ile	Phe	Leu	Met	Pro	Leu	Trp
			645						650					655	
Thr	Ser	Tyr	Thr	Val	Ser	Lys	Gln	Ala	Glu	Val	Ser	Ser	Val	Pro	Asp
		660					665						670		
His	Leu	Thr	Ser	Cys	Val	Arg	Pro	Asp	Val	Arg	Val	Ser	Pro	Ser	Phe

		675					680					685				
Ser	Gln	Asn	Cys	Leu	Ala	Tyr	Lys	Asn	Asp	Lys	Gln	Met	Ser	Tyr	Gly	
	690					695					700					
Phe	Leu	Phe	Pro	Pro	Tyr	Leu	Ser	Ser	Ser	Pro	Glu	Ala	Lys	Tyr	Asp	
705					710					715					720	
Ala	Phe	Leu	Val	Thr	Asn	Met	Val	Pro	Met	Tyr	Pro	Ala	Phe	Lys	Arg	
				725					730					735		
Val	Trp	Asn	Tyr	Phe	Gln	Arg	Val	Leu	Val	Lys	Lys	Tyr	Ala	Ser	Glu	
			740				745						750			
Arg	Asn	Gly	Val	Asn	Val	Ile	Ser	Gly	Pro	Ile	Phe	Asp	Tyr	Asp	Tyr	
	755					760					765					
Asp	Gly	Leu	His	Asp	Thr	Glu	Asp	Lys	Ile	Lys	Gln	Tyr	Val	Glu	Gly	
770					775						780					
Ser	Ser	Ile	Pro	Val	Pro	Thr	His	Tyr	Tyr	Ser	Ile	Ile	Thr	Ser	Cys	
785				790						795					800	
Leu	Asp	Phe	Thr	Gln	Pro	Ala	Asp	Lys	Cys	Asp	Gly	Pro	Leu	Ser	Val	
				805					810					815		
Ser	Ser	Phe	Ile	Leu	Pro	His	Arg	Pro	Asp	Asn	Glu	Glu	Ser	Cys	Asn	
			820				825						830			
Ser	Ser	Glu	Asp	Glu	Ser	Lys	Trp	Val	Glu	Glu	Leu	Met	Lys	Met	His	
	835					840					845					
Thr	Ala	Arg	Val	Arg	Asp	Ile	Glu	His	Leu	Thr	Ser	Leu	Asp	Phe	Phe	
	850				855					860						
Arg	Lys	Thr	Ser	Arg	Ser	Tyr	Pro	Glu	Ile	Leu	Thr	Leu	Lys	Thr	Tyr	
865				870						875					880	
Leu	His	Thr	Tyr	Glu	Ser	Glu	Ile									
				885												

SEQ. ID NO:6 - Extracellular Domain of ENPP3:

Glu	Lys	Gln	Gly	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp	Ala	Ser	Phe	Arg	
1				5					10					15		
Gly	Leu	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys	Asp	Arg	Gly	Asp	
			20					25					30			
Cys	Cys	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser	Thr	Arg	Ile	Trp	
	35					40					45					
Met	Cys	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Thr	Arg	Leu	Glu	Ala	Ser	Leu	
50					55					60						
Cys	Ser	Cys	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys	Cys	Ala	Asp	
65				70					75					80		
Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu	Glu	Asn	Cys	
			85					90					95			
Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp	Leu	Pro	Pro	
		100					105						110			
Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	Tyr	Thr	
	115					120					125					
Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr	Cys	Gly	Ile	
	130				135						140					
His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	
145				150					155					160		
His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	
			165					170					175			
Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe	Ser	Leu	Ser	
		180					185					190				
Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln	Pro	Met	Trp	

		195					200					205					
Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr	Phe	Trp	Pro		
	210					215					220						
Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	Tyr	Met	Pro		
225					230					235					240		
Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	Leu	Leu	Lys		
				245					250					255			
Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	Thr	Met	Tyr		
			260					265					270				
Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	Val	Ser	Ala		
	275						280					285					
Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	Gly	Met	Leu		
290					295					300							
Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	Asn	Ile	Ile		
305					310					315					320		
Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	Lys	Met	Glu		
				325					330					335			
Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	Met	Tyr	Glu		
			340				345						350				
Gly	Pro	Ala	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	Asp	Phe	Phe		
	355						360					365					
Ser	Phe	Asn	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	Arg	Lys	Pro		
370					375					380							
Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys	Arg	Leu		
385					390					395					400		
His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe	Val	Asp		
				405					410					415			
Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys	Gly	Gly		
			420					425					430				
Gly	Asn	His	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	Ala	Ile	Phe		
	435						440					445					
Leu	Ala	His	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	Glu	Pro	Phe		
	450					455					460						
Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu	Arg	Ile	Gln		
465					470					475					480		
Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys		
				485					490					495			
Val	Pro	Phe	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu	Val	Ser	Lys	Phe	Ser		
			500				505						510				
Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu	Asp	Cys	Phe		
	515					520						525					
Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val	Asn	Gln	Met		
	530				535						540						
Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys	Val	Asn	Leu		
545					550					555					560		
Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp	His	Cys	Leu		
				565					570					575			
Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala	Met	Arg	Met		
			580				585						590				
Pro	Met	Trp	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu	Gly	Asp	Thr	Ser	Pro		
	595					600						605					
Leu	Pro	Pro	Thr	Val	Pro	Asp	Cys	Leu	Arg	Ala	Asp	Val	Arg	Val	Pro		
	610					615					620						
Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu	Ala	Asp	Lys	Asn	Ile		
625					630					635					640		
Thr	His	Gly	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn	Arg	Thr	Ser	Asp	Ser		

				645					650					655			
Gln	Tyr	Asp	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val	Pro	Met	Tyr	Glu	Glu		
			660					665					670				
Phe	Arg	Lys	Met	Trp	Asp	Tyr	Phe	His	Ser	Val	Leu	Leu	Ile	Lys	His		
		675					680					685					
Ala	Thr	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro	Ile	Phe	Asp		
		690				695					700						
Tyr	Asn	Tyr	Asp	Gly	His	Phe	Asp	Ala	Pro	Asp	Glu	Ile	Thr	Lys	His		
705				710						715					720		
Leu	Ala	Asn	Thr	Asp	Val	Pro	Ile	Pro	Thr	His	Tyr	Phe	Val	Val	Leu		
			725						730					735			
Thr	Ser	Cys	Lys	Asn	Lys	Ser	His	Thr	Pro	Glu	Asn	Cys	Pro	Gly	Trp		
		740					745					750					
Leu	Asp	Val	Leu	Pro	Phe	Ile	Ile	Pro	His	Arg	Pro	Thr	Asn	Val	Glu		
		755				760					765						
Ser	Cys	Pro	Glu	Gly	Lys	Pro	Glu	Ala	Leu	Trp	Val	Glu	Glu	Arg	Phe		
	770					775					780						
Thr	Ala	His	Ile	Ala	Arg	Val	Arg	Asp	Val	Glu	Leu	Leu	Thr	Gly	Leu		
785				790						795					800		
Asp	Phe	Tyr	Gln	Asp	Lys	Val	Gln	Pro	Val	Ser	Glu	Ile	Leu	Gln	Leu		
			805						810					815			
Lys	Thr	Tyr	Leu	Pro	Thr	Phe	Glu	Thr	Thr	Ile							
		820						825									

SEQ. ID NO: 7 - NPP3 Amino Acid Sequence:

Met	Glu	Ser	Thr	Leu	Thr	Leu	Ala	Thr	Glu	Gln	Pro	Val	Lys	Lys	Asn		
1				5					10					15			
Thr	Leu	Lys	Lys	Tyr	Lys	Ile	Ala	Cys	Ile	Val	Leu	Leu	Ala	Leu	Leu		
			20					25					30				
Val	Ile	Met	Ser	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Arg	Lys	Leu		
		35				40					45						
Glu	Lys	Gln	Gly	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp	Ala	Ser	Phe	Arg		
	50					55					60						
Gly	Leu	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys	Asp	Arg	Gly	Asp		
65				70						75					80		
Cys	Cys	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser	Thr	Arg	Ile	Trp		
			85					90					95				
Met	Cys	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Thr	Arg	Leu	Glu	Ala	Ser	Leu		
		100					105						110				
Cys	Ser	Cys	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys	Cys	Ala	Asp		
		115				120					125						
Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu	Glu	Asn	Cys		
	130					135					140						
Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp	Leu	Pro	Pro		
145				150						155					160		
Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	Tyr	Thr		
			165						170					175			
Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr	Cys	Gly	Ile		
		180						185					190				
His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn		
	195					200						205					
His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile		
	210					215					220						
Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe	Ser	Leu	Ser		

225					230					235				240
Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln	Pro	Met
				245					250					255
Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr	Phe	Trp
			260					265					270	Pro
Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	Tyr	Met
		275					280					285		Pro
Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	Leu	Leu
	290					295					300			Lys
Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	Thr	Met
305					310					315				Tyr
Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	Val	Ser
				325					330					335
Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	Gly	Met
			340					345					350	Leu
Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	Asn	Ile
		355					360					365		Ile
Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	Lys	Met
	370					375					380			Glu
Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	Met	Tyr
385					390					395				400
Gly	Pro	Ala	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	Asp	Phe
				405					410					415
Ser	Phe	Asn	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	Arg	Lys
			420					425					430	Pro
Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys	Arg
	435						440					445		Leu
His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe	Val
	450					455					460			Asp
Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys	Gly
465					470					475				480
Gly	Asn	His	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	Ala	Ile
				485					490					495
Leu	Ala	His	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	Glu	Pro
			500					505					510	Phe
Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu	Arg	Ile
	515						520				525			Gln
Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu	Asn	His	Leu	Leu
	530					535					540			Lys
Val	Pro	Phe	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu	Val	Ser	Lys	Phe
545					550					555				560
Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu	Asp	Cys
				565					570					575
Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val	Asn	Gln
			580					585					590	Met
Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys	Val	Asn
	595						600					605		Leu
Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp	His	Cys
	610					615					620			Leu
Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala	Met	Arg
625					630					635				640
Pro	Met	Trp	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu	Gly	Asp	Thr	Ser
				645					650					655
Leu	Pro	Pro	Thr	Val	Pro	Asp	Cys	Leu	Arg	Ala	Asp	Val	Arg	Val
			660					665					670	Pro
Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu	Ala	Asp	Lys	Asn
														Ile

SEQ ID No: 8 - Azurocidin-ENPP3-FC

Single underline - Azurocidin signal sequence, Double underline - Beginning and end of ENPP3 sequence, Bold residues- Fc sequence, ** indicates the cleavage point of the signal sequence.

MTRLTVLALLAGLLASSRA**AKQGSCRKKCFDASFRGLENCRCDVACKDRGDCCWDFEDTC
 VESTRIWMCNKFRCGETRLEASLCSDDCLQRKDCCADYKSVCQGETSWLEENDTAQQSQCPGEGD
 LPPVILFSDMGFRAEYLYTWDTLMPNINKLKTGIIHISKYMRAMYPTKTFPNHYTIVTGLYPESHGIIID
 NNMYDVNLNKNFSLSSKEONNPAWWHGOPMNLTAMYOGLKAATYFWPGSEVAINGSFPSIYMPYNGSV

PFEERISTLLKWLDPKAERPRFYTMFEEDSSGHAGGPVSARVIKALQVVDHAFGMLMEGLKQRNL
 HNCVNIILLADHGMDQTYCNKMEYMTDYFPRINFFYMYEGPAPRIRAHNIPHDFFSFNSEEIVRNLSC
 RKPQDHFQPYLTPDLPKRLHYAKNVRIDKVHLFVDQQWLAVRSKSNNTNCGGGNHGYNNEFRSMEAI
 AHLPSFKEKTEVEPFENIEVYNLMCDLLRIQPAPNNGTHGSLNHLLKVPFYEP SHAEEVSKFSVCGFA
 NPLPTESLDCFCPHLQNSTQLEQVNQMLNLTQEEITATVKVNLFPGRPRVLQKNVDHCLLYHREYVSG
 FGKAMRMPMWSSYTPVQLGDTSPLPPTVPDCLRADVRVPPSESQKCSFYLDKNITHGFLYPPASNRT
 SDSQYDALITSNLVPMYEEFRKMWDYFHSVLLIKHATERNGVNVVSGPIFDYNYDGHFDAPDEITKHL
 ANTDPVPIPTHYFVVLTSCKNKSHTPENCPGWLVDLPFIIPHRPTNVESCPEGKPEALWVEERFTAHIA
 RVRDVELLTGLDFYQDKVQPVSEILQLKTYLPTFETTI**MKWVTFLLLLFVSGSAFSGVFRREAHKSE**
IAHRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCCKSLHTLFGDKL
CAIPNLRENYGELADCCTKQEPERNECFHQKDDNPSPPFERPEAEAMCTSFKENPTTFMGHYLHEV
ARRHPYFYAPELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERA
FKAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATISSKLQTC
CDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDVLGTFLEYYSRRHPDYSVSL
LRLAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQK
APQVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLV
ERRPCFSALTVDETYVPKEFKAETFTFHSIDICTLPEKEKQIKQTALAEVLKHKPKATAEQKLTVMDD
FAQFLDTCCKAADKDTCTFSTEGPNLVTRCKDALARSWSHPQFEK

Single underline - Azurocidin signal sequence, Double underline - Beginning and end of ENPP3 sequence, Bold residues - Albumin sequence, ** indicates the cleavage point of the signal sequence.

SEQ ID No: 10 - Azurocidin-ENPP3

MTRLTVLALLAGLLASSRA**AKQGSCRRKKCFDASFRGLENCRCDVACKDRGDCCWDFEDTC
 VESTRIWMCNKFRCGETRLEASLCSCSDCLQRKDCADYKSVQGETSWLEENCDTAQQSQCPEGFD
 LPPVILFMSDGFRAEYLYTWDTLMPNINKLKTGCIH SKYMRAMYPTKTFPNHYTIVTGLYPESHGIID
 NNMYDVNLNKNFSLSSKEQNNPAWWHGQPMNLAMYQGLKAATYFWPGSEVAINGSFPSIYMPYNGSV
 PFEERISTLLKWLDPKAERPRFYTMFEEDSSGHAGGPVSARVIKALQVVDHAFGMLMEGLKQRNL
 HNCVNIILLADHGMDQTYCNKMEYMTDYFPRINFFYMYEGPAPRIRAHNIPHDFFSFNSEEIVRNLSC
 RKPQDHFQPYLTPDLPKRLHYAKNVRIDKVHLFVDQQWLAVRSKSNNTNCGGGNHGYNNEFRSMEAI
 AHLPSFKEKTEVEPFENIEVYNLMCDLLRIQPAPNNGTHGSLNHLLKVPFYEP SHAEEVSKFSVCGFA
 NPLPTESLDCFCPHLQNSTQLEQVNQMLNLTQEEITATVKVNLFPGRPRVLQKNVDHCLLYHREYVSG
 FGKAMRMPMWSSYTPVQLGDTSPLPPTVPDCLRADVRVPPSESQKCSFYLDKNITHGFLYPPASNRT
 SDSQYDALITSNLVPMYEEFRKMWDYFHSVLLIKHATERNGVNVVSGPIFDYNYDGHFDAPDEITKHL
 ANTDPVPIPTHYFVVLTSCKNKSHTPENCPGWLVDLPFIIPHRPTNVESCPEGKPEALWVEERFTAHIA
 RVRDVELLTGLDFYQDKVQPVSEILQLKTYLPTFETTI

Single underline - Azurocidin signal sequence, Double underline - Beginning and end of ENPP3 sequence, ** indicates the cleavage point of the signal sequence.

SEQ. ID NO:11 - ENPP4 Amino Acid Sequence - Wild Type

	Met	Lys	Leu	Leu	Val	Ile	Leu	Leu	Phe	Ser	Gly	Leu	Ile	Thr	Gly
Phe	1				5					10					15
	Arg	Ser	Asp	Ser	Ser	Ser	Ser	Leu	Pro	Pro	Lys	Leu	Leu	Leu	Val
Ser					20					25					30
	Phe	Asp	Gly	Phe	Arg	Ala	Asp	Tyr	Leu	Lys	Asn	Tyr	Glu	Phe	Pro
His															

		35					40				45				
	Leu	Gln	Asn	Phe	Ile	Lys	Glu	Gly	Val	Leu	Val	Glu	His	Val	Lys
Asn															
		50					55				60				
	Val	Phe	Ile	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val	Thr
Gly															
	65					70				75					80
	Leu	Tyr	Glu	Glu	Ser	His	Gly	Ile	Val	Ala	Asn	Ser	Met	Tyr	Asp
Ala															
					85				90					95	
	Val	Thr	Lys	Lys	His	Phe	Ser	Asp	Ser	Asn	Asp	Lys	Asp	Pro	Phe
Trp															
					100				105					110	
	Trp	Asn	Glu	Ala	Val	Pro	Ile	Trp	Val	Thr	Asn	Gln	Leu	Gln	Glu
Asn															
					115			120				125			
	Arg	Ser	Ser	Ala	Ala	Ala	Met	Trp	Pro	Gly	Thr	Asp	Val	Pro	Ile
His															
		130					135				140				
	Asp	Thr	Ile	Ser	Ser	Tyr	Phe	Met	Asn	Tyr	Asn	Ser	Ser	Val	Ser
Phe															
	145					150					155				
160															
	Glu	Glu	Arg	Leu	Asn	Asn	Ile	Thr	Met	Trp	Leu	Asn	Asn	Ser	Asn
Pro															
					165				170					175	
	Pro	Val	Thr	Phe	Ala	Thr	Leu	Tyr	Trp	Glu	Glu	Pro	Asp	Ala	Ser
Gly															
					180				185				190		
	His	Lys	Tyr	Gly	Pro	Glu	Asp	Lys	Glu	Asn	Met	Ser	Arg	Val	Leu
Lys															
					195				200				205		
	Lys	Ile	Asp	Asp	Leu	Ile	Gly	Asp	Leu	Val	Gln	Arg	Leu	Lys	Met
Leu															
					210				215				220		
	Gly	Leu	Trp	Glu	Asn	Leu	Asn	Val	Ile	Ile	Thr	Ser	Asp	His	Gly
Met															
	225					230					235				
240															
	Thr	Gln	Cys	Ser	Gln	Asp	Arg	Leu	Ile	Asn	Leu	Asp	Ser	Cys	Ile
Asp															
					245				250					255	
	His	Ser	Tyr	Tyr	Thr	Leu	Ile	Asp	Leu	Ser	Pro	Val	Ala	Ala	Ile
Leu															
					260				265					270	
	Pro	Lys	Ile	Asn	Arg	Thr	Glu	Val	Tyr	Asn	Lys	Leu	Lys	Asn	Cys
Ser															
					275				280				285		
	Pro	His	Met	Asn	Val	Tyr	Leu	Lys	Glu	Asp	Ile	Pro	Asn	Arg	Phe
Tyr															
					290				295				300		
	Tyr	Gln	His	Asn	Asp	Arg	Ile	Gln	Pro	Ile	Ile	Leu	Val	Ala	Asp
Glu															
	305					310					315				
320															

His Gly Trp Thr Ile Val Leu Asn Glu Ser Ser Gln Lys Leu Gly Asp
 325 330 335
 His Gly Tyr Asp Asn Ser Leu Pro Ser Met His Pro Phe Leu Ala Ala
 340 345 350
 Val Gly Pro Ala Phe His Lys Gly Tyr Lys His Ser Thr Ile Asn Ile
 355 360 365
 Pro Asp Ile Tyr Pro Met Met Cys His Ile Leu Gly Leu Lys Pro His
 370 375 380
 Trp Asn Asn Gly Thr Phe Gly His Thr Lys Cys Leu Leu Val Asp Gln
 385 390 395
 400 Cys Ile Asn Leu Pro Glu Ala Ile Ala Ile Val Ile Gly Ser Leu
 Leu 405 410 415
 Leu Val Leu Thr Met Leu Thr Cys Leu Ile Ile Ile Met Gln Asn Arg
 420 425 430
 Asp Ser Val Pro Arg Pro Phe Ser Arg Leu Gln Leu Gln Glu Asp Asp
 435 440 445
 Asp Pro Leu Ile Gly
 450

SEQ. ID NO: 12 - ENPP51 Amino Acid Sequence

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu
Ser
 1 5 10 15
Leu Ser Thr Thr Phe Ser Leu Gln**Pro Ser Cys Ala Lys Glu Val
 Lys
 20 25 30
 Cys Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Ser Asn Cys Arg
 35 40 45
 Glu Asp Ala Ala Cys Val Ser Leu Gly Asn Cys Cys Leu Asp Phe Gln
 50 55 60
 Cys Thr Cys Val Glu Pro Thr His Ile Trp Thr Cys Asn Lys Phe Arg
 65 70 75 80
 Cys Gly Glu Lys Arg Leu Ser Arg Phe Val Cys Ser Cys Ala Asp Asp
 85 90 95
 Asp Lys Thr His Asn Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln
 100 105 110
 Glu Lys Lys Ser Trp Val Glu Glu Thr Cys Glu Ser Ile Asp Thr Pro
 115 120 125

	Cys	Pro	Ala	Glu	Phe	Glu	Ser	Pro	Pro	Thr	Leu	Leu	Phe	Ser	Leu
Asp															
		130					135				140				
	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu	Pro
Val															
	145					150					155				
160															
	Ile	Ser	Lys	Leu	Lys	Asn	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met	Arg
Pro															
					165				170					175	
	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val	Thr
Gly															
			180					185					190		
	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr	Asp
Pro															
		195					200					205			
	Lys	Met	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe	Asn
Pro															
		210					215				220				
	Leu	Trp	Tyr	Lys	Gly	Gln	Pro	Ile	Trp	Val	Thr	Ala	Asn	His	Gln
Glu															
	225					230					235				
240															
	Val	Lys	Ser	Gly	Thr	Tyr	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu	Ile
Asp															
				245				250					255		
	Gly	Ile	Leu	Pro	Asp	Ile	Tyr	Lys	Val	Tyr	Asn	Gly	Ser	Val	Pro
Phe															
			260					265				270			
	Glu	Glu	Arg	Ile	Leu	Ala	Val	Leu	Glu	Trp	Leu	Gln	Leu	Pro	Ser
His															
		275					280				285				
	Glu	Arg	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp	Ser
Ser															
		290					295				300				
	Gly	His	Ser	His	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala	Leu
Gln															
	305					310					315				
320															
	Lys	Val	Asp	Arg	Leu	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys	Asp
Leu															
				325				330					335		
	Gly	Leu	Asp	Lys	Cys	Leu	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His	Gly
Met															
			340					345				350			
	Glu	Gln	Gly	Ser	Cys	Lys	Lys	Tyr	Val	Tyr	Leu	Asn	Lys	Tyr	Leu
Gly															
		355					360				365				
	Asp	Val	Asn	Asn	Val	Lys	Val	Val	Tyr	Gly	Pro	Ala	Ala	Arg	Leu
Arg															
		370					375				380				
	Pro	Thr	Asp	Val	Pro	Glu	Thr	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu	Ala
Leu															
	385					390					395				
400															

	Ala	Lys	Asn	Leu	Ser	Cys	Arg	Glu	Pro	Asn	Gln	His	Phe	Arg	Pro
Tyr															
					405					410					415
Arg	Leu	Lys	Pro	Phe	Leu	Pro	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp
				420					425					430	
Leu	Ile	Glu	Pro	Leu	Thr	Phe	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala
			435					440					445		
Asp	Asn	Pro	Ser	Glu	Arg	Lys	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser
		450					455				460				
Ala	Asn	Leu	Phe	Ser	Asn	Met	Gln	Ala	Leu	Phe	Ile	Gly	Tyr	Gly	Pro
	465					470					475				
480															
Tyr	Phe	Lys	His	Gly	Ala	Glu	Val	Asp	Ser	Phe	Glu	Asn	Ile	Glu	Val
				485					490					495	
Gly	Asn	Leu	Met	Cys	Asp	Leu	Leu	Gly	Leu	Ile	Pro	Ala	Pro	Asn	Asn
			500						505					510	
Pro	Ser	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Lys	Pro	Ile	Tyr	Asn
		515					520					525			
Ser	Ser	His	Pro	Lys	Glu	Glu	Gly	Phe	Leu	Ser	Gln	Cys	Pro	Ile	Lys
		530				535					540				
Ile	Thr	Ser	Asn	Asp	Leu	Gly	Cys	Thr	Cys	Asp	Pro	Trp	Ile	Val	Pro
	545				550						555				
560															
Asp	Lys	Asp	Phe	Glu	Lys	Gln	Leu	Asn	Leu	Thr	Thr	Glu	Asp	Val	Asp
				565					570					575	
Lys	Ile	Tyr	His	Met	Thr	Val	Pro	Tyr	Gly	Arg	Pro	Arg	Ile	Leu	Leu
			580						585					590	
Tyr	Gln	His	Arg	Val	Cys	Leu	Leu	Gln	Gln	Gln	Gln	Phe	Leu	Thr	Gly
		595						600					605		
Ser	Ser	Leu	Asp	Leu	Leu	Met	Pro	Leu	Trp	Ala	Ser	Tyr	Thr	Phe	Leu
		610				615						620			
Asp	Asn	Asp	Gln	Phe	Ser	Arg	Asp	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln
	625					630					635				
640															
Ser	Leu	Arg	Ile	Pro	Leu	Ser	Pro	Val	His	Lys	Cys	Ser	Tyr	Tyr	Lys
				645					650				655		
Arg	Asn	Ser	Lys	Leu	Ser	Tyr	Gly	Phe	Leu	Thr	Pro	Pro	Arg	Leu	Asn
			660						665				670		
Val	Val	Ser	Asn	His	Ile	Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Ser	Asn	Ile

```

        675              680              685
Pro Met Tyr Gln Ser Phe Gln Val Ile Trp His Tyr Leu His Asp
Thr
        690              695              700
Leu Leu Gln Arg Tyr Ala His Glu Arg Asn Gly Ile Asn Val Val
Ser
705              710              715
720
Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Tyr Asp Ser Leu
Glu
        725              730              735
Ile Leu Lys Gln Asn Ser Arg Val Ile Arg Ser Gln Glu Ile Leu
Ile
        740              745              750
Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Gln Leu Ser
Glu
        755              760              765
Thr Pro Leu Glu Cys Ser Ala Leu Glu Ser Ser Ala Tyr Ile Leu
Pro
        770              775              780
His Arg Pro Asp Asn Ile Glu Ser Cys Thr His Gly Lys Arg Glu
Ser
785              790              795
800
Ser Trp Val Glu Glu Leu Leu Thr Leu His Arg Ala Arg Val Thr
Asp
        805              810              815
Val Glu Leu Ile Thr Gly Leu Ser Phe Tyr Gln Asp Arg Gln Glu
Ser
        820              825              830
Val Ser Glu Leu Leu Arg Leu Lys Thr His Leu Pro Ile Phe Ser
Gln
        835              840              845
Glu Asp
        850

```

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence

SEQ. ID NO: 13 - ENPP51 - ALB Amino Acid Sequence:

```

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu
Ser
1              5              10              15
Leu Ser Thr Thr Phe Ser Leu Gln**Pro Ser Cys Ala Lys Glu Val
Lys
        20              25              30
Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Ser Asn Cys Arg
Cys
        35              40              45
Asp Ala Ala Cys Val Ser Leu Gly Asn Cys Cys Leu Asp Phe Gln
Glu

```

	50		55		60										
	Thr	Cys	Val	Glu	Pro	Thr	His	Ile	Trp	Thr	Cys	Asn	Lys	Phe	Arg
Cys															
	65					70					75				80
	Gly	Glu	Lys	Arg	Leu	Ser	Arg	Phe	Val	Cys	Ser	Cys	Ala	Asp	Asp
Cys															
				85						90					95
	Lys	Thr	His	Asn	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys	Gln
Asp															
				100					105					110	
	Lys	Lys	Ser	Trp	Val	Glu	Glu	Thr	Cys	Glu	Ser	Ile	Asp	Thr	Pro
Glu															
			115					120					125		
	Cys	Pro	Ala	Glu	Phe	Glu	Ser	Pro	Pro	Thr	Leu	Leu	Phe	Ser	Leu
Asp															
		130					135					140			
	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu	Pro
Val															
	145					150					155				
160															
	Ile	Ser	Lys	Leu	Lys	Asn	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met	Arg
Pro															
				165					170					175	
	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val	Thr
Gly															
			180					185					190		
	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr	Asp
Pro															
		195					200					205			
	Lys	Met	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe	Asn
Pro															
		210					215				220				
	Leu	Trp	Tyr	Lys	Gly	Gln	Pro	Ile	Trp	Val	Thr	Ala	Asn	His	Gln
Glu															
	225					230					235				
240															
	Val	Lys	Ser	Gly	Thr	Tyr	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu	Ile
Asp															
				245					250					255	
	Gly	Ile	Leu	Pro	Asp	Ile	Tyr	Lys	Val	Tyr	Asn	Gly	Ser	Val	Pro
Phe															
			260					265					270		
	Glu	Glu	Arg	Ile	Leu	Ala	Val	Leu	Glu	Trp	Leu	Gln	Leu	Pro	Ser
His															
		275					280					285			
	Glu	Arg	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp	Ser
Ser															
		290				295					300				
	Gly	His	Ser	His	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala	Leu
Gln															
	305					310					315				
320															
	Lys	Val	Asp	Arg	Leu	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys	Asp
Leu															
				325					330					335	

	Gly	Leu	Asp	Lys	Cys	Leu	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His	Gly
Met															
				340					345					350	
	Glu	Gln	Gly	Ser	Cys	Lys	Lys	Tyr	Val	Tyr	Leu	Asn	Lys	Tyr	Leu
Gly															
			355					360					365		
	Asp	Val	Asn	Asn	Val	Lys	Val	Val	Tyr	Gly	Pro	Ala	Ala	Arg	Leu
Arg															
		370					375					380			
	Pro	Thr	Asp	Val	Pro	Glu	Thr	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu	Ala
Leu															
	385					390					395				
400															
	Ala	Lys	Asn	Leu	Ser	Cys	Arg	Glu	Pro	Asn	Gln	His	Phe	Arg	Pro
Tyr															
				405					410					415	
	Leu	Lys	Pro	Phe	Leu	Pro	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp
Arg															
			420					425					430		
	Ile	Glu	Pro	Leu	Thr	Phe	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala
Leu															
		435					440				445				
	Asn	Pro	Ser	Glu	Arg	Lys	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser
Asp															
		450				455					460				
	Asn	Leu	Phe	Ser	Asn	Met	Gln	Ala	Leu	Phe	Ile	Gly	Tyr	Gly	Pro
Ala															
	465					470					475				
480															
	Phe	Lys	His	Gly	Ala	Glu	Val	Asp	Ser	Phe	Glu	Asn	Ile	Glu	Val
Tyr															
				485				490					495		
	Asn	Leu	Met	Cys	Asp	Leu	Leu	Gly	Leu	Ile	Pro	Ala	Pro	Asn	Asn
Gly															
			500					505					510		
	Ser	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Lys	Pro	Ile	Tyr	Asn
Pro															
			515				520					525			
	Ser	His	Pro	Lys	Glu	Glu	Gly	Phe	Leu	Ser	Gln	Cys	Pro	Ile	Lys
Ser															
		530				535					540				
	Thr	Ser	Asn	Asp	Leu	Gly	Cys	Thr	Cys	Asp	Pro	Trp	Ile	Val	Pro
Ile															
	545				550						555				
560															
	Lys	Asp	Phe	Glu	Lys	Gln	Leu	Asn	Leu	Thr	Thr	Glu	Asp	Val	Asp
Asp															
				565				570					575		
	Ile	Tyr	His	Met	Thr	Val	Pro	Tyr	Gly	Arg	Pro	Arg	Ile	Leu	Leu
Lys															
			580				585					590			
	Gln	His	Arg	Val	Cys	Leu	Leu	Gln	Gln	Gln	Gln	Phe	Leu	Thr	Gly
Tyr															
		595				600					605				
	Ser	Leu	Asp	Leu	Leu	Met	Pro	Leu	Trp	Ala	Ser	Tyr	Thr	Phe	Leu
Ser															

	610		615		620										
Asp	Asn	Asp	Gln	Phe	Ser	Arg	Asp	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln
	625					630					635				
640	Leu	Arg	Ile	Pro	Leu	Ser	Pro	Val	His	Lys	Cys	Ser	Tyr	Tyr	Lys
Ser						645					650				655
Arg	Asn	Ser	Lys	Leu	Ser	Tyr	Gly	Phe	Leu	Thr	Pro	Pro	Arg	Leu	Asn
				660					665					670	
Val	Val	Ser	Asn	His	Ile	Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Ser	Asn	Ile
				675				680					685		
Thr	Pro	Met	Tyr	Gln	Ser	Phe	Gln	Val	Ile	Trp	His	Tyr	Leu	His	Asp
				690			695				700				
Ser	Leu	Leu	Gln	Arg	Tyr	Ala	His	Glu	Arg	Asn	Gly	Ile	Asn	Val	Val
	705					710					715				
720	Gly	Pro	Val	Phe	Asp	Phe	Asp	Tyr	Asp	Gly	Arg	Tyr	Asp	Ser	Leu
Glu															
				725					730					735	
Ile	Ile	Leu	Lys	Gln	Asn	Ser	Arg	Val	Ile	Arg	Ser	Gln	Glu	Ile	Leu
				740					745					750	
Glu	Pro	Thr	His	Phe	Phe	Ile	Val	Leu	Thr	Ser	Cys	Lys	Gln	Leu	Ser
				755				760					765		
Pro	Thr	Pro	Leu	Glu	Cys	Ser	Ala	Leu	Glu	Ser	Ser	Ala	Tyr	Ile	Leu
				770			775					780			
Ser	His	Arg	Pro	Asp	Asn	Ile	Glu	Ser	Cys	Thr	His	Gly	Lys	Arg	Glu
	785					790						795			
800	Ser	Trp	Val	Glu	Glu	Leu	Leu	Thr	Leu	His	Arg	Ala	Arg	Val	Thr
Asp															
				805					810					815	
Ser	Val	Glu	Leu	Ile	Thr	Gly	Leu	Ser	Phe	Tyr	Gln	Asp	Arg	Gln	Glu
				820					825					830	
Gln	Val	Ser	Glu	Leu	Leu	Arg	Leu	Lys	Thr	His	Leu	Pro	Ile	Phe	Ser
				835			840						845		
Leu	Glu	Asp	<u>Gly</u>	<u>Gly</u>	<u>Ser</u>	<u>Gly</u>	<u>Gly</u>	<u>Ser</u>	Met	Lys	Trp	Val	Thr	Phe	Leu
				850			855						860		
Arg	Leu	Leu	Phe	Val	Ser	Gly	Ser	Ala	Phe	Ser	Arg	Gly	Val	Phe	Arg
				865			870						875		
880	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg	Tyr	Asn	Asp	Leu	Gly
Glu															
				885					890					895	

Gln	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe	Ser	Gln	Tyr	Leu
				900					905					910	
Asp	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu	Val	Gln	Glu	Val	Thr
				915				920					925		
Lys	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp
				930				935					940		
Leu	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn
				945			950					955			
960	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys	Cys	Thr	Lys	Gln	Glu
Pro															
					965				970				975		
Leu	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Ser
				980				985					990		
Lys	Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe
				995				1000					1005		
	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala
	1010						1015					1020			
	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala
	1025						1030					1035			
	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp
	1040						1045					1050			
	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys
	1055						1060					1065			
	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met
	1070						1075					1080			
	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
	1085						1090					1095			
	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys
	1100						1105					1110			
	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly
	1115						1120					1125			
	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr
	1130						1135					1140			
	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys
	1145						1150					1155			
	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val
	1160						1165					1170			
	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp
	1175						1180					1185			
	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys
	1190						1195					1200			
	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His
	1205						1210					1215			
	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr
	1220						1225					1230			
	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
	1235						1240					1245			
	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu
	1250						1255					1260			


```

Pro Lys  Asn Leu Val Lys Thr  Asn Cys Asp Leu Tyr  Glu Lys Leu
1265                                1270                1275
Gly Glu  Tyr Gly Phe Gln Asn  Ala Ile Leu Val Arg  Tyr Thr Gln
1280                                1285                1290
Lys Ala  Pro Gln Val Ser Thr  Pro Thr Leu Val Glu  Ala Ala Arg
1295                                1300                1305
Asn Leu  Gly Arg Val Gly Thr  Lys Cys Cys Thr Leu  Pro Glu Asp
1310                                1315                1320
Gln Arg  Leu Pro Cys Val Glu  Asp Tyr Leu Ser Ala  Ile Leu Asn
1325                                1330                1335
Arg Val  Cys Leu Leu His Glu  Lys Thr Pro Val Ser  Glu His Val
1340                                1345                1350
Thr Lys  Cys Cys Ser Gly Ser  Leu Val Glu Arg Arg  Pro Cys Phe
1355
Ser Ala  Leu Thr Val Asp Glu  Thr Tyr Val Pro Lys  Glu Phe Lys
1370                                1375                1380
Ala Glu  Thr Phe Thr Phe His  Ser Asp Ile Cys Thr  Leu Pro Glu
1385                                1390                1395
Lys Glu  Lys Gln Ile Lys Lys  Gln Thr Ala Leu Ala  Glu Leu Val
1400                                1405                1410
Lys His  Lys Pro Lys Ala Thr  Ala Glu Gln Leu Lys  Thr Val Met
1415                                1420                1425
Asp Asp  Phe Ala Gln Phe Leu  Asp Thr Cys Cys Lys  Ala Ala Asp
1430                                1435                1440
Lys Asp  Thr Cys Phe Ser Thr  Glu Gly Pro Asn Leu  Val Thr Arg
1445                                1450                1455
Cys Lys  Asp Ala Leu Ala Arg  Ser Trp Ser His Pro  Gln Phe Glu
1460                                1465                1470
Lys

```

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 14 - ENPP5-NPP3-Fc sequence

```

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu
Ser
1           5           10           15
Leu Ser Thr Thr Phe Ser**Lys Gln Gly Ser Cys Arg Lys Lys Cys
Phe
           20           25           30
Asp Ala Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala
Cys
           35           40           45
Lys Asp Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val
Glu
           50           55           60
Ser Thr Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg
Leu
65           70           75           80

```

	Glu	Ala	Ser	Leu	Cys	Ser	Cys	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys
Asp															
					85					90					95
	Cys	Cys	Ala	Asp	Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp
Leu															
				100					105					110	
	Glu	Glu	Asn	Cys	Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly
Phe															
			115					120					125		
	Asp	Leu	Pro	Pro	Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala
Glu															
		130					135					140			
	Tyr	Leu	Tyr	Thr	Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu
Lys															
	145					150					155				
160															
	Thr	Cys	Gly	Ile	His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr
Lys															
				165					170					175	
	Thr	Phe	Pro	Asn	His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu
Ser															
			180					185					190		
	His	Gly	Ile	Ile	Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys
Asn															
		195					200					205			
	Phe	Ser	Leu	Ser	Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His
Gly															
		210				215					220				
	Gln	Pro	Met	Trp	Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala
Thr															
	225				230					235					
240															
	Tyr	Phe	Trp	Pro	Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro
Ser															
			245						250				255		
	Ile	Tyr	Met	Pro	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile
Ser															
			260					265				270			
	Thr	Leu	Leu	Lys	Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg
Phe															
		275				280					285				
	Tyr	Thr	Met	Tyr	Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly
Gly															
		290			295						300				
	Pro	Val	Ser	Ala	Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His
Ala															
	305			310						315					
320															
	Phe	Gly	Met	Leu	Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn
Cys															
			325					330				335			
	Val	Asn	Ile	Ile	Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr
Cys															
		340						345				350			
	Asn	Lys	Met	Glu	Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe
Phe															

			355				360				365				
	Tyr	Met	Tyr	Glu	Gly	Pro	Ala	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile
Pro															
		370					375					380			
	His	Asp	Phe	Phe	Ser	Phe	Asn	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu
Ser															
	385					390					395				
400															
	Cys	Arg	Lys	Pro	Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp
Leu															
				405						410				415	
	Pro	Lys	Arg	Leu	His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val
His															
			420					425					430		
	Leu	Phe	Val	Asp	Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn
Thr															
		435					440					445			
	Asn	Cys	Gly	Gly	Gly	Asn	His	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser
Met															
		450					455					460			
	Glu	Ala	Ile	Phe	Leu	Ala	His	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr
Glu															
	465					470					475				
480															
	Val	Glu	Pro	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp
Leu															
			485					490				495			
	Leu	Arg	Ile	Gln	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu
Asn															
			500					505				510			
	His	Leu	Leu	Lys	Val	Pro	Phe	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu
Val															
		515						520				525			
	Ser	Lys	Phe	Ser	Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu
Ser															
		530					535					540			
	Leu	Asp	Cys	Phe	Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu
Gln															
	545					550					555				
560															
	Val	Asn	Gln	Met	Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr
Val															
			565					570					575		
	Lys	Val	Asn	Leu	Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn
Val															
			580					585					590		
	Asp	His	Cys	Leu	Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly
Lys															
		595					600					605			
	Ala	Met	Arg	Met	Pro	Met	Trp	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu
Gly															
		610					615					620			
	Asp	Thr	Ser	Pro	Leu	Pro	Pro	Thr	Val	Pro	Asp	Cys	Leu	Arg	Ala
Asp															
	625					630					635				
640															

	Val	Arg	Val	Pro	Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu
Ala															
					645					650					655
	Asp	Lys	Asn	Ile	Thr	His	Gly	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn
Arg															
				660					665					670	
	Thr	Ser	Asp	Ser	Gln	Tyr	Asp	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val
Pro															
			675					680					685		
	Met	Tyr	Glu	Glu	Phe	Arg	Lys	Met	Trp	Asp	Tyr	Phe	His	Ser	Val
Leu															
		690					695					700			
	Leu	Ile	Lys	His	Ala	Thr	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser
Gly															
	705					710						715			
720															
	Pro	Ile	Phe	Asp	Tyr	Asn	Tyr	Asp	Gly	His	Phe	Asp	Ala	Pro	Asp
Glu															
				725					730					735	
	Ile	Thr	Lys	His	Leu	Ala	Asn	Thr	Asp	Val	Pro	Ile	Pro	Thr	His
Tyr															
			740					745					750		
	Phe	Val	Val	Leu	Thr	Ser	Cys	Lys	Asn	Lys	Ser	His	Thr	Pro	Glu
Asn															
		755					760					765			
	Cys	Pro	Gly	Trp	Leu	Asp	Val	Leu	Pro	Phe	Ile	Ile	Pro	His	Arg
Pro															
		770				775					780				
	Thr	Asn	Val	Glu	Ser	Cys	Pro	Glu	Gly	Lys	Pro	Glu	Ala	Leu	Trp
Val															
	785				790						795				
800															
	Glu	Glu	Arg	Phe	Thr	Ala	His	Ile	Ala	Arg	Val	Arg	Asp	Val	Glu
Leu															
				805				810					815		
	Leu	Thr	Gly	Leu	Asp	Phe	Tyr	Gln	Asp	Lys	Val	Gln	Pro	Val	Ser
Glu															
			820					825					830		
	Ile	Leu	Gln	Leu	Lys	Thr	Tyr	Leu	Pro	Thr	Phe	Glu	<u>Thr</u>	<u>Thr</u>	<u>Ile</u>
Asp															
		835					840					845			
	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
Gly															
		850				855					860				
	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
Ile															
	865				870						875				
880															
	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
Glu															
				885				890					895		
	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
His															
			900				905					910			
	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
Arg															

```

          915          920          925
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
Lys
          930          935          940
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
Glu
945          950          955
960
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
Tyr
          965          970          975
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
Leu
          980          985          990
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
Trp
          995          1000          1005
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
1010          1015          1020
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
1025          1030          1035
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
1040          1045          1050
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
1055          1060          1065
Ser Leu Ser Pro Gly Lys
1070

```

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP33; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 15- ENPP5-NPP3-Albumin sequence

```

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu
Ser
1          5          10          15
Leu Ser Thr Thr Phe Ser**Lys Gln Gly Ser Cys Arg Lys Lys Cys
Phe
          20          25          30
Asp Ala Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala
Cys
          35          40          45
Lys Asp Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val
Glu
          50          55          60
Ser Thr Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg
Leu
          65          70          75          80
Glu Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys
Asp

```

					85					90					95
	Cys	Cys	Ala	Asp	Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp
Leu															
					100				105					110	
	Glu	Glu	Asn	Cys	Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly
Phe															
					115				120				125		
	Asp	Leu	Pro	Pro	Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala
Glu															
		130						135				140			
	Tyr	Leu	Tyr	Thr	Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu
Lys															
	145					150					155				
160															
	Thr	Cys	Gly	Ile	His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr
Lys															
					165				170					175	
	Thr	Phe	Pro	Asn	His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu
Ser															
					180				185				190		
	His	Gly	Ile	Ile	Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys
Asn															
		195						200				205			
	Phe	Ser	Leu	Ser	Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His
Gly															
		210						215				220			
	Gln	Pro	Met	Trp	Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala
Thr															
	225					230					235				
240															
	Tyr	Phe	Trp	Pro	Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro
Ser															
					245				250				255		
	Ile	Tyr	Met	Pro	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile
Ser															
					260				265				270		
	Thr	Leu	Leu	Lys	Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg
Phe															
		275						280				285			
	Tyr	Thr	Met	Tyr	Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly
Gly															
		290						295				300			
	Pro	Val	Ser	Ala	Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His
Ala															
	305					310					315				
320															
	Phe	Gly	Met	Leu	Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn
Cys															
					325				330				335		
	Val	Asn	Ile	Ile	Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr
Cys															
					340				345				350		
	Asn	Lys	Met	Glu	Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe
Phe															
					355				360				365		

Tyr Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile
 Pro
 370 375 380
 His Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu
 Ser
 385 390 395
 400
 Cys Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp
 Leu
 405 410 415
 Pro Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val
 His
 420 425 430
 Leu Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn
 Thr
 435 440 445
 Asn Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser
 Met
 450 455 460
 Glu Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr
 Glu
 465 470 475
 480
 Val Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp
 Leu
 485 490 495
 Leu Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu
 Asn
 500 505 510
 His Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu
 Val
 515 520 525
 Ser Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu
 Ser
 530 535 540
 Leu Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu
 Gln
 545 550 555
 560
 Val Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr
 Val
 565 570 575
 Lys Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn
 Val
 580 585 590
 Asp His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly
 Lys
 595 600 605
 Ala Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu
 Gly
 610 615 620
 Asp Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala
 Asp
 625 630 635
 640

	Val	Arg	Val	Pro	Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu
Ala															
					645					650					655
	Asp	Lys	Asn	Ile	Thr	His	Gly	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn
Arg															
				660						665					670
	Thr	Ser	Asp	Ser	Gln	Tyr	Asp	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val
Pro															
			675						680					685	
	Met	Tyr	Glu	Glu	Phe	Arg	Lys	Met	Trp	Asp	Tyr	Phe	His	Ser	Val
Leu															
		690						695				700			
	Leu	Ile	Lys	His	Ala	Thr	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser
Gly															
	705						710					715			
720															
	Pro	Ile	Phe	Asp	Tyr	Asn	Tyr	Asp	Gly	His	Phe	Asp	Ala	Pro	Asp
Glu															
					725					730					735
	Ile	Thr	Lys	His	Leu	Ala	Asn	Thr	Asp	Val	Pro	Ile	Pro	Thr	His
Tyr															
				740					745					750	
	Phe	Val	Val	Leu	Thr	Ser	Cys	Lys	Asn	Lys	Ser	His	Thr	Pro	Glu
Asn															
			755						760				765		
	Cys	Pro	Gly	Trp	Leu	Asp	Val	Leu	Pro	Phe	Ile	Ile	Pro	His	Arg
Pro															
		770						775				780			
	Thr	Asn	Val	Glu	Ser	Cys	Pro	Glu	Gly	Lys	Pro	Glu	Ala	Leu	Trp
Val															
	785						790					795			
800															
	Glu	Glu	Arg	Phe	Thr	Ala	His	Ile	Ala	Arg	Val	Arg	Asp	Val	Glu
Leu															
					805					810					815
	Leu	Thr	Gly	Leu	Asp	Phe	Tyr	Gln	Asp	Lys	Val	Gln	Pro	Val	Ser
Glu															
				820					825					830	
	Ile	Leu	Gln	Leu	Lys	Thr	Tyr	Leu	Pro	Thr	Phe	Glu	<u>Thr</u>	<u>Thr</u>	<u>Ile</u>
Gly															
				835					840					845	
	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Met	Lys
Trp															
		850						855				860			
	Val	Thr	Phe	Leu	Leu	Leu	Leu	Phe	Val	Ser	Gly	Ser	Ala	Phe	Ser
Arg															
	865						870					875			
880															
	Gly	Val	Phe	Arg	Arg	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg
Tyr															
					885				890					895	
	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala
Phe															
				900					905					910	
	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu
Val															

	915		920		925	
	Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser					
Ala						
	930		935		940	
	Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu					
Cys						
	945		950		955	
960						
	Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys					
Cys						
		965		970		975
	Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys					
Asp						
		980		985		990
	Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala					
Met						
	995		1000		1005	
	Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr					
	1010		1015		1020	
	Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu					
	1025		1030		1035	
	Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys					
	1040		1045		1050	
	Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp					
	1055		1060		1065	
	Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met					
	1070		1075		1080	
	Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala					
	1085		1090		1095	
	Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe					
	1100		1105		1110	
	Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys					
	1115		1120		1125	
	Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala					
	1130		1135		1140	
	Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser					
	1145		1150		1155	
	Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His					
	1160		1165		1170	
	Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro					
	1175		1180		1185	
	Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn					
	1190		1195		1200	
	Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu					
	1205		1210		1215	
	Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg					
	1220		1225		1230	
	Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu					
	1235		1240		1245	
	Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln					
	1250		1255		1260	
	Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp					
	1265		1270		1275	
	Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu					
	1280		1285		1290	
	Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu					

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

[illegible]

	Met	Thr	Ser	Lys	Phe	Leu	Leu	Val	Ser	Phe	Ile	Leu	Ala	Ala	Leu
Ser															
	1				5					10					15
Val	Leu	Ser	Thr	Thr	Phe	Ser**	<u>Gly</u>	<u>Leu</u>	<u>Lys</u>	Pro	Ser	Cys	Ala	Lys	Glu
				20					25					30	
Arg	Lys	Ser	Cys	Lys	Gly	Arg	Cys	Phe	Glu	Arg	Thr	Phe	Gly	Asn	Cys
			35					40					45		
Gln	Cys	Asp	Ala	Ala	Cys	Val	Glu	Leu	Gly	Asn	Cys	Cys	Leu	Asp	Tyr
		50					55					60			
Arg	Glu	Thr	Cys	Ile	Glu	Pro	Glu	His	Ile	Trp	Thr	Cys	Asn	Lys	Phe
	65					70					75				80

	Cys	Gly	Glu	Lys	Arg	Leu	Thr	Arg	Ser	Leu	Cys	Ala	Cys	Ser	Asp
Asp															
					85					90					95
	Cys	Lys	Asp	Lys	Gly	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys
Gln															
				100					105					110	
	Gly	Glu	Lys	Ser	Trp	Val	Glu	Glu	Pro	Cys	Glu	Ser	Ile	Asn	Glu
Pro															
			115					120					125		
	Gln	Cys	Pro	Ala	Gly	Phe	Glu	Thr	Pro	Pro	Thr	Leu	Leu	Phe	Ser
Leu															
		130					135					140			
	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu
Pro															
	145					150					155				
160															
	Val	Ile	Ser	Lys	Leu	Lys	Lys	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met
Arg															
				165					170					175	
	Pro	Val	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val
Thr															
			180					185					190		
	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr
Asp															
		195					200					205			
	Pro	Lys	Met	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe
Asn															
		210				215					220				
	Pro	Glu	Trp	Tyr	Lys	Gly	Glu	Pro	Ile	Trp	Val	Thr	Ala	Lys	Tyr
Gln															
	225				230					235					
240															
	Gly	Leu	Lys	Ser	Gly	Thr	Phe	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu
Ile															
			245					250					255		
	Asn	Gly	Ile	Phe	Pro	Asp	Ile	Tyr	Lys	Met	Tyr	Asn	Gly	Ser	Val
Pro															
		260					265					270			
	Phe	Glu	Glu	Arg	Ile	Leu	Ala	Val	Leu	Gln	Trp	Leu	Gln	Leu	Pro
Lys															
		275				280					285				
	Asp	Glu	Arg	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp
Ser															
		290			295						300				
	Ser	Gly	His	Ser	Tyr	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala
Leu															
	305				310					315					
320															
	Gln	Arg	Val	Asp	Gly	Met	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys
Glu															
			325				330						335		
	Leu	Asn	Leu	His	Arg	Cys	Leu	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His
Gly															
		340				345					350				
	Met	Glu	Gln	Gly	Ser	Cys	Lys	Lys	Tyr	Ile	Tyr	Leu	Asn	Lys	Tyr
Leu															

			355					360				365			
	Gly	Asp	Val	Lys	Asn	Ile	Lys	Val	Ile	Tyr	Gly	Pro	Ala	Ala	Arg
Leu															
		370					375					380			
	Arg	Pro	Ser	Asp	Val	Pro	Asp	Lys	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu
Gly															
	385					390					395				
400															
	Ile	Ala	Arg	Asn	Leu	Ser	Cys	Arg	Glu	Pro	Asn	Gln	His	Phe	Lys
Pro															
				405					410					415	
	Tyr	Leu	Lys	His	Phe	Leu	Pro	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser
Asp															
			420					425					430		
	Arg	Ile	Glu	Pro	Leu	Thr	Phe	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu
Ala															
		435					440					445			
	Leu	Asn	Pro	Ser	Glu	Arg	Lys	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly
Ser															
	450					455				460					
	Asp	Asn	Val	Phe	Ser	Asn	Met	Gln	Ala	Leu	Phe	Val	Gly	Tyr	Gly
Pro															
	465					470				475					
480															
	Gly	Phe	Lys	His	Gly	Ile	Glu	Ala	Asp	Thr	Phe	Glu	Asn	Ile	Glu
Val															
				485				490					495		
	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu	Asn	Leu	Thr	Pro	Ala	Pro	Asn
Asn															
			500				505					510			
	Gly	Thr	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Asn	Pro	Val	Tyr
Thr															
		515				520					525				
	Pro	Lys	His	Pro	Lys	Glu	Val	His	Pro	Leu	Val	Gln	Cys	Pro	Phe
Thr															
		530				535					540				
	Arg	Asn	Pro	Arg	Asp	Asn	Leu	Gly	Cys	Ser	Cys	Asn	Pro	Ser	Ile
Leu															
	545					550					555				
560															
	Pro	Ile	Glu	Asp	Phe	Gln	Thr	Gln	Phe	Asn	Leu	Thr	Val	Ala	Glu
Glu															
				565				570					575		
	Lys	Ile	Ile	Lys	His	Glu	Thr	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val
Leu															
			580				585					590			
	Gln	Lys	Glu	Asn	Thr	Ile	Cys	Leu	Leu	Ser	Gln	His	Gln	Phe	Met
Ser															
		595				600					605				
	Gly	Tyr	Ser	Gln	Asp	Ile	Leu	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr
Val															
		610				615					620				
	Asp	Arg	Asn	Asp	Ser	Phe	Ser	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu
Tyr															
	625					630					635				
640															

Tyr Gln Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe
 645 650 655
 Leu Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln
 660 665 670
 Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr
 675 680 685
 His Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe
 690 695 700
 Val Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn
 705 710 715
 720 Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp
 Ser 725 730 735
 Ile Leu Glu Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu
 740 745 750
 Thr Leu Ile Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp
 755 760 765
 Ile Ser Gln Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe
 770 775 780
 His Leu Pro His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys
 785 790 795
 800 Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg
 Ile 805 810 815
 Lys Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg
 820 825 830
 Phe Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr
 835 840 845
 Pro Ser Gln Glu Asp Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 850 855 860
 Lys Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 865 870 875
 880 Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 885 890 895
 Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 900 905 910
 Tyr Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln

```

          915          920          925
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
Asp
          930          935          940
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
Leu
          945          950          955
960
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
Arg
          965          970          975
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
Lys
          980          985          990
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
Asp
          995          1000          1005
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
          1010          1015          1020
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
          1025          1030          1035
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
          1040          1045          1050
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
          1055          1060          1065
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
          1070          1075

```

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 18 - ENPP71-Fc Amino Acid Sequence

```

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
Leu
1          5          10          15
Ala Pro Gly Ala Gly Ala**Gly Leu Lys Pro Ser Cys Ala Lys Glu
Val
          20          25          30
Lys Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys
Arg
          35          40          45
Cys Asp Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr
Gln
          50          55          60
Glu Thr Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe
Arg
          65          70          75          80
Cys Gly Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp
Asp
          85          90          95

```

	Cys	Lys	Asp	Lys	Gly	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys
Gln															
				100					105					110	
	Gly	Glu	Lys	Ser	Trp	Val	Glu	Glu	Pro	Cys	Glu	Ser	Ile	Asn	Glu
Pro															
			115						120					125	
	Gln	Cys	Pro	Ala	Gly	Phe	Glu	Thr	Pro	Pro	Thr	Leu	Leu	Phe	Ser
Leu															
		130							135				140		
	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu
Pro															
	145							150					155		
160															
	Val	Ile	Ser	Lys	Leu	Lys	Lys	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met
Arg															
					165					170					175
	Pro	Val	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val
Thr															
				180					185					190	
	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr
Asp															
		195							200				205		
	Pro	Lys	Met	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe
Asn															
		210							215				220		
	Pro	Glu	Trp	Tyr	Lys	Gly	Glu	Pro	Ile	Trp	Val	Thr	Ala	Lys	Tyr
Gln															
	225								230				235		
240															
	Gly	Leu	Lys	Ser	Gly	Thr	Phe	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu
Ile															
					245					250					255
	Asn	Gly	Ile	Phe	Pro	Asp	Ile	Tyr	Lys	Met	Tyr	Asn	Gly	Ser	Val
Pro															
				260						265				270	
	Phe	Glu	Glu	Arg	Ile	Leu	Ala	Val	Leu	Gln	Trp	Leu	Gln	Leu	Pro
Lys															
			275							280				285	
	Asp	Glu	Arg	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp
Ser															
		290								295			300		
	Ser	Gly	His	Ser	Tyr	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala
Leu															
	305												315		
320															
	Gln	Arg	Val	Asp	Gly	Met	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys
Glu															
					325					330					335
	Leu	Asn	Leu	His	Arg	Cys	Leu	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His
Gly															
				340						345				350	
	Met	Glu	Gln	Gly	Ser	Cys	Lys	Lys	Tyr	Ile	Tyr	Leu	Asn	Lys	Tyr
Leu															
			355							360				365	
	Gly	Asp	Val	Lys	Asn	Ile	Lys	Val	Ile	Tyr	Gly	Pro	Ala	Ala	Arg
Leu															

	370		375		380
	Arg Pro Ser Asp Val	Pro Asp Lys Tyr Tyr	Ser Phe Asn Tyr Glu		
Gly	385	390	395		
400	Ile Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys				
Pro		405	410	415	
	Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser				
Asp		420	425	430	
	Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu				
Ala		435	440	445	
	Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly				
Ser		450	455	460	
	Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly				
Pro	465	470	475		
480	Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu				
Val		485	490	495	
	Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn				
Asn		500	505	510	
	Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr				
Thr		515	520	525	
	Pro Lys His Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe				
Thr		530	535	540	
	Arg Asn Pro Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile				
Leu	545	550	555		
560	Pro Ile Glu Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu				
Glu		565	570	575	
	Lys Ile Ile Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val				
Leu		580	585	590	
	Gln Lys Glu Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met				
Ser		595	600	605	
	Gly Tyr Ser Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr				
Val		610	615	620	
	Asp Arg Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu				
Tyr	625	630	635		
640	Gln Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe				
Tyr		645	650	655	

Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln
 Leu
 660 665 670
 Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr
 Asn
 675 680 685
 Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe
 His
 690 695 700
 Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn
 Val
 705 710 715
 720
 Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp
 Ser
 725 730 735
 Leu Glu Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu
 Ile
 740 745 750
 Leu Ile Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp
 Thr
 755 760 765
 Ser Gln Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe
 Ile
 770 775 780
 Leu Pro His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys
 His
 785 790 795
 800
 Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg
 Ile
 805 810 815
 Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg
 Lys
 820 825 830
 Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr
 Phe
 835 840 845
 Ser Gln Glu Asp Leu Ile Asn **Asp Lys Thr His Thr Cys Pro Pro**
Cys
 850 855 860
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
Pro
 865 870 875
 880
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
Cys
 885 890 895
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
Trp
 900 905 910
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
Glu
 915 920 925
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
Leu

	930		935		940										
	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser
Asn															
	945				950						955				
960															
	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys
Gly															
				965						970					975
	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu
Glu															
				980						985					990
	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe
Tyr															
				995						1000					1005
	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu
	1010						1015					1020			
	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser
	1025						1030					1035			
	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln
	1040						1045					1050			
	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His
	1055						1060					1065			
	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	
	1070						1075					1080			

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 19 - ENPP71 (lacking NPP1 N-Terminus GLK) Amino Acid Sequence:

	Met	Arg	Gly	Pro	Ala	Val	Leu	Leu	Thr	Val	Ala	Leu	Ala	Thr	Leu
Leu															
	1			5					10					15	
	Ala	Pro	Gly	Ala	Gly	Ala	**	Pro	Ser	Cys	Ala	Lys	Glu	Val	Lys
Cys															
				20					25					30	
	Lys	Gly	Arg	Cys	Phe	Glu	Arg	Thr	Phe	Gly	Asn	Cys	Arg	Cys	Asp
Ala															
				35					40					45	
	Ala	Cys	Val	Glu	Leu	Gly	Asn	Cys	Cys	Leu	Asp	Tyr	Gln	Glu	Thr
Cys															
				50					55					60	
	Ile	Glu	Pro	Glu	His	Ile	Trp	Thr	Cys	Asn	Lys	Phe	Arg	Cys	Gly
Glu															
	65					70					75				80
	Lys	Arg	Leu	Thr	Arg	Ser	Leu	Cys	Ala	Cys	Ser	Asp	Asp	Cys	Lys
Asp															
				85					90					95	
	Lys	Gly	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys	Gln	Gly	Glu
Lys															
				100					105					110	

	Ser	Trp	Val	Glu	Glu	Pro	Cys	Glu	Ser	Ile	Asn	Glu	Pro	Gln	Cys
Pro															
			115					120					125		
	Ala	Gly	Phe	Glu	Thr	Pro	Pro	Thr	Leu	Leu	Phe	Ser	Leu	Asp	Gly
Phe															
		130					135					140			
	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu	Pro	Val	Ile
Ser															
	145					150					155				
160															
	Lys	Leu	Lys	Lys	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met	Arg	Pro	Val
Tyr															
					165					170				175	
	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val	Thr	Gly	Leu
Tyr															
			180					185					190		
	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr	Asp	Pro	Lys
Met															
		195					200					205			
	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe	Asn	Pro	Glu
Trp															
		210					215					220			
	Tyr	Lys	Gly	Glu	Pro	Ile	Trp	Val	Thr	Ala	Lys	Tyr	Gln	Gly	Leu
Lys															
	225					230					235				
240															
	Ser	Gly	Thr	Phe	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu	Ile	Asn	Gly
Ile															
				245					250					255	
	Phe	Pro	Asp	Ile	Tyr	Lys	Met	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu
Glu															
			260					265					270		
	Arg	Ile	Leu	Ala	Val	Leu	Gln	Trp	Leu	Gln	Leu	Pro	Lys	Asp	Glu
Arg															
		275					280					285			
	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp	Ser	Ser	Gly
His															
		290					295					300			
	Ser	Tyr	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala	Leu	Gln	Arg
Val															
	305					310					315				
320															
	Asp	Gly	Met	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys	Glu	Leu	Asn
Leu															
				325					330					335	
	His	Arg	Cys	Leu	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His	Gly	Met	Glu
Gln															
			340					345					350		
	Gly	Ser	Cys	Lys	Lys	Tyr	Ile	Tyr	Leu	Asn	Lys	Tyr	Leu	Gly	Asp
Val															
		355					360					365			
	Lys	Asn	Ile	Lys	Val	Ile	Tyr	Gly	Pro	Ala	Ala	Arg	Leu	Arg	Pro
Ser															
		370					375					380			
	Asp	Val	Pro	Asp	Lys	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu	Gly	Ile	Ala
Arg															

	385		390		395										
400	Asn	Leu	Ser	Cys	Arg	Glu	Pro	Asn	Gln	His	Phe	Lys	Pro	Tyr	Leu
Lys															
				405				410						415	
Glu	His	Phe	Leu	Pro	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp	Arg	Ile
				420				425						430	
Pro	Pro	Leu	Thr	Phe	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala	Leu	Asn
			435					440					445		
Val	Ser	Glu	Arg	Lys	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser	Asp	Asn
		450					455					460			
Lys	Phe	Ser	Asn	Met	Gln	Ala	Leu	Phe	Val	Gly	Tyr	Gly	Pro	Gly	Phe
	465						470					475			
480	His	Gly	Ile	Glu	Ala	Asp	Thr	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn
Leu															
				485				490						495	
His	Met	Cys	Asp	Leu	Leu	Asn	Leu	Thr	Pro	Ala	Pro	Asn	Asn	Gly	Thr
				500				505						510	
His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Asn	Pro	Val	Tyr	Thr	Pro	Lys
			515					520					525		
Pro	Pro	Lys	Glu	Val	His	Pro	Leu	Val	Gln	Cys	Pro	Phe	Thr	Arg	Asn
		530					535					540			
Glu	Arg	Asp	Asn	Leu	Gly	Cys	Ser	Cys	Asn	Pro	Ser	Ile	Leu	Pro	Ile
	545						550					555			
560	Asp	Phe	Gln	Thr	Gln	Phe	Asn	Leu	Thr	Val	Ala	Glu	Glu	Lys	Ile
Ile															
				565				570						575	
Glu	Lys	His	Glu	Thr	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys
				580				585						590	
Ser	Asn	Thr	Ile	Cys	Leu	Leu	Ser	Gln	His	Gln	Phe	Met	Ser	Gly	Tyr
			595					600					605		
Asn	Gln	Asp	Ile	Leu	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr	Val	Asp	Arg
		610					615					620			
Phe	Asp	Ser	Phe	Ser	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln	Asp
	625						630					635			
640	Arg	Ile	Pro	Leu	Ser	Pro	Val	His	Lys	Cys	Ser	Phe	Tyr	Lys	Asn
Asn															
				645				650						655	
Asn	Thr	Lys	Val	Ser	Tyr	Gly	Phe	Leu	Ser	Pro	Pro	Gln	Leu	Asn	Lys
				660				665						670	

Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val
 Pro
 675 680 685
 Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr
 Leu
 690 695 700
 Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser
 Gly
 705 710 715
 720
 Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu
 Asn
 725 730 735
 Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile
 Pro
 740 745 750
 Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln
 Thr
 755 760 765
 Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro
 His
 770 775 780
 Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser
 Ser
 785 790 795
 800
 Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp
 Val
 805 810 815
 Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro
 Val
 820 825 830
 Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln
Glu
 835 840 845
Asp

Singly underlined: signal peptide sequence; double-underlined:
 beginning and end of NPP3; ** = cleavage position at the signal
 peptide sequence

SEQ. ID NO: 20 -ENPP71 (lacking NPP1 N-Terminus GLK) - Fc
Amino Acid Sequence:

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
Leu
 1 5 10 15
Ala Pro Gly Ala Gly Ala**Pro Ser Cys Ala Lys Glu Val Lys Ser
 Cys
 20 25 30
 Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp
 Ala
 35 40 45

	Ala	Cys	Val	Glu	Leu	Gly	Asn	Cys	Cys	Leu	Asp	Tyr	Gln	Glu	Thr
Cys		50					55				60				
	Ile	Glu	Pro	Glu	His	Ile	Trp	Thr	Cys	Asn	Lys	Phe	Arg	Cys	Gly
Glu		65				70					75				80
	Lys	Arg	Leu	Thr	Arg	Ser	Leu	Cys	Ala	Cys	Ser	Asp	Asp	Cys	Lys
Asp					85					90					95
	Lys	Gly	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys	Gln	Gly	Glu
Lys				100					105				110		
	Ser	Trp	Val	Glu	Glu	Pro	Cys	Glu	Ser	Ile	Asn	Glu	Pro	Gln	Cys
Pro				115				120					125		
	Ala	Gly	Phe	Glu	Thr	Pro	Pro	Thr	Leu	Leu	Phe	Ser	Leu	Asp	Gly
Phe		130					135				140				
	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu	Pro	Val	Ile
Ser		145				150					155				
160															
	Lys	Leu	Lys	Lys	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met	Arg	Pro	Val
Tyr					165				170				175		
	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val	Thr	Gly	Leu
Tyr				180				185				190			
	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr	Asp	Pro	Lys
Met				195				200				205			
	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe	Asn	Pro	Glu
Trp				210				215				220			
	Tyr	Lys	Gly	Glu	Pro	Ile	Trp	Val	Thr	Ala	Lys	Tyr	Gln	Gly	Leu
Lys															
240		225				230					235				
	Ser	Gly	Thr	Phe	Phe	Trp	Pro	Gly	Ser	Asp	Val	Glu	Ile	Asn	Gly
Ile															
				245					250				255		
	Phe	Pro	Asp	Ile	Tyr	Lys	Met	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu
Glu				260					265				270		
	Arg	Ile	Leu	Ala	Val	Leu	Gln	Trp	Leu	Gln	Leu	Pro	Lys	Asp	Glu
Arg															
		275					280					285			
	Pro	His	Phe	Tyr	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp	Ser	Ser	Gly
His															
		290					295					300			
	Ser	Tyr	Gly	Pro	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala	Leu	Gln	Arg
Val															
320		305				310					315				
	Asp	Gly	Met	Val	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys	Glu	Leu	Asn
Leu															

82

Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg
 Asn
 610 615 620
 Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp
 Phe
 625 630 635
 640
 Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn
 Asn
 645 650 655
 Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys
 Asn
 660 665 670
 Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val
 Pro
 675 680 685
 Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr
 Leu
 690 695 700
 Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser
 Gly
 705 710 715
 720
 Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu
 Asn
 725 730 735
 Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile
 Pro
 740 745 750
 Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln
 Thr
 755 760 765
 Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro
 His
 770 775 780
 Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser
 Ser
 785 790 795
 800
 Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp
 Val
 805 810 815
 Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro
 Val
 820 825 830
 Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln
Glu
 835 840 845
Asp Leu Ile Asn Asp **Lys Thr His Thr Cys Pro Pro Cys Pro Ala**
Pro
 850 855 860
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
Lys
 865 870 875
 880

Val Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 885 890 895
 Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 900 905 910
 Tyr Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 915 920 925
 Asp Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 930 935 940
 Leu Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 945 950 955
 960 Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 Arg
 965 970 975
 Lys Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
 980 985 990
 Asp Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 995 1000 1005
 Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 1010 1015 1020
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
 1025 1030 1035
 Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 1040 1045 1050
 Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 1055 1060 1065
 Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 1070 1075

Singly underlined: signal peptide sequence; double-underlined:
 beginning and end of NPP1; ** = cleavage position at the signal
 peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 21 - ENPP71 (lacking NPP1 N-Terminus GLK) - ALB
Amino Acid Sequence

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
1 5 10 15
Ala Pro Gly Ala Gly Ala**Pro Ser Cys Ala Lys Glu Val Lys Ser
 Cys
 20 25 30
 Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp
 Ala
 35 40 45
 Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr
 Cys
 50 55 60

Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly
 Glu 65 70 75 80
 Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys
 Asp 85 90 95
 Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu
 Lys 100 105 110
 Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys
 Pro 115 120 125
 Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly
 Phe 130 135 140
 Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile
 Ser 145 150 155
 160
 Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val
 Tyr 165 170 175
 Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu
 Tyr 180 185 190
 Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys
 Met 195 200 205
 Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu
 Trp 210 215 220
 Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu
 Lys 225 230 235
 240
 Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly
 Ile 245 250 255
 Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu
 Glu 260 265 270
 Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu
 Arg 275 280 285
 Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly
 His 290 295 300
 Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg
 Val 305 310 315
 320
 Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn
 Leu 325 330 335
 His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu
 Gln

86

Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp
 Phe 625 630 635
 640 Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn
 Asn 645 650 655
 Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys
 Asn 660 665 670
 Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val
 Pro 675 680 685
 Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr
 Leu 690 695 700
 Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser
 Gly 705 710 715
 720 Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu
 Asn 725 730 735
 Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile
 Pro 740 745 750
 Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln
 Thr 755 760 765
 Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro
 His 770 775 780
 Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser
 Ser 785 790 795
 800 Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp
 Val 805 810 815
 Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro
 Val 820 825 830
 Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln
 Glu 835 840 845
 Asp Arg Ser Gly Ser Gly Gly Ser **Met Lys Trp Val Thr Phe Leu**
 Leu 850 855 860
Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg
 Arg 865 870 875
 880 Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly
 Glu 885 890 895

	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe	Ser	Gln	Tyr	Leu
Gln															
				900					905					910	
	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu	Val	Gln	Glu	Val	Thr
Asp															
				915				920					925		
	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp
Lys															
				930				935					940		
	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn
Leu															
				945			950					955			
960															
	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys	Cys	Thr	Lys	Gln	Glu
Pro															
							965			970				975	
	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Ser
Leu															
							980			985				990	
	Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe
Lys															
				995				1000					1005		
	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala
	1010						1015					1020			
	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala
	1025						1030					1035			
	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp
	1040						1045					1050			
	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys
	1055						1060					1065			
	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met
	1070						1075					1080			
	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
	1085						1090					1095			
	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys
	1100						1105					1110			
	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly
	1115						1120					1125			
	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr
	1130						1135					1140			
	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys
	1145						1150					1155			
	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val
	1160						1165					1170			
	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp
	1175						1180					1185			
	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys
	1190						1195					1200			
	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His
	1205						1210					1215			
	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr
	1220						1225					1230			
	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
	1235						1240					1245			
	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu
	1250						1255					1260			

Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu
	1265					1270					1275			
Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln
	1280					1285					1290			
Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg
	1295					1300					1305			
Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp
	1310					1315					1320			
Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn
	1325					1330					1335			
Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val
	1340					1345					1350			
Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe
	1355					1360					1365			
Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys
	1370					1375					1380			
Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu
	1385					1390					1395			
Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val
	1400					1405					1410			
Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met
	1415					1420					1425			
Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp
	1430					1435					1440			
Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg
	1445					1450					1455			
Cys	Lys	Asp	Ala	Leu	Ala	Arg	Ser	Trp	Ser	His	Pro	Gln	Phe	Glu
	1460					1465					1470			

Lys

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 22 - ENPP7-NPP3-Fc sequence:

	Met	Arg	Gly	Pro	Ala	Val	Leu	Leu	Thr	Val	Ala	Leu	Ala	Thr	Leu
Leu															
	1				5				10					15	
	Ala	Pro	Gly	Ala	**	Lys	Gln	Gly	Ser	Cys	Arg	Lys	Lys	Cys	Phe
Ala															Asp
				20					25					30	
	Ser	Phe	Arg	Gly	Leu	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys
Asp															
			35					40				45			
	Arg	Gly	Asp	Cys	Cys	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser
Thr															
		50				55					60				
	Arg	Ile	Trp	Met	Cys	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Arg	Leu	Glu
Ala															
	65				70				75					80	
	Ser	Leu	Cys	Ser	Cys	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys
Cys															

					85					90					95
	Ala	Asp	Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu
Glu															
				100					105					110	
	Asn	Cys	Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp
Leu															
			115					120					125		
	Pro	Pro	Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr
Leu															
		130					135					140			
	Tyr	Thr	Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr
Cys															
	145					150					155				
160															
	Gly	Ile	His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr
Phe															
				165					170					175	
	Pro	Asn	His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His
Gly															
			180					185					190		
	Ile	Ile	Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe
Ser															
		195					200					205			
	Leu	Ser	Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln
Pro															
		210				215					220				
	Met	Trp	Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr
Phe															
	225				230				235						
240															
	Trp	Pro	Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile
Tyr															
			245					250				255			
	Met	Pro	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr
Leu															
			260				265					270			
	Leu	Lys	Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr
Thr															
		275				280						285			
	Met	Tyr	Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro
Val															
		290			295						300				
	Ser	Ala	Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe
Gly															
	305			310					315						
320															
	Met	Leu	Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val
Asn															
			325			330						335			
	Ile	Ile	Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn
Lys															
		340			345						350				
	Met	Glu	Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr
Met															
		355			360						365				

Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His
 Asp 370 375 380
 Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys
 Arg 385 390 395
 400
 Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro
 Lys 405 410 415
 Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu
 Phe 420 425 430
 Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn
 Cys 435 440 445
 Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu
 Ala 450 455 460
 Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val
 Glu 465 470 475
 480
 Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu
 Arg 485 490 495
 Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His
 Leu 500 505 510
 Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser
 Lys 515 520 525
 Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu
 Asp 530 535 540
 Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val
 Asn 545 550 555
 560
 Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys
 Val 565 570 575
 Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp
 His 580 585 590
 Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala
 Met 595 600 605
 Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp
 Thr 610 615 620
 Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val
 Arg 625 630 635
 640

Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp
 Lys
 645 650 655
 Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr
 Ser
 660 665 670
 Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met
 Tyr
 675 680 685
 Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu
 Ile
 690 695 700
 Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro
 Ile
 705 710 715
 720
 Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile
 Thr
 725 730 735
 Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe
 Val
 740 745 750
 Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys
 Pro
 755 760 765
 Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr
 Asn
 770 775 780
 Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu
 Glu
 785 790 795
 800
 Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu
 Thr
 805 810 815
 Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile
 Leu
 820 825 830
 Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile **Asp Lys**
 Thr
 835 840 845
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 Ser
 850 855 860
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 Arg
 865 870 875
 880
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 Pro
 885 890 895
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 Ala
 900 905 910
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 Val

915 920 925
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 Tyr
 930 935 940
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 Thr
 945 950 955
 960
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 Leu
 965 970 975
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 Cys
 980 985 990
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 Ser
 995 1000 1005
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 1010 1015 1020
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 1025 1030 1035
 Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 1040 1045 1050
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 1055 1060 1065
 Ser Pro Gly Lys
 1070

Singly underlined: signal peptide sequence; double-underlined:
 beginning and end of NPP3; ** = cleavage position at the signal
 peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 23 - ENPP71-Albumin

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
 Leu
 1 5 10 15
Ala Pro Gly Ala Gly Leu Lys**Pro Ser Cys Ala Lys Glu Val Lys
 Ser
 20 25 30
 Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys
 Asp
 35 40 45
 Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu
 Thr
 50 55 60
 Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys
 Gly
 65 70 75 80
 Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys
 Lys
 85 90 95
 Asp Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly
 Glu
 100 105 110

Cys Lys Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln
 115 120 125
 Gly Pro Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp
 130 135 140
 Ile Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val
 145 150 155
 160 Ser Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro
 Val
 165 170 175
 Leu Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly
 180 185 190
 Lys Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro
 195 200 205
 Glu Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro
 210 215 220
 Leu Trp Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly
 225 230 235
 240 Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn
 Gly
 245 250 255
 Glu Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe
 260 265 270
 Glu Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp
 275 280 285
 Gly Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser
 290 295 300
 Arg His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln
 305 310 315
 320 Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu
 Asn
 325 330 335
 Glu Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met
 340 345 350
 Asp Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly
 355 360 365
 Pro Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg
 370 375 380
 Ala Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile

	385		390		395										
400	Arg	Asn	Leu	Ser	Cys	Arg	Glu	Pro	Asn	Gln	His	Phe	Lys	Pro	Tyr
Leu															
					405					410					415
	Lys	His	Phe	Leu	Pro	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp	Arg
Ile															
				420					425						430
	Glu	Pro	Leu	Thr	Phe	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala	Leu
Asn															
				435					440					445	
	Pro	Ser	Glu	Arg	Lys	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser	Asp
Asn															
		450					455					460			
	Val	Phe	Ser	Asn	Met	Gln	Ala	Leu	Phe	Val	Gly	Tyr	Gly	Pro	Gly
Phe															
	465					470					475				
480															
	Lys	His	Gly	Ile	Glu	Ala	Asp	Thr	Phe	Glu	Asn	Ile	Glu	Val	Tyr
Asn															
					485				490						495
	Leu	Met	Cys	Asp	Leu	Leu	Asn	Leu	Thr	Pro	Ala	Pro	Asn	Asn	Gly
Thr															
				500					505					510	
	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Asn	Pro	Val	Tyr	Thr	Pro
Lys															
			515				520					525			
	His	Pro	Lys	Glu	Val	His	Pro	Leu	Val	Gln	Cys	Pro	Phe	Thr	Arg
Asn															
		530					535					540			
	Pro	Arg	Asp	Asn	Leu	Gly	Cys	Ser	Cys	Asn	Pro	Ser	Ile	Leu	Pro
Ile															
	545					550					555				
560															
	Glu	Asp	Phe	Gln	Thr	Gln	Phe	Asn	Leu	Thr	Val	Ala	Glu	Glu	Lys
Ile															
				565					570						575
	Ile	Lys	His	Glu	Thr	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val	Leu	Gln
Lys															
				580					585					590	
	Glu	Asn	Thr	Ile	Cys	Leu	Leu	Ser	Gln	His	Gln	Phe	Met	Ser	Gly
Tyr															
			595					600					605		
	Ser	Gln	Asp	Ile	Leu	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr	Val	Asp
Arg															
		610					615					620			
	Asn	Asp	Ser	Phe	Ser	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln
Asp															
	625					630					635				
640															
	Phe	Arg	Ile	Pro	Leu	Ser	Pro	Val	His	Lys	Cys	Ser	Phe	Tyr	Lys
Asn															
				645					650						655
	Asn	Thr	Lys	Val	Ser	Tyr	Gly	Phe	Leu	Ser	Pro	Pro	Gln	Leu	Asn
Lys															
				660					665					670	

	Asn	Ser	Ser	Gly	Ile	Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Thr	Asn	Ile
Val															
			675					680					685		
	Pro	Met	Tyr	Gln	Ser	Phe	Gln	Val	Ile	Trp	Arg	Tyr	Phe	His	Asp
Thr															
		690					695					700			
	Leu	Leu	Arg	Lys	Tyr	Ala	Glu	Glu	Arg	Asn	Gly	Val	Asn	Val	Val
Ser															
	705					710					715				
720															
	Gly	Pro	Val	Phe	Asp	Phe	Asp	Tyr	Asp	Gly	Arg	Cys	Asp	Ser	Leu
Glu															
				725						730				735	
	Asn	Leu	Arg	Gln	Lys	Arg	Arg	Val	Ile	Arg	Asn	Gln	Glu	Ile	Leu
Ile															
			740						745					750	
	Pro	Thr	His	Phe	Phe	Ile	Val	Leu	Thr	Ser	Cys	Lys	Asp	Thr	Ser
Gln															
		755						760				765			
	Thr	Pro	Leu	His	Cys	Glu	Asn	Leu	Asp	Thr	Leu	Ala	Phe	Ile	Leu
Pro															
		770					775				780				
	His	Arg	Thr	Asp	Asn	Ser	Glu	Ser	Cys	Val	His	Gly	Lys	His	Asp
Ser															
	785					790					795				
800															
	Ser	Trp	Val	Glu	Glu	Leu	Leu	Met	Leu	His	Arg	Ala	Arg	Ile	Thr
Asp															
				805					810					815	
	Val	Glu	His	Ile	Thr	Gly	Leu	Ser	Phe	Tyr	Gln	Gln	Arg	Lys	Glu
Pro															
			820						825				830		
	Val	Ser	Asp	Ile	Leu	Lys	Leu	Lys	Thr	His	Leu	Pro	Thr	Phe	Ser
<u>Gln</u>															
		835						840				845			
	<u>Glu Asp</u>	Gly	Gly	Ser	Gly	Gly	Ser	Met	Lys	Trp	Val	Thr	Phe	Leu	
Leu															
		850					855				860				
	Leu	Leu	Phe	Val	Ser	Gly	Ser	Ala	Phe	Ser	Arg	Gly	Val	Phe	Arg
Arg															
	865					870					875				
880															
	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg	Tyr	Asn	Asp	Leu	Gly
Glu															
				885					890					895	
	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe	Ser	Gln	Tyr	Leu
Gln															
			900					905					910		
	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu	Val	Gln	Glu	Val	Thr
Asp															
		915					920				925				
	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp
Lys															
		930				935				940					
	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn
Leu															

97

1340	Thr Lys Cys Cys Ser Gly Ser	1345	Leu Val Glu Arg Arg	1350	Pro Cys Phe
1355	Ser Ala Leu Thr Val Asp Glu	1360	Thr Tyr Val Pro Lys	1365	Glu Phe Lys
1370	Ala Glu Thr Phe Thr Phe His	1375	Ser Asp Ile Cys Thr	1380	Leu
1385		1390		1395	

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 24 - ENPP7-NPP3-Albumin

	<u>Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu</u>																			
<u>Leu</u>	1	5	10	15																
	<u>Ala Pro Gly Ala**Lys Gln Gly</u> Ser Cys Arg Lys Lys Cys Phe Asp																			
Ala																				
	20	25	30																	
	Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys																			
Asp																				
	35	40	45																	
	Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser																			
Thr																				
	50	55	60																	
	Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu Glu																			
Ala																				
	65	70	75	80																
	Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys																			
Cys																				
	85	90	95																	
	Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu																			
Glu																				
	100	105	110																	
	Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp																			
Leu																				
	115	120	125																	
	Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr																			
Leu																				
	130	135	140																	
	Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr																			
Cys																				
	145	150	155																	
160																				
	Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr																			
Phe																				
	165	170	175																	
	Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His																			
Gly																				
	180	185	190																	
	Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe																			
Ser																				

		195					200			205						
	Leu	Ser	Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln	
Pro																
		210					215			220						
	Met	Trp	Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr	
Phe																
	225						230					235				
240																
	Trp	Pro	Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	
Tyr																
					245					250					255	
	Met	Pro	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	
Leu																
				260					265					270		
	Leu	Lys	Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	
Thr																
		275					280					285				
	Met	Tyr	Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	
Val																
		290					295					300				
	Ser	Ala	Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	
Gly																
	305						310					315				
320																
	Met	Leu	Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	
Asn																
					325				330						335	
	Ile	Ile	Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	
Lys																
				340				345				350				
	Met	Glu	Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	
Met																
		355					360					365				
	Tyr	Glu	Gly	Pro	Ala	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	
Asp																
		370					375					380				
	Phe	Phe	Ser	Phe	Asn	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	
Arg																
	385						390					395				
400																
	Lys	Pro	Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	
Lys																
					405				410						415	
	Arg	Leu	His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	
Phe																
				420					425					430		
	Val	Asp	Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	
Cys																
		435					440					445				
	Gly	Gly	Gly	Asn	His	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	
Ala																
		450					455					460				
	Ile	Phe	Leu	Ala	His	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	
Glu																
	465						470					475				
480																

Arg	Pro	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu
				485						490					495
Leu	Ile	Gln	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu	Asn	His
				500						505					510
Lys	Leu	Lys	Val	Pro	Phe	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu	Val	Ser
				515						520					525
Asp	Phe	Ser	Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu
				530						535					540
Asn	Cys	Phe	Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val
				545						550					555
560															
Val	Gln	Met	Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys
His	Asn	Leu	Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp
Met	Cys	Leu	Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala
Thr	Arg	Met	Pro	Met	Trp	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu	Gly	Asp
Arg															
640															
Lys	Val	Pro	Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu	Ala	Asp
Ser	Asn	Ile	Thr	His	Gly	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn	Arg	Thr
Tyr	Asp	Ser	Gln	Tyr	Asp	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val	Pro	Met
Ile	Glu	Glu	Phe	Arg	Lys	Met	Trp	Asp	Tyr	Phe	His	Ser	Val	Leu	Leu
Ile	Lys	His	Ala	Thr	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro
720															
Thr	Phe	Asp	Tyr	Asn	Tyr	Asp	Gly	His	Phe	Asp	Ala	Pro	Asp	Glu	Ile
Val	Lys	His	Leu	Ala	Asn	Thr	Asp	Val	Pro	Ile	Pro	Thr	His	Tyr	Phe
Pro	Val	Leu	Thr	Ser	Cys	Lys	Asn	Lys	Ser	His	Thr	Pro	Glu	Asn	Cys

101

1055	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys
1070	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala
1085	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu
1100	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys
1115	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu
1130	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu
1145	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu
1160	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile
1175	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala
1190	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser
1205	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala
1220	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn
1235	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu
1250	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr
1265	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg
1280	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu
1295	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu
1310	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala
1325	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser
1340	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg
1355	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys
1370	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr
1385	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala
1400	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys
1415	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys
1430	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu
1445	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala						
1460															

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 25 - ENPP7-ENPP3-Albumin

	Met	Arg	Gly	Pro	Ala	Val	Leu	Leu	Thr	Val	Ala	Leu	Ala	Thr	Leu
Leu	1				5					10					15
	Ala	Pro	Gly	Ala	**Lys	Gln	Gly	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp
Ala				20				25					30		
	Ser	Phe	Arg	Gly	Leu	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys
Asp			35				40					45			
	Arg	Gly	Asp	Cys	Cys	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser
Thr		50				55					60				
	Arg	Ile	Trp	Met	Cys	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Arg	Leu	Glu
Ala	65				70				75					80	
	Ser	Leu	Cys	Ser	Cys	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys
Cys				85				90					95		
	Ala	Asp	Tyr	Lys	Ser	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu
Glu				100				105				110			
	Asn	Cys	Asp	Thr	Ala	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp
Leu				115				120				125			
	Pro	Pro	Val	Ile	Leu	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr
Leu															
	130					135					140				
	Tyr	Thr	Trp	Asp	Thr	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr
Cys															
	145				150				155						
160															
	Gly	Ile	His	Ser	Lys	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr
Phe															
				165				170				175			
	Pro	Asn	His	Tyr	Thr	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His
Gly															
			180					185				190			
	Ile	Ile	Asp	Asn	Asn	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe
Ser															
		195						200				205			
	Leu	Ser	Ser	Lys	Glu	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln
Pro															
		210						215				220			
	Met	Trp	Leu	Thr	Ala	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr
Phe															
	225				230						235				
240															

Tyr Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile
 245 250 255
 Leu Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr
 260 265 270
 Thr Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr
 275 280 285
 Val Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro
 290 295 300
 Gly Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe
 305 310 315
 320 Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val
 Asn 325 330 335
 Lys Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn
 340 345 350
 Met Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr
 355 360 365
 Asp Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His
 370 375 380
 Arg Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys
 385 390 395
 400 Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro
 Lys 405 410 415
 Phe Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu
 420 425 430
 Cys Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn
 435 440 445
 Ala Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu
 450 455 460
 Glu Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val
 465 470 475
 480 Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu
 Arg 485 490 495
 Leu Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His
 500 505 510
 Lys Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser

		515				520			525						
	Phe	Ser	Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu
Asp															
		530				535			540						
	Cys	Phe	Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val
Asn															
	545					550			555						
560															
	Gln	Met	Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys
Val															
				565					570					575	
	Asn	Leu	Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp
His															
			580					585					590		
	Cys	Leu	Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala
Met															
		595					600					605			
	Arg	Met	Pro	Met	Trp	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu	Gly	Asp
Thr															
		610				615					620				
	Ser	Pro	Leu	Pro	Pro	Thr	Val	Pro	Asp	Cys	Leu	Arg	Ala	Asp	Val
Arg															
	625					630			635						
640															
	Val	Pro	Pro	Ser	Glu	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu	Ala	Asp
Lys															
				645				650					655		
	Asn	Ile	Thr	His	Gly	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn	Arg	Thr
Ser															
			660					665					670		
	Asp	Ser	Gln	Tyr	Asp	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val	Pro	Met
Tyr															
		675						680					685		
	Glu	Glu	Phe	Arg	Lys	Met	Trp	Asp	Tyr	Phe	His	Ser	Val	Leu	Leu
Ile															
		690						695					700		
	Lys	His	Ala	Thr	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro
Ile															
	705						710						715		
720															
	Phe	Asp	Tyr	Asn	Tyr	Asp	Gly	His	Phe	Asp	Ala	Pro	Asp	Glu	Ile
Thr															
				725					730					735	
	Lys	His	Leu	Ala	Asn	Thr	Asp	Val	Pro	Ile	Pro	Thr	His	Tyr	Phe
Val															
			740					745					750		
	Val	Leu	Thr	Ser	Cys	Lys	Asn	Lys	Ser	His	Thr	Pro	Glu	Asn	Cys
Pro															
		755						760					765		
	Gly	Trp	Leu	Asp	Val	Leu	Pro	Phe	Ile	Ile	Pro	His	Arg	Pro	Thr
Asn															
		770						775					780		
	Val	Glu	Ser	Cys	Pro	Glu	Gly	Lys	Pro	Glu	Ala	Leu	Trp	Val	Glu
Glu															
	785						790						795		
800															

Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu
 Thr
 805 810 815
 Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile
 Leu
 820 825 830
 Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Asp Lys
 Thr
 835 840 845
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 Ser
 850 855 860
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 Arg
 865 870 875
 880
 Thr Pro Glu Val Thr Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 Gly
 885 890 895
 Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val
 Ser
 900 905 910
 Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys
 Ser
 915 920 925
 Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys
 Gly
 930 935 940
 Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr
 Asp
 945 950 955
 960
 Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr
 Cys
 965 970 975
 Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr
 Leu
 980 985 990
 Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr
 Gly
 995 1000 1005
 Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu
 1010 1015 1020
 Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe
 1025 1030 1035
 Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn
 1040 1045 1050
 Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg
 1055 1060 1065
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln
 1070 1075 1080
 Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu
 1085 1090 1095
 Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu
 1100 1105 1110
 Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys

1115	Phe Gly Glu Arg Ala Phe	1120	Lys Ala Trp Ala Val	1125	Ala Arg Leu Ser
1130	Gln Thr Phe Pro Asn Ala	1135	Asp Phe Ala Glu Ile	1140	Thr Lys Leu Ala
1145	Thr Asp Leu Thr Lys Val	1150	Asn Lys Glu Cys Cys	1155	His Gly Asp Leu
1160	Leu Glu Cys Ala Asp Asp	1165	Arg Ala Glu Leu Ala	1170	Lys Tyr Met Cys
1175	Glu Asn Gln Ala Thr Ile	1180	Ser Ser Lys Leu Gln	1185	Thr Cys Cys Asp
1190	Lys Pro Leu Leu Lys Lys	1195	Ala His Cys Leu Ser	1200	Glu Val Glu His
1205	Asp Thr Met Pro Ala Asp	1210	Leu Pro Ala Ile Ala	1215	Ala Asp Phe Val
1220	Glu Asp Gln Glu Val Cys	1225	Lys Asn Tyr Ala Glu	1230	Ala Lys Asp Val
1235	Phe Leu Gly Thr Phe Leu	1240	Tyr Glu Tyr Ser Arg	1245	Arg His Pro Asp
1250	Tyr Ser Val Ser Leu Leu	1255	Leu Arg Leu Ala Lys	1260	Lys Tyr Glu Ala
1265	Thr Leu Glu Lys Cys Cys	1270	Ala Glu Ala Asn Pro	1275	Pro Ala Cys Tyr
1280	Gly Thr Val Leu Ala Glu	1285	Phe Gln Pro Leu Val	1290	Glu Glu Pro Lys
1295	Asn Leu Val Lys Thr Asn	1300	Cys Asp Leu Tyr Glu	1305	Lys Leu Gly Glu
1310	Tyr Gly Phe Gln Asn Ala	1315	Ile Leu Val Arg Tyr	1320	Thr Gln Lys Ala
1325	Pro Gln Val Ser Thr Pro	1330	Thr Leu Val Glu Ala	1335	Ala Arg Asn Leu
1340	Gly Arg Val Gly Thr Lys	1345	Cys Cys Thr Leu Pro	1350	Glu Asp Gln Arg
1355	Leu Pro Cys Val Glu Asp	1360	Tyr Leu Ser Ala Ile	1365	Leu Asn Arg Val
1370	Cys Leu Leu His Glu Lys	1375	Thr Pro Val Ser Glu	1380	His Val Thr Lys
1385	Cys Cys Ser Gly Ser Leu	1390	Val Glu Arg Arg Pro	1395	Cys Phe Ser Ala
1400	Leu Thr Val Asp Glu Thr	1405	Tyr Val Pro Lys Glu	1410	Phe Lys Ala Glu
1415	Thr Phe Thr Phe His Ser	1420	Asp Ile Cys Thr Leu	1425	Pro Glu Lys Glu
1430	Lys Gln Ile Lys Lys Gln	1435	Thr Ala Leu Ala Glu	1440	Leu Val Lys His
1445	Lys Pro Lys Ala Thr Ala	1450	Glu Gln Leu Lys Thr	1455	Val Met Asp Asp
1460	Phe Ala Gln Phe Leu Asp	1465	Thr Cys Cys Lys Ala	1470	Ala Asp Lys Asp
1475	Thr Cys Phe Ser Thr Glu	1480	Gly Pro Asn Leu Val	1485	Thr Arg Cys Lys
1490	Asp Ala Leu Ala	1495		1500	
1505					

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 26 - ENPP71 Amino Acid Sequence

	Met	Arg	Gly	Pro	Ala	Val	Leu	Leu	Thr	Val	Ala	Leu	Ala	Thr	Leu
<u>Leu</u>	1			5				10					15		
	Ala	Pro	Gly	Ala	Gly	Ala	**Gly	Leu	Lys	Pro	Ser	Cys	Ala	Lys	Glu
Val				20				25					30		
	Lys	Ser	Cys	Lys	Gly	Arg	Cys	Phe	Glu	Arg	Thr	Phe	Gly	Asn	Cys
Arg				35				40					45		
	Cys	Asp	Ala	Ala	Cys	Val	Glu	Leu	Gly	Asn	Cys	Cys	Leu	Asp	Tyr
Gln				50			55				60				
	Glu	Thr	Cys	Ile	Glu	Pro	Glu	His	Ile	Trp	Thr	Cys	Asn	Lys	Phe
Arg															
	65			70				75					80		
	Cys	Gly	Glu	Lys	Arg	Leu	Thr	Arg	Ser	Leu	Cys	Ala	Cys	Ser	Asp
Asp															
				85				90					95		
	Cys	Lys	Asp	Lys	Gly	Asp	Cys	Cys	Ile	Asn	Tyr	Ser	Ser	Val	Cys
Gln															
				100				105					110		
	Gly	Glu	Lys	Ser	Trp	Val	Glu	Glu	Pro	Cys	Glu	Ser	Ile	Asn	Glu
Pro															
				115				120					125		
	Gln	Cys	Pro	Ala	Gly	Phe	Glu	Thr	Pro	Pro	Thr	Leu	Leu	Phe	Ser
Leu															
				130				135					140		
	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	His	Thr	Trp	Gly	Gly	Leu	Leu
Pro															
	145			150				155							
160															
	Val	Ile	Ser	Lys	Leu	Lys	Lys	Cys	Gly	Thr	Tyr	Thr	Lys	Asn	Met
Arg															
				165				170					175		
	Pro	Val	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr	Ser	Ile	Val
Thr															
				180				185					190		
	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn	Lys	Met	Tyr
Asp															
				195				200					205		
	Pro	Lys	Met	Asn	Ala	Ser	Phe	Ser	Leu	Lys	Ser	Lys	Glu	Lys	Phe
Asn															
				210				215					220		
	Pro	Glu	Trp	Tyr	Lys	Gly	Glu	Pro	Ile	Trp	Val	Thr	Ala	Lys	Tyr
Gln															
	225			230				235							
240															

Ile Gly Leu Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu
 245 250 255
 Pro Asn Gly Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val
 260 265 270
 Lys Phe Glu Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro
 275 280 285
 Ser Asp Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp
 290 295 300
 Leu Ser Gly His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala
 305 310 315
 320 Gln Arg Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys
 Glu 325 330 335
 Gly Leu Asn Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His
 340 345 350
 Leu Met Glu Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr
 355 360 365
 Leu Gly Asp Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg
 370 375 380
 Gly Arg Pro Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu
 385 390 395
 400 Ile Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys
 Pro 405 410 415
 Asp Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser
 420 425 430
 Ala Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu
 435 440 445
 Ser Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly
 450 455 460
 Pro Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly
 465 470 475
 480 Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu
 Val 485 490 495
 Asn Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn
 500 505 510
 Thr Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr

		515				520			525						
	Pro	Lys	His	Pro	Lys	Glu	Val	His	Pro	Leu	Val	Gln	Cys	Pro	Phe
Thr															
		530				535			540						
	Arg	Asn	Pro	Arg	Asp	Asn	Leu	Gly	Cys	Ser	Cys	Asn	Pro	Ser	Ile
Leu															
	545					550					555				
560															
	Pro	Ile	Glu	Asp	Phe	Gln	Thr	Gln	Phe	Asn	Leu	Thr	Val	Ala	Glu
Glu															
					565				570						575
	Lys	Ile	Ile	Lys	His	Glu	Thr	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val
Leu															
				580					585					590	
	Gln	Lys	Glu	Asn	Thr	Ile	Cys	Leu	Leu	Ser	Gln	His	Gln	Phe	Met
Ser															
		595				600							605		
	Gly	Tyr	Ser	Gln	Asp	Ile	Leu	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr
Val															
		610				615							620		
	Asp	Arg	Asn	Asp	Ser	Phe	Ser	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu
Tyr															
	625					630							635		
640															
	Gln	Asp	Phe	Arg	Ile	Pro	Leu	Ser	Pro	Val	His	Lys	Cys	Ser	Phe
Tyr															
					645				650						655
	Lys	Asn	Asn	Thr	Lys	Val	Ser	Tyr	Gly	Phe	Leu	Ser	Pro	Pro	Gln
Leu															
				660				665						670	
	Asn	Lys	Asn	Ser	Ser	Gly	Ile	Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Thr
Asn															
		675				680							685		
	Ile	Val	Pro	Met	Tyr	Gln	Ser	Phe	Gln	Val	Ile	Trp	Arg	Tyr	Phe
His															
		690				695							700		
	Asp	Thr	Leu	Leu	Arg	Lys	Tyr	Ala	Glu	Glu	Arg	Asn	Gly	Val	Asn
Val															
	705					710							715		
720															
	Val	Ser	Gly	Pro	Val	Phe	Asp	Phe	Asp	Tyr	Asp	Gly	Arg	Cys	Asp
Ser															
					725				730						735
	Leu	Glu	Asn	Leu	Arg	Gln	Lys	Arg	Arg	Val	Ile	Arg	Asn	Gln	Glu
Ile															
				740				745						750	
	Leu	Ile	Pro	Thr	His	Phe	Phe	Ile	Val	Leu	Thr	Ser	Cys	Lys	Asp
Thr															
		755				760							765		
	Ser	Gln	Thr	Pro	Leu	His	Cys	Glu	Asn	Leu	Asp	Thr	Leu	Ala	Phe
Ile															
		770				775							780		
	Leu	Pro	His	Arg	Thr	Asp	Asn	Ser	Glu	Ser	Cys	Val	His	Gly	Lys
His															
	785					790							795		
800															

```

      Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg
Ile
      805      810      815
      Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg
Lys
      820      825      830
      Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr
Phe
      835      840      845
      Ser Gln Glu Asp
      850

```

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence

SEQ. ID NO: 27 - ENPP121 Amino Acid Sequence

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Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu
Gly
1      5      10      15
Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg
Gly
      20      25      30
Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala
Ser
      35      40      45
Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala
Ala
      50      55      60
Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser
Leu
      65      70      75      80
Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly**Phe Thr Ala
Gly
      85      90      95
Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg
Cys
      100      105      110
Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val
Glu
      115      120      125
Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro
Glu
      130      135      140
His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu
Thr
      145      150      155
      160
Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp
Cys
      165      170      175

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Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val
 Glu
 180 185 190
 Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe
 Glu
 195 200 205
 Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu
 Tyr
 210 215 220
 Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys
 Lys
 225 230 235
 240
 Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys
 Thr
 245 250 255
 Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser
 His
 260 265 270
 Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser
 Phe
 275 280 285
 Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly
 Glu
 290 295 300
 Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr
 Phe
 305 310 315
 320
 Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp
 Ile
 325 330 335
 Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu
 Ala
 340 345 350
 Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe
 Tyr
 355 360 365
 Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly
 Pro
 370 375 380
 Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met
 Val
 385 390 395
 400
 Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys
 Leu
 405 410 415
 Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys
 Lys
 420 425 430
 Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile
 Lys
 435 440 445
 Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro
 Asp

	450		455		460										
	Lys	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu	Gly	Ile	Ala	Arg	Asn	Leu	Ser
Cys															
	465					470					475				
480															
	Arg	Glu	Pro	Asn	Gln	His	Phe	Lys	Pro	Tyr	Leu	Lys	His	Phe	Leu
Pro															
					485					490				495	
	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp	Arg	Ile	Glu	Pro	Leu	Thr
Phe															
			500						505					510	
	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala	Leu	Asn	Pro	Ser	Glu	Arg
Lys															
			515					520				525			
	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser	Asp	Asn	Val	Phe	Ser	Asn
Met															
		530					535				540				
	Gln	Ala	Leu	Phe	Val	Gly	Tyr	Gly	Pro	Gly	Phe	Lys	His	Gly	Ile
Glu															
	545					550					555				
560															
	Ala	Asp	Thr	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp
Leu															
					565				570					575	
	Leu	Asn	Leu	Thr	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu
Asn															
			580					585					590		
	His	Leu	Leu	Lys	Asn	Pro	Val	Tyr	Thr	Pro	Lys	His	Pro	Lys	Glu
Val															
		595						600				605			
	His	Pro	Leu	Val	Gln	Cys	Pro	Phe	Thr	Arg	Asn	Pro	Arg	Asp	Asn
Leu															
		610					615					620			
	Gly	Cys	Ser	Cys	Asn	Pro	Ser	Ile	Leu	Pro	Ile	Glu	Asp	Phe	Gln
Thr															
	625					630					635				
640															
	Gln	Phe	Asn	Leu	Thr	Val	Ala	Glu	Glu	Lys	Ile	Ile	Lys	His	Glu
Thr															
					645				650					655	
	Leu	Pro	Tyr	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Glu	Asn	Thr	Ile
Cys															
			660					665					670		
	Leu	Leu	Ser	Gln	His	Gln	Phe	Met	Ser	Gly	Tyr	Ser	Gln	Asp	Ile
Leu															
		675					680					685			
	Met	Pro	Leu	Trp	Thr	Ser	Tyr	Thr	Val	Asp	Arg	Asn	Asp	Ser	Phe
Ser															
		690				695					700				
	Thr	Glu	Asp	Phe	Ser	Asn	Cys	Leu	Tyr	Gln	Asp	Phe	Arg	Ile	Pro
Leu															
	705					710					715				
720															
	Ser	Pro	Val	His	Lys	Cys	Ser	Phe	Tyr	Lys	Asn	Asn	Thr	Lys	Val
Ser															
					725				730					735	

Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly
 Ile
 740 745 750
 Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln
 Ser
 755 760 765
 Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys
 Tyr
 770 775 780
 Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe
 Asp
 785 790 795
 800
 Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln
 Lys
 805 810 815
 Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe
 Phe
 820 825 830
 Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His
 Cys
 835 840 845
 Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp
 Asn
 850 855 860
 Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu
 Glu
 865 870 875
 880
 Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile
 Thr
 885 890 895
 Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile
 Leu
 900 905 910
 Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp
 915 920 925

Singly underlined: signal peptide sequence; double-underlined:
 beginning and end of NPP1; ** = cleavage position at the signal
 peptide sequence

SEQ. ID. NO: 28 - ENPP121-Fc Amino Acid Sequence

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu
 Gly
 1 5 10 15
 Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg
 Gly
 20 25 30
 Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala
 Ser
 35 40 45

Ala Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala
 50 55 60
 Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser
Leu 65 70 75 80
Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly**Phe Thr Ala
Gly
 85 90 95
Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg
 Cys 100 105 110
 Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val
 Glu 115 120 125
 Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro
 Glu 130 135 140
 His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu
 Thr 145 150 155
 160
 Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp
 Cys 165 170 175
 Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val
 Glu 180 185 190
 Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe
 Glu 195 200 205
 Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu
 Tyr 210 215 220
 Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys
 Lys 225 230 235
 240
 Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys
 Thr 245 250 255
 Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser
 His 260 265 270
 Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser
 Phe 275 280 285
 Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly
 Glu 290 295 300
 Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr
 Phe 305 310 315
 320
 Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp
 Ile

				325					330					335	
	Tyr	Lys	Met	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Leu
Ala															
				340					345					350	
	Val	Leu	Gln	Trp	Leu	Gln	Leu	Pro	Lys	Asp	Glu	Arg	Pro	His	Phe
Tyr															
				355				360					365		
	Thr	Leu	Tyr	Leu	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ser	Tyr	Gly
Pro															
				370				375					380		
	Val	Ser	Ser	Glu	Val	Ile	Lys	Ala	Leu	Gln	Arg	Val	Asp	Gly	Met
Val															
				385				390					395		
400															
	Gly	Met	Leu	Met	Asp	Gly	Leu	Lys	Glu	Leu	Asn	Leu	His	Arg	Cys
Leu															
					405					410					415
	Asn	Leu	Ile	Leu	Ile	Ser	Asp	His	Gly	Met	Glu	Gln	Gly	Ser	Cys
Lys															
				420					425					430	
	Lys	Tyr	Ile	Tyr	Leu	Asn	Lys	Tyr	Leu	Gly	Asp	Val	Lys	Asn	Ile
Lys															
				435				440					445		
	Val	Ile	Tyr	Gly	Pro	Ala	Ala	Arg	Leu	Arg	Pro	Ser	Asp	Val	Pro
Asp															
				450				455				460			
	Lys	Tyr	Tyr	Ser	Phe	Asn	Tyr	Glu	Gly	Ile	Ala	Arg	Asn	Leu	Ser
Cys															
				465				470				475			
480															
	Arg	Glu	Pro	Asn	Gln	His	Phe	Lys	Pro	Tyr	Leu	Lys	His	Phe	Leu
Pro															
					485					490					495
	Lys	Arg	Leu	His	Phe	Ala	Lys	Ser	Asp	Arg	Ile	Glu	Pro	Leu	Thr
Phe															
				500					505					510	
	Tyr	Leu	Asp	Pro	Gln	Trp	Gln	Leu	Ala	Leu	Asn	Pro	Ser	Glu	Arg
Lys															
				515				520					525		
	Tyr	Cys	Gly	Ser	Gly	Phe	His	Gly	Ser	Asp	Asn	Val	Phe	Ser	Asn
Met															
				530				535				540			
	Gln	Ala	Leu	Phe	Val	Gly	Tyr	Gly	Pro	Gly	Phe	Lys	His	Gly	Ile
Glu															
				545				550				555			
560															
	Ala	Asp	Thr	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp
Leu															
					565				570					575	
	Leu	Asn	Leu	Thr	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu
Asn															
				580					585				590		
	His	Leu	Leu	Lys	Asn	Pro	Val	Tyr	Thr	Pro	Lys	His	Pro	Lys	Glu
Val															
				595				600				605			

His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn
 Leu
 610 615 620
 Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln
 Thr
 625 630 635
 640
 Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu
 Thr
 645 650 655
 Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile
 Cys
 660 665 670
 Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile
 Leu
 675 680 685
 Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe
 Ser
 690 695 700
 Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro
 Leu
 705 710 715
 720
 Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys Val
 Ser
 725 730 735
 Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly
 Ile
 740 745 750
 Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln
 Ser
 755 760 765
 Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys
 Tyr
 770 775 780
 Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe
 Asp
 785 790 795
 800
 Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln
 Lys
 805 810 815
 Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe
 Phe
 820 825 830
 Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His
 Cys
 835 840 845
 Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp
 Asn
 850 855 860
 Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu
 Glu
 865 870 875
 880

Thr Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile
 885 890 895
 Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile
 Leu 900 905 910
 Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp Leu Ile
 Asn 915 920 925
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 Gly 930 935 940
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 Met 945 950 955
 960
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 His 965 970 975
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 Val 980 985 990
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 Tyr 995 1000 1005
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 1010 1015 1020
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 1025 1030 1035
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 1040 1045 1050
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
 1055 1060 1065
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 1070 1075 1080
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
 1085 1090 1095
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 1100 1105 1110
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 1115 1120 1125
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
 1130 1135 1140
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 1145 1150 1155

Singly underlined: signal peptide sequence; double-underlined:
 beginning and end of NPP1; ** = cleavage position at the signal
 peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 29 - ENPP121-ALB Amino Acid Sequence:

Gly Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu
 1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg
 Gly
 20 25 30
 Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala
 Ser
 35 40 45
 Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala
 Ala
 50 55 60
 Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser
 Leu
 65 70 75 80
Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly**Phe Thr Ala
Gly
 85 90 95
Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg
 Cys
 100 105 110
 Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val
 Glu
 115 120 125
 Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro
 Glu
 130 135 140
 His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu
 Thr
 145 150 155
 160
 Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp
 Cys
 165 170 175
 Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val
 Glu
 180 185 190
 Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe
 Glu
 195 200 205
 Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu
 Tyr
 210 215 220
 Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys
 Lys
 225 230 235
 240
 Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys
 Thr
 245 250 255
 Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser
 His
 260 265 270
 Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser
 Phe
 275 280 285
 Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly
 Glu
 290 295 300

Phe Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr
 305 310 315
 320 Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp
 Ile 325 330 335
 Ala Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu
 340 345 350
 Tyr Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe
 355 360 365
 Pro Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly
 370 375 380
 Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met
 385 390 395
 400 Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys
 Leu 405 410 415
 Lys Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys
 420 425 430
 Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile
 435 440 445
 Asp Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro
 450 455 460
 Cys Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser
 465 470 475
 480 Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu
 Pro 485 490 495
 Phe Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu Thr
 500 505 510
 Lys Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg
 515 520 525
 Met Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn
 530 535 540
 Glu Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile
 545 550 555
 560 Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp
 Leu 565 570 575

Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu
 Asn
 580 585 590
 His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu
 Val
 595 600 605
 His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn
 Leu
 610 615 620
 Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln
 Thr
 625 630 635
 640
 Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu
 Thr
 645 650 655
 Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile
 Cys
 660 665 670
 Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile
 Leu
 675 680 685
 Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe
 Ser
 690 695 700
 Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro
 Leu
 705 710 715
 720
 Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys Val
 Ser
 725 730 735
 Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly
 Ile
 740 745 750
 Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln
 Ser
 755 760 765
 Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys
 Tyr
 770 775 780
 Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe
 Asp
 785 790 795
 800
 Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln
 Lys
 805 810 815
 Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe
 Phe
 820 825 830
 Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His
 Cys
 835 840 845
 Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp
 Asn

	850		855		860
	Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu				
Glu					
	865		870		875
880					
	Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile				
Thr					
		885		890	895
	Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile				
Leu					
		900		905	910
	Lys Leu Lys Thr His Leu Pro Thr Phe Ser <u>Gln Glu Asp</u> Arg Ser				
Gly					
		915		920	925
	Ser Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe				
Val					
		930		935	940
	Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His				
Lys					
	945		950		955
960					
	Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe				
Lys					
		965		970	975
	Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser				
Tyr					
		980		985	990
	Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys				
Thr					
		995		1000	1005
	Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His				
	1010		1015		1020
	Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu				
	1025		1030		1035
	Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu				
	1040		1045		1050
	Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu				
	1055		1060		1065
	Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe				
	1070		1075		1080
	Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val				
	1085		1090		1095
	Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr				
	1100		1105		1110
	Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala				
	1115		1120		1125
	Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu				
	1130		1135		1140
	Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser				
	1145		1150		1155
	Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala				
	1160		1165		1170
	Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr				
	1175		1180		1185
	Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His				
	1190		1195		1200

Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys
	1205					1210					1215			
Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr
	1220					1225					1230			
Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu
	1235					1240					1245			
Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala
	1250					1255					1260			
Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala
	1265					1270					1275			
Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg
	1280					1285					1290			
His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys
	1295					1300					1305			
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro
	1310					1315					1320			
Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu
	1325					1330					1335			
Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys
	1340					1345					1350			
Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr
	1355					1360					1365			
Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala
	1370					1375					1380			
Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu
	1385					1390					1395			
Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu
	1400					1405					1410			
Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His
	1415					1420					1425			
Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys
	1430					1435					1440			
Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe
	1445					1450					1455			
Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro
	1460					1465					1470			
Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu
	1475					1480					1485			
Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val
	1490					1495					1500			
Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala
	1505					1510					1515			
Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr
	1520					1525					1530			
Arg	Cys	Lys	Asp	Ala	Leu	Ala	Arg	Ser	Trp	Ser	His	Pro	Gln	Phe
	1535					1540					1545			
Glu	Lys													
	1550													

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 30 - ENPP121-NPP3-Fc sequence

	Met	Glu	Arg	Asp	Gly	Cys	Ala	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Glu
Gly	1				5					10					15
	Gly	Arg	Ala	Pro	Arg	Glu	Gly	Pro	Ala	Gly	Asn	Gly	Arg	Asp	Arg
Gly					20					25					30
	Arg	Ser	His	Ala	Ala	Glu	Ala	Pro	Gly	Asp	Pro	Gln	Ala	Ala	Ala
Ser					35					40					45
	Leu	Leu	Ala	Pro	Met	Asp	Val	Gly	Glu	Glu	Pro	Leu	Glu	Lys	Ala
Ala					50					55					60
	Arg	Ala	Arg	Thr	Ala	Lys	Asp	Pro	Asn	Thr	Tyr	Lys	Ile	Ile	Ser
Leu															
	65				70					75					80
	Phe	Thr	Phe	Ala	Val	Gly	Val	Asn	Ile	Cys	Leu	Gly	Phe	Thr	
Ala*	<u>Lys</u>														
					85					90					95
	<u>Gln</u>	<u>Gly</u>	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp	Ala	Ser	Phe	Arg	Gly
Leu															
					100					105					110
	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys	Asp	Arg	Gly	Asp	Cys
Cys															
					115					120					125
	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser	Thr	Arg	Ile	Trp	Met
Cys															
					130					135					140
	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Arg	Leu	Glu	Ala	Ser	Leu	Cys	Ser
Cys															
	145				150					155					
160															
	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys	Cys	Ala	Asp	Tyr	Lys
Ser															
					165					170					175
	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu	Glu	Asn	Cys	Asp	Thr
Ala															
					180					185					190
	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp	Leu	Pro	Pro	Val	Ile
Leu															
					195					200					205
	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	Tyr	Thr	Trp	Asp
Thr															
					210					215					220
	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr	Cys	Gly	Ile	His	Ser
Lys															
	225				230					235					
240															
	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr
Thr															
					245					250					255
	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn
Asn															
					260					265					270
	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe	Ser	Leu	Ser	Ser	Lys
Glu															
					275					280					285

	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln	Pro	Met	Trp	Leu	Thr
Ala															
		290					295				300				
	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr	Phe	Trp	Pro	Gly	Ser
Glu															
	305					310					315				
320															
	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	Tyr	Met	Pro	Tyr	Asn
Gly															
				325						330				335	
	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	Leu	Leu	Lys	Trp	Leu
Asp															
			340						345				350		
	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	Thr	Met	Tyr	Phe	Glu
Glu															
		355					360					365			
	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	Val	Ser	Ala	Arg	Val
Ile															
		370				375					380				
	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	Gly	Met	Leu	Met	Glu
Gly															
	385					390					395				
400															
	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	Asn	Ile	Ile	Leu	Leu
Ala															
				405					410				415		
	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	Lys	Met	Glu	Tyr	Met
Thr															
			420					425				430			
	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	Met	Tyr	Glu	Gly	Pro
Ala															
		435					440				445				
	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	Asp	Phe	Phe	Ser	Phe
Asn															
		450				455			460						
	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	Arg	Lys	Pro	Asp	Gln
His															
	465					470			475						
480															
	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys	Arg	Leu	His	Tyr
Ala															
				485					490				495		
	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe	Val	Asp	Gln	Gln
Trp															
			500					505				510			
	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys	Gly	Gly	Gly	Asn
His															
		515					520				525				
	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	Ala	Ile	Phe	Leu	Ala
His															
		530				535			540						
	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	Glu	Pro	Phe	Glu	Asn
Ile															
	545					550			555						
560															

Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg Ile Gln Pro Ala
 Pro
 565 570 575
 Asn Asn Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Val Pro
 Phe
 580 585 590
 Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys Phe Ser Val Cys
 Gly
 595 600 605
 Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp Cys Phe Cys Pro
 His
 610 615 620
 Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn Gln Met Leu Asn
 Leu
 625 630 635
 640
 Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val Asn Leu Pro Phe
 Gly
 645 650 655
 Arg Pro Arg Val Leu Gln Lys Asn Val Asp His Cys Leu Leu Tyr
 His
 660 665 670
 Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met Arg Met Pro Met
 Trp
 675 680 685
 Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr Ser Pro Leu Pro
 Pro
 690 695 700
 Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg Val Pro Pro Ser
 Glu
 705 710 715
 720
 Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys Asn Ile Thr His
 Gly
 725 730 735
 Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser Asp Ser Gln Tyr
 Asp
 740 745 750
 Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr Glu Glu Phe Arg
 Lys
 755 760 765
 Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile Lys His Ala Thr
 Glu
 770 775 780
 Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile Phe Asp Tyr Asn
 Tyr
 785 790 795
 800
 Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His Leu Ala
 Asn
 805 810 815
 Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu Thr Ser
 Cys
 820 825 830
 Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp Leu Asp
 Val

	835		840		845
Pro	Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu Ser Cys				
	850		855		860
His	Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe Thr Ala				
880	865		870		875
Tyr	Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr Gly Leu Asp Phe				
		885		890	895
Tyr	Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu Gln Leu Lys Thr				
		900		905	910
Pro	Leu <u>Pro Thr Phe Glu Thr Thr Ile</u> Asp Lys Thr His Thr Cys Pro				
		915		920	925
Pro	Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe				
		930		935	940
Thr	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val				
960	945		950		955
Asn	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe				
		965		970	975
Arg	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro				
		980		985	990
Val	Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr				
		995		1000	1005
	Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val				
	1010		1015		1020
	Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys				
	1025		1030		1035
	Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro				
	1040		1045		1050
	Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu				
	1055		1060		1065
	Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Thr Glu Ser				
	1070		1075		1080
	Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu				
	1085		1090		1095
	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp				
	1100		1105		1110
	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met				
	1115		1120		1125
	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu				
	1130		1135		1140
	Ser Pro Gly Lys				
	1145				

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP1; ** = cleavage position at the signal peptide sequence; bold residues indicate Fc sequence

SEQ. ID NO: 31 - ENPP121-NPP3-Albumin sequence

	Met	Glu	Arg	Asp	Gly	Cys	Ala	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Glu
Gly	1				5					10					15
	Gly	Arg	Ala	Pro	Arg	Glu	Gly	Pro	Ala	Gly	Asn	Gly	Arg	Asp	Arg
Gly					20					25					30
	Arg	Ser	His	Ala	Ala	Glu	Ala	Pro	Gly	Asp	Pro	Gln	Ala	Ala	Ala
Ser					35					40					45
	Leu	Leu	Ala	Pro	Met	Asp	Val	Gly	Glu	Glu	Pro	Leu	Glu	Lys	Ala
Ala					50					55					60
	Arg	Ala	Arg	Thr	Ala	Lys	Asp	Pro	Asn	Thr	Tyr	Lys	Ile	Ile	Ser
Leu					65					70					80
	<u>Phe</u>	<u>Thr</u>	<u>Phe</u>	<u>Ala</u>	<u>Val</u>	<u>Gly</u>	<u>Val</u>	<u>Asn</u>	<u>Ile</u>	<u>Cys</u>	<u>Leu</u>	<u>Gly</u>	<u>Phe</u>	<u>Thr</u>	
Ala**	<u>Lys</u>														
					85					90					95
	<u>Gln</u>	<u>Gly</u>	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp	Ala	Ser	Phe	Arg	Gly
Leu					100					105					110
	Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys	Asp	Arg	Gly	Asp	Cys
Cys					115					120					125
	Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser	Thr	Arg	Ile	Trp	Met
Cys					130					135					140
	Asn	Lys	Phe	Arg	Cys	Gly	Glu	Arg	Leu	Glu	Ala	Ser	Leu	Cys	Ser
Cys					145					150					155
160															
	Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys	Cys	Ala	Asp	Tyr	Lys
Ser					165					170					175
	Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu	Glu	Asn	Cys	Asp	Thr
Ala					180					185					190
	Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp	Leu	Pro	Pro	Val	Ile
Leu					195					200					205
	Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	Tyr	Thr	Trp	Asp
Thr					210					215					220
	Leu	Met	Pro	Asn	Ile	Asn	Lys	Leu	Lys	Thr	Cys	Gly	Ile	His	Ser
Lys					225					230					235
240															

	Tyr	Met	Arg	Ala	Met	Tyr	Pro	Thr	Lys	Thr	Phe	Pro	Asn	His	Tyr
Thr															
					245					250					255
	Ile	Val	Thr	Gly	Leu	Tyr	Pro	Glu	Ser	His	Gly	Ile	Ile	Asp	Asn
Asn															
				260					265					270	
	Met	Tyr	Asp	Val	Asn	Leu	Asn	Lys	Asn	Phe	Ser	Leu	Ser	Ser	Lys
Glu															
			275					280					285		
	Gln	Asn	Asn	Pro	Ala	Trp	Trp	His	Gly	Gln	Pro	Met	Trp	Leu	Thr
Ala															
		290					295				300				
	Met	Tyr	Gln	Gly	Leu	Lys	Ala	Ala	Thr	Tyr	Phe	Trp	Pro	Gly	Ser
Glu															
	305					310					315				
320															
	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	Tyr	Met	Pro	Tyr	Asn
Gly															
				325					330					335	
	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	Leu	Leu	Lys	Trp	Leu
Asp															
			340					345					350		
	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	Thr	Met	Tyr	Phe	Glu
Glu															
		355					360					365			
	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	Val	Ser	Ala	Arg	Val
Ile															
		370				375					380				
	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	Gly	Met	Leu	Met	Glu
Gly															
	385				390					395					
400															
	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	Asn	Ile	Ile	Leu	Leu
Ala															
				405					410				415		
	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	Lys	Met	Glu	Tyr	Met
Thr															
			420					425					430		
	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	Met	Tyr	Glu	Gly	Pro
Ala															
		435				440					445				
	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	Asp	Phe	Phe	Ser	Phe
Asn															
		450				455				460					
	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	Arg	Lys	Pro	Asp	Gln
His															
	465				470					475					
480															
	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys	Arg	Leu	His	Tyr
Ala															
				485				490					495		
	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe	Val	Asp	Gln	Gln
Trp															
			500					505				510			
	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys	Gly	Gly	Gly	Asn
His															

				515				520				525			
	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	Ala	Ile	Phe	Leu	Ala
His															
			530					535				540			
	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	Glu	Pro	Phe	Glu	Asn
Ile															
	545					550					555				
560															
	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu	Arg	Ile	Gln	Pro	Ala
Pro															
					565				570					575	
	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu	Asn	His	Leu	Leu	Lys	Val	Pro
Phe															
				580				585					590		
	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu	Val	Ser	Lys	Phe	Ser	Val	Cys
Gly															
			595					600				605			
	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu	Asp	Cys	Phe	Cys	Pro
His															
		610					615				620				
	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val	Asn	Gln	Met	Leu	Asn
Leu															
	625					630					635				
640															
	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys	Val	Asn	Leu	Pro	Phe
Gly															
				645				650				655			
	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp	His	Cys	Leu	Leu	Tyr
His															
			660					665				670			
	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala	Met	Arg	Met	Pro	Met
Trp															
			675					680				685			
	Ser	Ser	Tyr	Thr	Val	Pro	Gln	Leu	Gly	Asp	Thr	Ser	Pro	Leu	Pro
Pro															
		690					695				700				
	Thr	Val	Pro	Asp	Cys	Leu	Arg	Ala	Asp	Val	Arg	Val	Pro	Pro	Ser
Glu															
	705					710					715				
720															
	Ser	Gln	Lys	Cys	Ser	Phe	Tyr	Leu	Ala	Asp	Lys	Asn	Ile	Thr	His
Gly															
				725				730					735		
	Phe	Leu	Tyr	Pro	Pro	Ala	Ser	Asn	Arg	Thr	Ser	Asp	Ser	Gln	Tyr
Asp															
			740					745				750			
	Ala	Leu	Ile	Thr	Ser	Asn	Leu	Val	Pro	Met	Tyr	Glu	Glu	Phe	Arg
Lys															
		755					760				765				
	Met	Trp	Asp	Tyr	Phe	His	Ser	Val	Leu	Leu	Ile	Lys	His	Ala	Thr
Glu															
		770				775				780					
	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro	Ile	Phe	Asp	Tyr	Asn
Tyr															
	785				790						795				
800															

Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His Leu Ala
 Asn
 805 810 815
 Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu Thr Ser
 Cys
 820 825 830
 Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp Leu Asp
 Val
 835 840 845
 Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu Ser Cys
 Pro
 850 855 860
 Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe Thr Ala
 His
 865 870 875
 880
 Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr Gly Leu Asp Phe
 Tyr
 885 890 895
 Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu Gln Leu Lys Thr
 Tyr
 900 905 910
 Leu Pro Thr Phe Glu Thr Thr Ile Gly Gly Gly Ser Gly Gly Gly
 Gly
 915 920 925
 Ser Gly Gly Gly Gly Ser **Met Lys Trp Val Thr Phe Leu Leu Leu**
 Leu
 930 935 940
Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu
 Ala
 945 950 955
 960
 His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln
 His
 965 970 975
 Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys
 Cys
 980 985 990
 Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe
 Ala
 995 1000 1005
 Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser
 1010 1015 1020
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
 1025 1030 1035
 Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu
 1040 1045 1050
 Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
 1055 1060 1065
 Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr
 1070 1075 1080
 Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His
 1085 1090 1095
 Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
 1100 1105 1110
 Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala

1115	Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	1120	Leu	Asp	Gly	Val	1125
1130	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	1135	Arg	Met	Lys	Cys	1140
1145	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	1150	Lys	Ala	Trp	Ala	1155
1160	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	1165	Asp	Phe	Ala	Glu	1170
1175	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	1180	Asn	Lys	Glu	Cys	1185
1190	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	1195	Arg	Ala	Glu	Leu	1200
1205	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	1210	Ser	Ser	Lys	Leu	1215
1220	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	1225	Ala	His	Cys	Leu	1230
1235	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	1240	Leu	Pro	Ala	Ile	1245
1250	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	1255	Lys	Asn	Tyr	Ala	1260
1265	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	1270	Tyr	Glu	Tyr	Ser	1275
1280	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	1285	Leu	Arg	Leu	Ala	1290
1295	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	1300	Ala	Glu	Ala	Asn	1305
1310	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	1315	Phe	Gln	Pro	Leu	1320
1325	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	1330	Cys	Asp	Leu	Tyr	1335
1340	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	1345	Ile	Leu	Val	Arg	1350
1355	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	1360	Thr	Leu	Val	Glu	1365
1370	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	1375	Cys	Cys	Thr	Leu	1380
1385	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	1390	Tyr	Leu	Ser	Ala	1395
1400	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	1405	Thr	Pro	Val	Ser	1410
1415	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	1420	Val	Glu	Arg	Arg	1425
1430	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	1435	Tyr	Val	Pro	Lys	1440
1445	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	1450	Asp	Ile	Cys	Thr	1455
1460	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	1465	Thr	Ala	Leu	Ala	1470
1475	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	1480	Glu	Gln	Leu	Lys	1485
1490	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	1495	Thr	Cys	Cys	Lys	1500
1505	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	1510	Gly	Pro	Asn	Leu	1515
1520	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala			1525					1530

1535

1540

Singly underlined: signal peptide sequence; double-underlined: beginning and end of NPP3; ** = cleavage position at the signal peptide sequence; bold residues indicate albumin sequence

SEQ. ID NO: 32 - ENPP121GLK Protein Export Signal Sequence

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu
 Gly 1 5 10 15
 Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg
 Gly 20 25 30
 Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala
 Ser 35 40 45
 Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala
 Ala 50 55 60
 Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser
Leu 65 70 75 80
Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala
Gly 85 90 95
Leu Lys

SEQ. ID NO: 33 - Albumin Sequence

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 Met 1 5 10 15
 Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala
 Phe 20 25 30
 Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala
 His 35 40 45
 Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu
 Ile 50 55 60
 Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala
 Lys 65 70 75 80
 Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp
 Glu 85 90 95
 Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 Lys 100 105 110

Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala
 Asp
 115 120 125
 Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 His
 130 135 140
 Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala
 Glu
 145 150 155
 160
 Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly
 His
 165 170 175
 Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 Glu
 180 185 190
 Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys
 Cys
 195 200 205
 Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly
 Val
 210 215 220
 Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys
 Ser
 225 230 235
 240
 Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 Ala
 245 250 255
 Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr
 Lys
 260 265 270
 Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
 Asp
 275 280 285
 Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met
 Cys
 290 295 300
 Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp
 Lys
 305 310 315
 320
 Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp
 Thr
 325 330 335
 Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp
 Gln
 340 345 350
 Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 Thr
 355 360 365
 Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser
 Leu
 370 375 380
 Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys
 Cys

385 390 395
 400 Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu
 Phe
 405 410 415
 Asp Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys
 420 425 430
 Val Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu
 435 440 445
 Glu Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val
 450 455 460
 Pro Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu
 465 470 475
 480 Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile
 Leu
 485 490 495
 Val Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His
 500 505 510
 Ser Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
 515 520 525
 Glu Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala
 530 535 540
 Lys Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu
 545 550 555
 560 Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys
 Pro
 565 570 575
 Gln Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala
 580 585 590
 Ser Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe
 595 600 605
 Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
 610 615 620

SEQ. ID NO: 34 - Human IgG Fc domain, Fc

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 Gly
 1 5 10 15
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 Met
 20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 His
 35 40 45
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 Val
 50 55 60
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 Tyr
 65 70 75 80
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 Gly
 85 90 95
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 Ile
 100 105 110
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 Val
 115 120 125
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
 Ser
 130 135 140
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 Glu
 145 150 155
 160
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 Pro
 165 170 175
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 Val
 180 185 190
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 Met
 195 200 205
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 Ser
 210 215 220
 Pro Gly Lys
 225

SEQ. ID NO: 35 - Albumin Sequence

Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser
 Ala
 1 5 10 15
 Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile
 Ala
 20 25 30
 His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val
 Leu
 35 40 45
 Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His
 Ala
 50 55 60

Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala
 Asp 65 70 75 80
 Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 Asp 85 90 95
 Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu
 Ala 100 105 110
 Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
 Gln 115 120 125
 His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu
 Ala 130 135 140
 Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met
 Gly 145 150 155
 160 His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala
 Pro 165 170 175
 Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln
 Cys 180 185 190
 Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp
 Gly 195 200 205
 Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys
 Cys 210 215 220
 Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 Val 225 230 235
 240 Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile
 Thr 245 250 255
 Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His
 Gly 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr
 Met 275 280 285
 Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys
 Asp 290 295 300
 Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His
 Asp 305 310 315
 320 Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu
 Asp 325 330 335
 Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 Gly

				340					345				350		
	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val
Ser															
			355					360					365		
	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys
Cys															
		370					375					380			
	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala
Glu															
	385					390					395				
400															
	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn
Cys															
				405					410					415	
	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile
Leu															
			420					425					430		
	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu
Val															
		435					440					445			
	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr
Leu															
		450				455			460						
	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala
Ile															
	465				470				475						
480															
	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu
His															
			485					490				495			
	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys
Phe															
		500					505				510				
	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys
Ala															
		515					520				525				
	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys
Glu															
		530				535			540						
	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His
Lys															
	545				550				555						
560															
	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe
Ala															
			565				570				575				
	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys
Phe															
		580				585			590						
	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu
Ala															
		595				600			605						
	Arg	Ser	Trp	Ser	His	Pro	Gln	Phe	Glu	Lys					
		610				615									

SEQ. ID NO: 36 - ENPP2 Signal Peptide

Leu Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly
 1 5 10 15
 Phe Thr Ala

SEQ. ID NO: 37 - Signal Sequence ENPP7

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
 Leu
 1 5 10 15
 Ala Pro Gly Ala
 20

SEQ. ID NO: 38 - Signal sequence ENPP7

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu
 Leu
 1 5 10 15
 Ala Pro Gly Ala Gly Ala
 20

SEQ. ID NO: 39 - Signal Sequence ENPP1-2-1

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu
 Gly
 1 5 10 15
 Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg
 Gly
 20 25 30
 Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala
 Ser
 35 40 45
 Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala
 Ala
 50 55 60
 Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser
 Leu
 65 70 75 80
Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala
 85 90 95

SEQ. ID NO: 40 - exENPP3

Leu Leu Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu
 Arg
 1 5 10 15
 Lys

SEQ. ID NO: 41 - Signal Sequence ENPP5:

Ser Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu
 1 5 10 15
 Leu Ser Thr Thr Phe Ser
 20

SEQ ID NO: 42 - Signal Sequence - Azurocidin

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala
 Ser

Ser Arg Ala

SEQ. ID NO: 43 - Linker

Asp Ser Ser

SEQ. ID NO: 44 - Linker

Glu Ser Ser

SEQ. ID NO: 45 - Linker

Arg Gln Gln

SEQ. ID NO: 46 - Linker

Lys Arg

SEQ. ID NO: 47 - Linker

(Arg)_m ; m=0-15

SEQ. ID NO: 48 - Linker

Gly Asp Ser Ser Ser Glu Glu Lys Phe Leu Arg Arg Ile Gly Arg Phe

SEQ. ID NO: 49 - Linker

Glu Glu Glu Glu Glu Glu Glu Pro Arg Gly Asp Thr

1 5 10

SEQ. ID NO: 50 - Linker

Ala Pro Trp His Leu Ser Ser Gln Tyr Ser Arg Thr

1 5 10

SEQ. ID NO: 51 - Linker

Ser Thr Leu Pro Ile Pro His Glu Phe Ser Arg Glu

1 5 10

SEQ. ID NO: 52 - Linker

Val Thr Lys His Leu Asn Gln Ile Ser Gln Ser Tyr

1 5 10

SEQ. ID NO: 53 - Linker

(Glu)_m; m=1-15

SEQ. ID NO: 54 - Linker

Leu Ile Asn

SEQ. ID NO: 55 - Linker

Gly Gly Ser Gly Gly Ser

1 5

SEQ. ID NO: 56 - Linker

Arg Ser Gly Ser Gly Gly Ser

1 5

SEQ. ID NO: 57 - Linker

(Asp)_m; m=1-15

1

SEQ. ID NO: 58 - Linker

Lys Leu Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Arg

1 5 10 15

SEQ. ID NO: 59 - Linker

Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10 15

SEQ. ID NO: 60 - Linker

Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10

SEQ. ID NO: 61 - Linker

Met Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10

SEQ. ID NO: 62 - Linker

Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10

SEQ. ID NO: 63 - Linker

Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10

SEQ. ID NO: 64 - Linker

Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5 10

SEQ. ID NO: 65 - Linker

Leu Gly Leu Gly Leu Gly Leu Arg Lys

1 5

SEQ. ID NO: 66 - Linker

Gly Leu Gly Leu Gly Leu Arg Lys

1 5

SEQ. ID NO: 67 - Linker

Leu Gly Leu Gly Leu Arg Lys

1 5

SEQ. ID NO: 68 - Linker

Gly Leu Gly Leu Arg Lys

1 5

SEQ. ID NO: 69 - Linker

Leu Gly Leu Arg Lys

1 5

SEQ. ID NO: 70 - Linker

Gly Leu Arg Lys

1

SEQ. ID NO: 71 - Linker

Leu Arg Lys

1

SEQ. ID NO: 72 - Linker

Arg Lys

1

SEQ. ID NO: 73 - Linker(Lys)_m; m=0-15

1

SEQ. ID NO: 74 -LinkerD_m; m=1-15SEQ. ID NO: 75 -Linker(GGGS)_n; n=1-10SEQ. ID NO: 76 - ENPP3 Nucleotide sequence

atggaatcta cgttgacttt agcaacggaa caacctgtta agaagaacac tcttaagaaa	60
tataaaatag cttgcattgt tcttcttgct ttgctgggtga tcatgtcact tggattaggc	120
ctggggccttg gactcaggaa actggaaaag caaggcagct gcaggaagaa gtgctttgat	180
gcatcattta gaggactgga gaactgccgg tgtgatgtgg catgtaaaga ccgagggtgat	240
tgctgctggg attttgaaga cacctgtgtg gaatcaactc gaatatggat gtgcaataaa	300
tttcgttgtg gagagaccag attagaggcc agcctttgct cttgttcaga tgactgtttg	360
cagaggaaaag attgctgtgc tgactataag agtgtttgcc aaggagaaac ctcatggctg	420
gaagaaaact gtgacacagc ccagcagtct cagtgccag aagggtttga cctgccacca	480
gttatcttgt tttctatgga tggatttaga gctgaatatt tatacacatg ggatacttta	540
atgccaaata tcaataaact gaaaacatgt ggaattcatt caaaatacat gagagctatg	600
tatcctacca aaaccttccc aaatcattac accattgtca cgggcttgta tccagagtca	660
catggcatca ttgacaataa tatgtatgat gtaaactctca acaagaattt ttcaactttc	720
tcaaaggaac aaaataatcc agcctgggtg catgggcaac caatgtggct gacagcaatg	780
tatcaaggtt taaaagccgc tacctacttt tggcccgat cagaagtggc tataaatggc	840
tcctttcctt ccatatacat gccttacaac ggaagtgtcc cathttgaaga gaggatttct	900

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acactgttaa aatggctgga cctgccccaa gctgaaagac ccagggttta taccatgtat      960
tttgaagaac ctgattcctc tggacatgca ggtggaccag tcagtgccag agtaattaaa      1020
gccttacagg tagtagatca tgcttttggg atgttgatgg aaggcctgaa gcagcggaat      1080
ttgcacaact gtgtcaatat catccttctg gctgaccatg gaatggacca gacttattgt      1140
aacaagatgg aatacatgac tgattatfff cccagaataa acttcttcta catgtacgaa      1200
gggcctgccc cccgcatccg agctcataat atacctcatg acttttttag ttttaattct      1260
gaggaaattg ttagaaacct cagttgccga aaacctgatc agcatttcaa gccctatttg      1320
actcctgatt tgccaaagcg actgcactat gccagaacg tcagaatcga caaagttcat      1380
ctctttgtgg atcaacagtg gctggctgtt aggagtaa at caaatacaaa ttgtggagga      1440
ggcaaccatg gttataacaa tgagtttagg agcatggagg ctatctttct ggcacatgga      1500
cccagtttta aagagaagac tgaagttgaa ccatttgaaa atattgaagt ctataaccta      1560
atgtgtgatc ttctacgcat tcaaccagca ccaaacaatg gaacccatgg tagtttaaac      1620
catcttctga aggtgccttt ttatgagcca tcccatgcag aggagggtgc aaagttttct      1680
gtttgtggct ttgctaatec attgcccaca gagtctcttg actgtttctg ccctcaccta      1740
caaaatagta ctcagctgga acaagtgaat cagatgctaa atctcaccca agaagaaata      1800
acagcaacag tgaaagtaaa tttgccattt gggaggccta gggtagtgca gaagaacgtg      1860
gaccactgtc tcctttacca cagggaatat gtcagtggat ttggaaaagc tatgaggatg      1920
cccatgtgga gttcatacac agtccccagc ttgggagaca catcgctctt gcctccact      1980
gtcccagact gtctgcgggc tgatgtcagg gttcctcctt ctgagagcca aaaatgttcc      2040
ttctatttag cagacaagaa tatcacccac ggcttctctt atcctcctgc cagcaataga      2100
acatcagata gccaatatga tgctttaatt actagcaatt tggtagctat gtatgaagaa      2160
ttcagaaaaa tgtgggacta cttccacagt gttcttctta taaaacatgc cacagaaaga      2220
aatggagtaa atgtggtagg tggaccaata tttgattata attatgatgg ccattttgat      2280
gtccagatg aaattaccaa acatttagcc aacctgatg ttcccatccc aacacactac      2340
tttgtggtgc tgaccagttg taaaaacaag agccacacac cggaaaactg ccctgggtgg      2400
ctggatgtcc taccctttat catccctcac cgacctacca acgtggagag ctgtcctgaa      2460
ggtaaacagc aagctctttg ggttgaagaa agatttacag ctcacattgc ccgggtccgt      2520
gatgtagaac ttctcactgg gcttgacttc tatcaggata aagtgcagcc tgtctctgaa      2580
atthtgcaac taaagacata ttaccaaca tttgaaacca ctatt      2625

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SEQ. ID NO: 77 - ENPP1 Nucleotide sequence:

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atggaacggg acggctgtgc cggcggagga tcaagaggcg gagaaggcgg cagagcccct      60
agagaaggac ctgccggcaa cggcagagac agaggcagat ctcatgccgc cgaagcccct      120
ggcgatcctc aggtgctgctg ttctctgctg gccccatgg atgtgggcga ggaacctctg      180

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gaaaaggccg ccagagccag aaccgccaag gaccccaaca cctacaaggt gctgagcctg	240
gtgctgtccg tgtgcgtgct gaccaccatc ctgggctgca tcttcggcct gaagcccagc	300
tgcgccaaag aagtgaagtc ctgcaagggc cgggtgcttcg agcggacctt cggcaactgc	360
agatgcgacg ccgcctgtgt ggaactgggc aactgctgcc tggactacca ggaaacctgc	420
atcgagcccg agcacatctg gacctgcaac aagttcagat gcggcgagaa gcggctgacc	480
agatccctgt gtgcctgcag cgacgactgc aaggacaagg gcgactgctg catcaactac	540
agcagcgtgt gccagggcga gaagtcctgg gtggaagaac cctgcgagag catcaacgag	600
ccccagtgcc ctgcccggctt cgagacacct cctacctgc tgttcagcct ggacggcttt	660
cgggcccagt acctgcacac atggggaggc ctgctgcccg tgatcagcaa gctgaagaag	720
tgcggcacct acaccaagaa catgcggccc gtgtaccca ccaagacctt ccccaaccac	780
tactccatcg tgaccggcct gtaccccgag agccacggca tcatcgacaa caagatgtac	840
gaccccaaga tgaacgccag cttcagcctg aagtccaaag agaagttcaa ccccgagtgg	900
tataagggcg agcccatctg ggtcaccgcc aagtaccagg gcctgaaaag cggcacattc	960
ttttggcccg gcagcgacgt ggaaatcaac ggcatcttcc ccgacatcta taagatgtac	1020
aacggcagcg tgcccttcga ggaacggatc ctggctgtgc tgcatgggt gcagctgccc	1080
aaggatgagc ggccccactt ctacacctg tacctggaag aacctgacag cagcggccac	1140
agctacggcc ctgtgtccag cgaagtgatc aaggccctgc agcgggtgga cggcatggtg	1200
ggaatgctga tggacggcct gaaagagctg aacctgcaca gatgcctgaa cctgatcctg	1260
atcagcgacc acggcatgga acagggatcc tgcaagaagt acatctacct gaacaagtac	1320
ctgggcgacg tgaagaacat caaagtgatc tacggcccag ccgccagact gaggcctagc	1380
gacgtgcccg acaagtacta cagcttcaac tacgagggaa tcgcccggaa cctgagctgc	1440
agagagccca accagcactt caagccctac ctgaagcact tcctgcccga gcggctgcac	1500
ttcgccaaga gcgacagaat cgagcccctg accttctacc tggaccccca gtggcagctg	1560
gcccgaatc ccagcgagag aaagtactgc ggcagcgggt tccacggctc cgacaacgtg	1620
ttcagcaaca tgcaggccct gttcgtgggc tacggaccgc gctttaagca cggcatcgag	1680
gccgacacct tcgagaacat cgagggtgtac aatctgatgt gcgacctgct gaatctgacc	1740
cctgccccca acaatggcac ccacggcagc ctgaaccatc tgctgaagaa ccccggtgac	1800
accctaagc accccaaaga ggtgcacccc ctggtgcagt gccccttcac cagaaacccc	1860
agagacaacc tgggctgtag ctgcaacccc agcatcctgc ccatcgagga cttccagacc	1920
cagttcaacc tgaccgtggc cgaggaaaag atcatcaagc acgagacact gccctacggc	1980
agaccccggtg tgctgcagaa agagaacacc atctgcctgc tgagccagca ccagttcatg	2040
agcggctact ccaggacat cctgatgccc ctgtggacca gctacaccgt ggaccggaac	2100
gacagcttct ccaccgagga tttcagcaac tgccgtgtacc aggatttcg gatccccctg	2160
agccccgtgc acaagtgcag cttctacaag aacaacacca aggtgtccta cggcttcctg	2220

agccctcccc agctgaacaa gaacagctcc ggcattctaca gcgaggccct gctgactacc	2280
aacatcgtgc ccatgtacca gagcttccaa gtgatctggc ggtacttcca cgacaccctg	2340
ctgcggaagt acgccgaaga acggaacggc gtgaacgtgg tgtccggccc agtgttcgac	2400
ttcgactacg acggcagatg tgacagcctg gaaaatctgc ggcagaaaag aagagtgate	2460
cggaaaccagg aaattctgat ccctaccac ttctttatcg tgctgacaag ctgcaaggat	2520
accagccaga cccccctgca ctgcgagaac ctggataccc tggccttcac cctgcctcac	2580
cggaccgaca acagcgagag ctgtgtgcac ggcaagcacg acagctcttg ggtggaagaa	2640
ctgctgatgc tgcaccgggc cagaatcacc gatgtggaac acatcaccgg cctgagcttt	2700
taccagcagc ggaaagaacc cgtgtccgat atcctgaagc tgaaaacca tctgcccacc	2760
ttcagccagg aagat	2775

SEQ ID NO: 78 - Azurocidin-ENPP1-FC Nucleotide sequence

ggtaccgccaccatgacaagactgacagtgctggctctgctggccggactggtggcctcttctagagc
tgctccttcctgcgccaaagaagtgaagtcctgcaagggcagatgcttcgagcggaccttcggcaact
 gtagatgtgacgccgcttgctggaactgggcaactgctgacctggactaccaagagacatgcatcgag
 cccgagcacatctggacctgcaacaagttcagatgcggcgagaagcggctgaccagatctctgtgctgc
 ctgctctgacgactgcaaggacaagggcactgctgcatcaactactcctctgtgtgcccagggcgaga
 agtcctgggttgaagaacctgcgagtcctcatcaacgagcctcagtgtcctgcccggcttcgagacact
 cctactctgctgttctccctggatggcttcagagccgagtagcctgcatacttggggaggcctgctgcc
 agtgatctccaagctgaagaagtgcggcacctacaccaagaacatgaggcctgtgtaccctaccaaga
 cattcccccaacctactccatcgtgaccggcctgtatcctgagagccacggcatcatcgacaacaag
 atgtacgacccccaaagatgaacgcctccttcagcctgaagtcctaaagagaagttcaaccccgagtggta
 taagggcgagcctatctgggtcaccgctaagtaccagggaactgaagtctggcaccttcttttggcctg
 gctccgacgtggaaatcaacggcatcttccccgacatctataagatgtacaacggctccgtgcctttc
 gaggaacgcattctggctgttctgcagtggtgctgcagctgcctaaggatgagaggcctcacttctacac
 cctgtacctggaagaacctgactcctccggccactcttatggcctgtgtcctctgaagtgatcaagg
 cctgcagcagtgagcgggaatggctcggaatgctgatggacggcctgaaagagctgaacctgcacaga
 tgacctgaacctgatcctgatctccgaccacggcatggaacaggggagctgcaagaagtacatctacct
 gaacaagtacctgggcgacgtgaagaacatcaaagtgatctacggcccagccgagactgaggcctt
 ctgatgtgctgacaagtactactccttcaactacgaggggaatcgcccggaaacctgtcctgcagagag
 cctaaccagcacttcaagccctacctgaagcactttctgcctaagcggtgcacttcgccaagtctga
 cagaatcgagccccctgaccttctatctggacctcagtggcagctggcctgaatcctagcgagagaa
 agtactgtggctccggcttccacggctccgacaacgtgttctctaataatgcaggccctgttcgtcggc
 tacggccctggctttaaacacggcatcgaggccgacaccttcgagaacatcgagggtgtacaatctgat
 gtgtgacctgtgaatctgacctgtctcctaacaacggcaccacggatctctgaacctatctgtga
 agaatcccggtgtacacccttaagcaccctaaagaggttcaccctctgggtccagtgctcctttcaccaga
 aatcctcgggacaacctgggtgctcttgcaacccttctatcctgcctatcgaggactttcagaccca
 gttcaacctgaccgtggccgaggaaaagatcatcaagcacgagacactgccctacggcagacctagag
 tgctgcagaaagagaacacccatctgcctgctgtcccagcaccagttcatgtccggctactcccaggac
 atcctgatgctctgtggacctcctacaccgtggaccggaacgatagcttctccaccgaggacttcag
 caactgcctgtaccaggatttcagaatccctctgagccccgtgcacaagtgcagcttctacaagaaca
 acaccaaggtgtcctacggcttctgtctcctccacagctgaacaagaactccagcggcatctactct
 gaggccctgctgaccaccaacatcgtgcccattgtaccagtccctccaagtgtctggcgggtacttcca
 cgacaccctgtgaggaagtacgccgaagaaagaaacggcgtgaacgtggtgtctggccccgtgttcg
 acttcgactacgacggcagatgcgactctctggaaaacctgcggcagaaaagacgagtgtccggaat
 caagagatcctgattcctacacacttctttatcgtgctgaccagctgcaaggatacctctcagacccc
 tctgactgcgagaatctggacaccttgcccttcattctgcctcacagaaccgacaactccgagtcct
 gtgtgcacggcaagcacgactcctcttgggtcgaagaactgctgatgctgcaccggggcagaatcacc

gatgtggaacacatcacccggcctgagcttctaccagcagcggaagaacctgtgtccgatatcctgaa
 gctgaaaacccatctgccaaccttcagccaagaggacctgatcaacgacaagacccacacctgtcctc
 catgtcctgctccagaactgctcggaggccctctgtgttctgtttccacctaagccaaaggacaca
 ctgatgatctctcggacccctgaagtgacctgctgtggtggtgatgtgtctcacgaagatcccgaagt
 caagttcaattggtacgtggacggcgtggaagtgcacaacgccaaagaccaagcctagagaggaacagt
 acaactccacctacagagtgggtgtccgtgctgactgtgctgcaccaggattggctgaacggcaaagag
 tacaagtgc aaagtgtccaacaaggctctgcccgtcctatcgaaaagaccatctccaaggctaaggg
 ccagcctcgggaacctcaggtttacaccctgcctccatctcgggaagagatgaccaagaaccaggtgt
 ccctgacctgcctgggtcaagggttctacccttccgatatcgccgtggaatgggagtc caatggccag
 cctgagaacaactacaagacaacccctcctgtgctggacagcgacggctcattcttctgtactctaa
 gctgacagtggacaagtcccgggtggcagcaaggcaatgtgttttctgtctgtgatgcacgaggccc
 tccacaatcactacaccagaagtccctgtctctgtcccttggaatgatagctcgag

Legend - **bold** = start/stop codon; underlined = nucleotide sequence of signal peptide.

SEQ ID NO: 79 - Azurocidin-ENPP3-FC Nucleotide sequence

atgaccagactgacctgctggccctgctggccggcctgctggccagcagcagagccgcca
 gcagggcagctgcagaaagaagtgtctcgacgccagcttcagaggcctggagaactgcagatgcgacg
 tggcctgcaaggacagaggcgactgctgctgggacttcgaggacacctgcgtggagagcaccagaatc
 tggatgtgcaacaagttcagatgcggcgagaccagactggaggccagcctgtgcagctgcagcgacga
 ctgcctgcagagaaaggactgctgcgccgactacaagagcgtgtgccagggcgagaccagctggctgg
 aggagaactgcgacaccgcccagcagagccagtgccccgagggttcgacctgcccccgctgatcctg
 ttcagcatggacggcttcagagccgagtagctgtacacctgggacaccctgatgcccacatcaaca
 gctgaagacctgcggcatccacagcaagtacatgagagccatgtacccaccaagaccttccccacc
 actacaccatcgtgaccggcctgtaccccgagagccacggcatcatcgacaacaacatgtacgacgtg
 aacctgaacaagaacttcagcctgagcagcaaggagcagaacaaccccgccctggtggcagggccagcc
 catgaacctgaccgccatgtaccagggtcctgaaggccgcccactacttctggcccgccagcgaggtgg
 ccatcaacggcagcttccccagcatctacatgccctacaacggcagcgtgcccttcgaggagagaatc
 agcaccctgctgaagtggctggacctgcccaggccgagagaccagattctacaccatgtacttcga
 ggagcccgcagcagcgccacgcggcgcccgctgagcgccagagtgatcaaggccctgcaggtgg
 tggaccacgccttcggcatgctgatggaggccctgaagcagagaaacctgcacaactgcgtgaacatc
 atcctgctggccgaccacggcatggaccagacctactgcaacaagatggagtacatgaccgactactt
 cccagaatcaacttcttctacatgtacgagggtcccgccccagaatcagagcccaacatcccc
 acgacttcttcagcttcaacagcgaggagatcgtgagaaacctgagctgcagaaagcccagaccagcac
 ttcaagccctacctgacccccgacctgcccagagactgcactacgccaagaacgtgagaatcgaca
 ggtgcacctgttcgtggaccagcagtggtggcgtgagaagcaagagcaacaccaactgcggcgccg
 gcaaccacggctacaacaacgagttcagaagcatggaggccatcttcttgcccacggccccagcttc
 aaggagaagaccgaggtggagcccttcgagaacatcgaggtgtacaacctgatgtgcacctgctgag
 aatccagcccgcacccaacaacggcacccacggcagcctgaaccacctgctgaaggtgcccttctacg
 agcccagccacgcggaggaggtgagcaagttcagcgtgtgcggttcgccaacccccctgccaccgag
 agcctggactgcttctgccccacctgcagaacagcaccagctggagcaggtgaaccagatgctgaa
 cctgaccagaggagatcaccgccacctgaaggtgaacctgcccttcggcagaccagagtgctgc
 agaagaactgtggaccactgcctgctgtaccacagagagtacgtgagcggttcggcaaggccatgaga
 atgcccattgtggagcagctacaccgtgccccagctggcgacaccagccccctgccccccacctgccc
 cgactgcctgagagccgacgtgagagtgccccccagcgagagccagaagtgcagcttctacctggccg
 acaagaacatcacccacggcttctgtaccccccgccagcaacagaaccagcgacagccagtagcag
 gccctgatcaccagcaacctgggtgcccatgtacgaggagttcagaaagatgtgggactacttccacag
 cgtgctgctgatcaagcagccaccgagagaaacggcgtgaacgtggtgagcggtcccatcttcgact
 acaactacgacggccacttcgacgccccgacgagatcaccaagcacctggccaacaccgacgtgccc
 atccccaccactacttctgtgggtgctgaccagctgcaagaacaagagccacacccccgagaactgccc
 cggctggctggacgtgctgcccttcattcatccccacagaccaccaacgtggagagctgccccgagg
 gcaagcccggaggccctgtgggtggaggagagattcaccgcccacatcgccagagtgagagacgtggag

ctgctgaccggcctggacttctaccaggacaaggtgcagcccgtagcgagatcctgcagctgaagac
ctacctgccaccttcgagaccaccatcgacaagaccacacctgccccccctgccccgccccgagc
tgctgggcgccccagcgtgttctgttccccccaagcccaaggacaccctgatgatcagcagaacc
cccaggtgacctgcgtggtggtggacgtgagccacgaggacccccgaggtgaagtccaactggtacgt
ggacggcgtggaggtgcacaacgccaaagaccaagcccagagaggagcagtacaacagcacctacagag
tggtgagcgtgctgaccgtgctgcaccaggactggctgaacggcaaggagtacaagtgaagggtgagc
aacaaggccctgccccgcccccatcgagaagaccatcagcaaggccaagggccagcccagagagccccca
ggtgtacaccctgccccccagcagagaggagatgaccaagaaccaggtgagcctgacctgcctggtga
agggcttctaccccagcgcacatcgccgtggagtgaggagagcaacggccagcccagagaacaactacaag
accaccccccccgctgctggacagcgcagcggcagcttcttctgtacagcaagctgaccgtggacaagag
cagatggcagcagggcaacgtgttcagctgcagcgtgatgcacgaggccctgcacaaccactacacc
agaagagcctgagcctgagccccggcaag

Cloning and Expression of ENPP1 and ENPP3 fusion polypeptides

ENPP1, or an ENPP1 polypeptide, is prepared as described in US 2015/0359858 A1, which is incorporated herein in its entirety by reference. ENPP1 is a transmembrane protein localized to the cell surface with distinct intramembrane domains. In order to express ENPP1 as a soluble extracellular protein, the transmembrane domain of ENPP1 may be swapped for the transmembrane domain of ENPP2 or a signal peptide sequence such as Azurocidin, which results in the accumulation of soluble, recombinant ENPP1 in the extracellular fluid of the baculovirus cultures. Signal sequences of any other known proteins may be used to target the extracellular domain of ENPP1 for secretion as well, such as but not limited to the signal sequence of the immunoglobulin kappa and lambda light chain proteins. Further, the disclosure should not be construed to be limited to the polypeptides described herein, but also includes polypeptides comprising any enzymatically active truncation of the ENPP1 extracellular domain.

ENPP1 is made soluble by omitting the transmembrane domain. Human ENPP1 (SEQ ID NO:1) was modified to express a soluble, recombinant protein by replacing its transmembrane region (e.g., residues 77-98) with the corresponding subdomain of human ENPP2 (NCBI accession NP 00112433 5, e.g., residues 12-30) or Azurocidin signal sequence (SEQ ID 42).

The modified ENPP1 sequence was cloned into a modified pFastbac FIT vector possessing a TEV protease cleavage site followed by a C-terminus 9-F IIS tag, and cloned and expressed in insect cells, and both proteins were expressed in a baculovirus system as described previously (*Albright, et al., 2012, Blood 120:4432-4440; Saunders, et al., 2011, J. Biol. Chem. 18:994-1004; Saunders, et al., 2008, Mol. Cancer Ther. 7:3352-3362*), resulting in the accumulation of soluble, recombinant protein in the extracellular fluid.

ENPP3 is poorly exported to the cell surface. Soluble ENPP3 polypeptide is constructed by replacing the signal sequence of ENPP3 with the native signal sequence of other ENPPs or Azurocidin or suitable signal sequences. Several examples of ENPP3 fusion constructs are disclosed in WO 2017/087936 . Soluble ENPP3 constructs are prepared by using the signal export signal sequence of other ENPP enzymes, such as but not limited to ENPP7 and/or ENPP5. Soluble ENPP3 constructs are prepared using a signal sequence comprised of a combination of the signal sequences of ENPP1 and ENPP2 ("ENPP1-2-1" or "ENPP121" hereinafter). Signal sequences of any other known proteins may be used to target the extracellular domain of ENPP3 for secretion as well, such as but not limited to the signal sequence of the immunoglobulin kappa and lambda light chain proteins. Further, the disclosure should not be construed to be limited to the constructs described herein, but also includes constructs comprising any enzymatically active truncation of the ENPP3 extracellular domain.

In certain embodiments, the ENPP3 polypeptide is soluble. In some embodiments, the polypeptide of the disclosure includes an ENPP3 polypeptide that lacks the ENPP3 transmembrane domain. In another embodiment, the polypeptide of the disclosure includes an ENPP3 polypeptide wherein the ENPP3 transmembrane domain has been removed and replaced with the transmembrane domain of another polypeptide, such as, by way of non-limiting example, ENPP2, ENPP5 or ENPP7 or Azurocidin signal sequence.

In some embodiments, the polypeptide of the disclosure comprises an IgG Fc domain. In certain embodiments, the polypeptide of the disclosure comprises an albumin domain. In other embodiments, the albumin domain is located at the C terminal region of the ENPP3 polypeptide. In yet other embodiments, the IgG Fc domain is located at the C terminal region of the ENPP3 polypeptide. In yet other embodiments, the presence of IgG Fc domain or albumin domain improves half-life, solubility, reduces immunogenicity and increases the activity of the ENPP3 polypeptide.

In certain embodiments, the polypeptide of the disclosure comprises a signal peptide resulting in the secretion of a precursor of the ENPP3 polypeptide, which undergoes proteolytic processing to yield the ENPP3 polypeptide. In other embodiments, the signal peptide is selected from the group consisting of signal peptides of ENPP2, ENPP5 and ENPP7. In yet other embodiments, the signal peptide is selected from the group consisting of SEQ ID NOs: 36-42.

In certain embodiments, the IgG Fc domain or the albumin domain is connected to the C terminal region of the ENPP3 polypeptide by a linker region. In other embodiments, the linker is selected from SEQ ID NOs: 43-75, where n is an integer ranging from 1-20.

Production and Purification of ENPP1 and ENPP3 fusion polypeptides

To produce soluble, recombinant ENPP1 polypeptide for in vitro use, polynucleotide encoding the extracellular domain of ENPP1 (Human NPP1 (NCBI accession NP_006199)) was fused to the Fc domain of IgG (referred to as "ENPP1-Fc") and was expressed in stable CHO cell lines. In some embodiments, ENPP1 polynucleotide encoding residues 96 to 925 of NCBI accession NP_006199 were fused to Fc domain to generate ENPP1 polypeptide.

Alternately the ENPP1 polypeptide can also be expressed from HEK293 cells, Baculovirus insect cell system or CHO cells or Yeast *Pichia* expression system using suitable vectors. The ENPP1 polypeptide can be produced in either adherent or suspension cells. Preferably the ENPP1 polypeptide is expressed in CHO cells. To establish stable cell lines the nucleic acid sequence encoding ENPP1 constructs are cloned into an appropriate vector for large scale protein production.

ENPP3 is produced by establishing stable transfections in either CHO or HEK293 mammalian cells. ENPP3 polynucleotide encoding ENPP3 (Human NPP3 (UniProtKB/Swiss-Prot: O14638.2) was fused to the Fc domain of IgG (referred to as "ENPP3-Fc") and was expressed in stable CHO cell lines. In some embodiments, ENPP3 polynucleotide encoding residues 49-875 of UniProtKB/Swiss-Prot: O14638.2 was fused to Fc domain to generate ENPP3 polypeptide. The ENPP3 polypeptide can be produced in either adherent or suspension cells. To establish stable cell lines the nucleic acid sequence encoding NPP3 fusion polypeptides of the disclosure into an appropriate vector for large scale protein production. There are a variety of these vectors available from commercial sources and any of those can be used. ENPP3 polypeptides are produced following the protocols established in WO 2017/087936, the contents of which are hereby incorporated by reference in their entirety. ENPP1 polypeptides are produced following the protocols established in *Albright, et al, 2015, Nat Commun. 6:10006*, the contents of which are hereby incorporated by reference in their entirety.

A suitable plasmid containing the desired polypeptide constructs of ENPP1 or ENPP3 can be stably transfected into expression plasmid using established techniques such as electroporation or lipofectamine, and the cells can be grown under antibiotic selection to enhance for stably transfected cells. Clones of single, stably transfected cells are then established and screened for high expressing clones of the desired fusion protein. Screening of the single cell clones for ENPP1 or ENPP3 polypeptide expression can be accomplished in a high-throughput manner in 96 well plates using the synthetic enzymatic substrate pNP-TMP as previously described (*Saunders, et al, 2008, Mol. Cancer Therap. 7(10):3352-62; Albright, et al, 2015, Nat Commun. 6:10006*).

Upon identification of high expressing clones for ENPP3 or ENPP1 polypeptides through screening, protein production can be accomplished in shaking flasks or bio-reactors previously described for ENPP1 (*Albright, et al, 2015, Nat Commun. 6:10006*). Purification of ENPP3 or ENPP1 polypeptides can be accomplished using a combination of standard purification techniques known in the art. These techniques are well known in art and are selected from techniques such as column chromatograph, ultracentrifugation, filtration, and precipitation. Column chromatographic purification is accomplished using affinity chromatography such as protein-A and protein-G resins, metal affinity resins such as nickel or copper, hydrophobic exchange chromatography, and reverse-phase high-pressure chromatography (HPLC) using C8-C14 resins. Ion exchange may also be employed, such as anion and cation exchange chromatography using commercially available resins such as Q-sepharose (anion exchange) and SP-sepharose (cation exchange), blue sepharose resin and blue-sephadex resin, and hydroxyapatite resins. Size exclusion chromatography using commercially available S-75 and S200 Superdex resins can also be employed, as known in the art. Buffers used to solubilize the protein and provide the selection media for the above described chromatographic steps, are standard biological buffers known to practitioners of the art and science of protein chemistry.

Some examples of buffers that are used in preparation include citrate, phosphate, acetate, tris(hydroxymethyl)aminomethane, saline buffers, glycine-HCL buffers, Cacodylate buffers, and sodium barbital buffers, which are well known in art. Using a single techniques, or a series of techniques in combination, and the appropriate buffer systems purified ENPP3 and the crude starting material side by side on a Coomassie stained polyacrylamide gel after a single purification step. The ENPP3 protein can then be additionally purified using additional techniques and/or chromatographic steps as described above, to reach substantially higher

purity such as ~99% purity adjusted to the appropriate pH, one can purify the ENPP1 or ENPP3 polypeptides described to greater than 99% purity from crude material.

Following purification, ENPP1-Fc or ENPP3-Fc was dialyzed into PBS supplemented with Zn²⁺ and Mg²⁺ (PBSplus) concentrated to between 5 and 7 mg/ml, and frozen at -80 °C in aliquots of 200-500 µl. Aliquots were thawed immediately prior to use and the specific activity of the solution was adjusted to 31.25 au/ml (or about 0.7 mg/ml depending on the preparation) by dilution in PBSplus.

Dosage & Mode of Administration

In another embodiment, the hsNPP1 or hsNPP3 is administered in one or more doses containing about 1.0 mg/kg to about 5.0 mg/kg NPP1 or about 1.0 mg/kg to about 5.0 mg/kg NPP3 respectively. In another embodiment, the hsNPP1 or hsNPP3 is administered in one or more doses containing about 1.0 mg/kg to about 10.0 mg/kg NPP1 or about 1.0 mg/kg to about 10.0 mg/kg NPP3.

The time period between doses of the hsNPP1 or hsNPP3 is at least 2 days and can be longer, for example at least 3 days, at least 1 week, 2 weeks or 1 month. In one embodiment, the administration is weekly, bi-weekly, or monthly.

The recombinant hsNPP1 or hsNPP3 can be administered in any suitable way, such as intravenously, subcutaneously, or intraperitoneally.

The recombinant hsNPP1 or hsNPP3 can be administered in combination with one or more additional therapeutic agents. Exemplary therapeutic agents include, but are not limited to Bisphosphonate, Statins, Fibrates, Niacin, Aspirin, Clopidogrel, and warfarin.

In some embodiments, the recombinant hsNPP1 or hsNPP3 and additional therapeutic agent are administered separately and are administered concurrently or sequentially. In some embodiments, the recombinant hsNPP1 or hsNPP3 is administered prior to administration of the additional therapeutic agent. In some embodiments, the recombinant hsNPP1 or hsNPP3 is administered after administration of the additional therapeutic agent. In other embodiments, the recombinant hsNPP1 or hsNPP3 and additional therapeutic agent are administered together.

Nucleic Acid Administration and Therapy

Viral Vectors for *in vivo* expression of ENPP1 and ENPP3

The nucleic acids encoding the polypeptide(s) useful within the disclosure may be used in gene therapy protocols for the treatment of the diseases or disorders contemplated herein. The improved construct encoding the polypeptide(s) can be inserted into the appropriate gene therapy vector and administered to a patient to treat or prevent the diseases or disorder of interest.

Vectors, such as viral vectors, have been used in the prior art to introduce genes into a wide variety of different target cells. Typically, the vectors are exposed to the target cells so that transformation can take place in a sufficient proportion of the cells to provide a useful therapeutic or prophylactic effect from the expression of the desired polypeptide (e.g., a receptor). The transfected nucleic acid may be permanently incorporated into the genome of each of the targeted cells, providing long lasting effect, or alternatively the treatment may have to be repeated periodically. In certain embodiments, the (viral) vector transfects liver cells *in vivo* with genetic material encoding the polypeptide(s) of the disclosure.

A variety of vectors, both viral vectors and plasmid vectors are known in the art (see for example U.S. Patent No. 5,252,479 and WO 93/07282). In particular, a number of viruses have been used as gene transfer vectors, including papovaviruses, such as SV40, vaccinia virus, herpes viruses including HSV and EBV, and retroviruses. Many gene therapy protocols in the prior art have employed disabled murine retroviruses. Several recently issued patents are directed to methods and compositions for performing gene therapy (see for example U.S. Patent Nos. 6,168,916; 6,135,976; 5,965,541 and 6,129,705). Each of the foregoing patents is incorporated by reference in its entirety herein. Hence, genetic material such as a polynucleotide comprising an NPP1 or an NPP3 sequence can be introduced to a mammal in order to treat VSMC proliferation.

Certain modified viruses are often used as vectors to carry a coding sequence because after administration to a mammal, a virus infects a cell and expresses the encoded protein. Modified viruses useful according to the disclosure are derived from viruses which include, for example: parvovirus, picornavirus, pseudorabies virus, hepatitis virus A, B or C, papillomavirus, papovavirus (such as polyoma and SV40) or herpes virus (such as Epstein-Barr Virus, Varicella Zoster Virus, Cytomegalovirus, Herpes Zoster and Herpes Simplex Virus types 1 and 2), an RNA virus or a retrovirus, such as the Moloney murine leukemia virus or a lentivirus (i.e. derived from Human Immunodeficiency Virus, Feline

Immunodeficiency Virus, equine infectious anemia virus, etc.). Among DNA viruses useful according to the disclosure are: Adeno-associated viruses adenoviruses, Alphaviruses, and Lentiviruses.

A viral vector is generally administered by injection, most often intravenously (by IV) directly into the body, or directly into a specific tissue, where it is taken up by individual cells. Alternately, a viral vector may be administered by contacting the viral vector *ex vivo* with a sample of the patient's cells, thereby allowing the viral vector to infect the cells, and cells containing the vector are then returned to the patient. Once the viral vector is delivered, the coding sequence expressed and results in a functioning protein. Generally, the infection and transduction of cells by viral vectors occur by a series of sequential events as follows: interaction of the viral capsid with receptors on the surface of the target cell, internalization by endocytosis, intracellular trafficking through the endocytic/ proteasomal compartment, endosomal escape, nuclear import, virion uncoating, and viral DNA double-strand conversion that leads to the transcription and expression of the recombinant coding sequence interest. (Colella *et al.*, *Mol Ther Methods Clin Dev.* 2017 Dec 1;8:87-104.).

Adeno-Associated Viral Vectors according to the disclosure

AAV refers to viruses belonging to the genus Dependovirus of the Parvoviridae family. The AAV genome is approximately 4.7 kilobases long and is composed of linear single-stranded deoxyribonucleic acid (ssDNA) which may be either positive- or negative-sensed. The genome comprises inverted terminal repeats (ITRs) at both ends of the DNA strand, and two open reading frames (ORFs): rep and cap. The rep frame is made of four overlapping genes encoding non-structural replication (Rep) proteins required for the AAV life cycle. The cap frame contains overlapping nucleotide sequences of structural VP capsid proteins: VP1, VP2 and VP3, which interact together to form a capsid of an icosahedral symmetry.

The terminal 145 nucleotides are self-complementary and are organized so that an energetically stable intramolecular duplex forming a T-shaped hairpin may be formed. These hairpin structures function as an origin for viral DNA replication, serving as primers for the cellular DNA polymerase complex. Following wild type AAV infection in mammalian cells the rep genes (i.e. Rep78 and Rep52) are expressed from the P5 promoter and the P19 promoter, respectively, and both Rep proteins have a function in the replication of the viral

genome. A splicing event in the rep ORF results in the expression of actually four Rep proteins (i.e. Rep78, Rep68, Rep52 and Rep40). However, it has been shown that the unspliced mRNA, encoding Rep78 and Rep52 proteins, in mammalian cells are sufficient for AAV vector production. Also in insect cells the Rep78 and Rep52 proteins suffice for AAV vector production.

AAV is a helper-dependent virus, that is, it requires co-infection with a helper virus (e.g., adenovirus, herpesvirus, or vaccinia virus) in order to form functionally complete AAV virions. In the absence of co-infection with a helper virus, AAV establishes a latent state in which the viral genome inserts into a host cell chromosome or exists in an episomal form, but infectious virions are not produced. Subsequent infection by a helper virus "rescues" the integrated genome, allowing it to be replicated and packaged into viral capsids, thereby reconstituting the infectious virion. While AAV can infect cells from different species, the helper virus must be of the same species as the host cell. Thus, for example, human AAV replicates in canine cells that have been co-infected with a canine adenovirus.

To produce infectious recombinant AAV (rAAV) containing a heterologous nucleic acid sequence, a suitable host cell line can be transfected with an AAV vector containing the heterologous nucleic acid sequence, but lacking the AAV helper function genes, rep and cap. The AAV-helper function genes can then be provided on a separate vector. Also, only the helper virus genes necessary for AAV production (i.e., the accessory function genes) can be provided on a vector, rather than providing a replication-competent helper virus (such as adenovirus, herpesvirus, or vaccinia).

Collectively, the AAV helper function genes (i.e., rep and cap) and accessory function genes can be provided on one or more vectors. Helper and accessory function gene products can then be expressed in the host cell where they will act in trans on rAAV vectors containing the heterologous nucleic acid sequence. The rAAV vector containing the heterologous nucleic acid sequence will then be replicated and packaged as though it were a wild-type (wt) AAV genome, forming a recombinant virion. When a patient's cells are infected with the resulting rAAV virions, the heterologous nucleic acid sequence enters and is expressed in the patient's cells.

Because the patient's cells lack the rep and cap genes, as well as the accessory function genes, the rAAV cannot further replicate and package their genomes. Moreover, without a source of 5 rep and cap genes, wtAAV cannot be formed in the patient's cells.

The AAV vector typically lacks rep and cap frames. Such AAV vectors can be replicated and packaged into infectious viral particles when present in a host cell that has been transfected with a vector encoding and expressing rep and cap gene products (i.e. AAV Rep and Cap proteins), and wherein the host cell has been transfected with a vector which encodes and expresses a protein from the adenovirus open reading frame E4orf6.

Delivery of a protein of interest to the cells of a mammal is accomplished by first generating an AAV vector comprising DNA encoding the protein of interest and then administering the vector to the mammal. Thus, the disclosure should be construed to include AAV vectors comprising DNA encoding the polypeptide(s) of interest. Once armed with the present disclosure, the generation of AAV vectors comprising DNA encoding this/these polypeptide(s) will be apparent to the skilled artisan.

In one embodiment, the disclosure relates to an adeno-associated viral (AAV) expression vector comprising a sequence encoding mammal ENPP1 or mammal ENPP3, and upon administration to a mammal the vector expresses an ENPP1 or ENPP3 precursor in a cell, the precursor including an Azurocidin signal peptide fused at its carboxy terminus to the amino terminus of ENPP1 or ENPP3. The ENPP1 or ENPP3 precursor may include a stabilizing domain, such as an IgG Fc region or human albumin. Upon secretion of the precursor from the cell, the signal peptide is cleaved off and enzymatically active soluble mammal ENPP1 or ENPP3 is provided extracellularly.

An AAV expression vector may include an expression cassette comprising a transcriptional regulatory region operatively linked to a nucleotide sequence comprising a transcriptional regulatory region operatively linked to a recombinant nucleic acid sequence encoding a polypeptide comprising an Azurocidin signal peptide sequence and an ectonucleotide pyrophosphatase/phosphodiesterase (ENPP1) polypeptide sequence.

In some embodiments, the expression cassette comprises a promoter and enhancer, the Kozak sequence GCCACCATGG, a nucleotide sequence encoding mammal NPP1 protein or a nucleotide sequence encoding mammal NPP3 protein, other suitable regulatory elements and a polyadenylation signal.

In some embodiments, the AAV recombinant genome of the AAV vector according to the disclosure lacks the rep open reading frame and/or the cap open reading frame.

The AAV vector according to the disclosure comprises a capsid from any serotype. In general, the AAV serotypes have genomic sequences of significant homology at the amino acid and the nucleic acid levels, provide an identical set of genetic functions, and replicate and assemble through practically identical mechanisms. In particular, the AAV of the present disclosure may belong to the serotype 1 of AAV (AAV1), AAV2, AAV3 (including types 3A and 3B), AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAVrh10, AAV11, avian AAV, bovine AAV, canine AAV, equine AAV, or ovine AAV.

Examples of the sequences of the genome of the different AAV serotypes may be found in the literature or in public databases such as GenBank. For example, GenBank accession numbers NC_001401.2 (AAV2), NC_001829.1 (AAV4), NC_006152.1 (AAV5), AF028704.1 (AAV6), NC_006260.1 (AAV7), NC_006261.1 (AAV8), AX753250.1 (AAV9) and AX753362.1 (AAV10).

In some embodiments, the adeno-associated viral vector according to the disclosure comprises a capsid derived from a serotype selected from the group consisting of the AAV2, AAV5, AAV7, AAV8, AAV9, AAV10 and AAVrh10 serotypes. In another embodiment, the serotype of the AAV is AAV8. If the viral vector comprises sequences encoding the capsid proteins, these may be modified so as to comprise an exogenous sequence to direct the AAV to a particular cell type or types, or to increase the efficiency of delivery of the targeted vector to a cell, or to facilitate purification or detection of the AAV, or to reduce the host response.

In certain embodiments, the rAAV vector of the disclosure comprises several essential DNA elements. In certain embodiments, these DNA elements include at least two copies of an AAV ITR sequence, a promoter/enhancer element, a transcription termination signal, any necessary 5' or 3' untranslated regions which flank DNA encoding the protein of interest or a biologically active fragment thereof. The rAAV vector of the disclosure may also include a portion of an intron of the protein of interest. Also, optionally, the rAAV vector of the disclosure comprises DNA encoding a mutated polypeptide of interest.

In certain embodiments, the vector comprises a promoter/regulatory sequence that comprises a promiscuous promoter which is capable of driving expression of a heterologous gene to high levels in many different cell types. Such promoters include but are not limited to the cytomegalovirus (CMV) immediate early promoter/enhancer sequences, the Rous sarcoma virus promoter/enhancer sequences and the like. In certain embodiments, the

promoter/regulatory sequence in the rAAV vector of the disclosure is the CMV immediate early promoter/enhancer. However, the promoter sequence used to drive expression of the heterologous gene may also be an inducible promoter, for example, but not limited to, a steroid inducible promoter, or may be a tissue specific promoter, such as, but not limited to, the skeletal α -actin promoter which is muscle tissue specific and the muscle creatine kinase promoter/enhancer, and the like.

In certain embodiments, the rAAV vector of the disclosure comprises a transcription termination signal. While any transcription termination signal may be included in the vector of the disclosure, in certain embodiments, the transcription termination signal is the SV40 transcription termination signal.

In certain embodiments, the rAAV vector of the disclosure comprises isolated DNA 5 encoding the polypeptide of interest, or a biologically active fragment of the polypeptide of interest. The disclosure should be construed to include any mammalian sequence of the polypeptide of interest, which is either known or unknown. Thus, the disclosure should be construed to include genes from mammals other than humans, which polypeptide functions in a substantially similar manner to the human polypeptide. Preferably, the nucleotide sequence comprising the gene encoding the polypeptide of interest is about 50% homologous, more preferably about 70% homologous, even more preferably about 80% homologous and most preferably about 90% homologous to the gene encoding the polypeptide of interest.

Further, the disclosure should be construed to include naturally occurring variants or recombinantly derived mutants of wild type protein sequences, which variants or mutants render the polypeptide encoded thereby either as therapeutically effective as full-length polypeptide, or even more therapeutically effective than full-length polypeptide in the gene therapy methods of the disclosure.

The disclosure should also be construed to include DNA encoding variants which retain the polypeptide's biological activity. Such variants include proteins or polypeptides which have been or may be modified using recombinant DNA technology, such that the protein or polypeptide possesses additional properties which enhance its suitability for use in the methods described herein, for example, but not limited to, variants conferring enhanced stability on the protein in plasma and enhanced specific activity of the protein. Analogs can differ from naturally occurring proteins or peptides by conservative amino acid sequence differences or by modifications which do not affect sequence, or by both. For example,

conservative amino acid changes may be made, which although they alter the primary sequence of the protein or peptide, do not normally alter its function.

The disclosure is not limited to the specific rAAV vector exemplified in the experimental examples; rather, the disclosure should be construed to include any suitable AAV vector, including, but not limited to, vectors based on AAV-1, AAV-3, AAV-4 and AAV-6, and the like. Also included in the disclosure is a method of treating a mammal having a disease or disorder in an amount effective to provide a therapeutic effect.

The method comprises administering to the mammal an rAAV vector encoding the polypeptide of interest. Preferably, the mammal is a human. Typically, the number of viral vector genomes/mammal which are administered in a single injection ranges from about 1×10^8 to about 5×10^{16} . Preferably, the number of viral vector genomes/mammal which are administered in a single injection is from about 1×10^{10} to about 1×10^{15} ; more preferably, the number of viral vector genomes/mammal which are administered in a single injection is from about 5×10^{10} to about 5×10^{15} ; and, most preferably, the number of viral vector genomes which are administered to the mammal in a single injection is from about 5×10^{10} to about 5×10^{14} .

When the method of the disclosure comprises multiple site simultaneous injections, or several multiple site injections comprising injections into different sites over a period of several hours (for example, from about less than one hour to about two or three hours) the total number of viral vector genomes administered may be identical, or a fraction thereof or a multiple thereof, 15 to that recited in the single site injection method.

For administration of the rAAV vector of the disclosure in a single site injection, in certain embodiments a composition comprising the virus is injected directly into an organ of the subject (such as, but not limited to, the liver of the subject).

For administration to the mammal, the rAAV vector may be suspended in a pharmaceutically acceptable carrier, for example, HEPES buffered saline at a pH of about 7.8. Other useful pharmaceutically acceptable carriers include, but are not limited to, glycerol, water, saline, ethanol and other pharmaceutically acceptable salt solutions such as phosphates and salts of organic acids. Examples of these and other pharmaceutically acceptable carriers are described in Remington's Pharmaceutical Sciences (1991, Mack Publication Co., New Jersey). The rAAV vector of the disclosure may also be provided in the form of a kit, the kit comprising, for example, a freeze-dried preparation of vector in a dried

salts formulation, sterile water for suspension of the vector/salts composition and instructions for suspension of the vector and administration of the same to the mammal

The published application, US 2017/0290926 –Smith et al., the contents of which are incorporated by reference in their entirety herein, describes in detail the process by which AAV vectors are generated, delivered and administered.

RNA based in vivo expression of ENPP1 and ENPP3 polypeptides

The present disclosure provides compositions and methods for the production and delivery of recombinant double-stranded RNA molecules (dsRNA that encode ENPP1 or ENPP3 polypeptides described herein. The double stranded RNA particle (dsRP) can contain a dsRNA molecule enclosed in a capsid or coat protein. The dsRNA molecule can be a viral genome or portion of a genome, which can be derived from a wild-type viral genome. The RNA molecule can encode an RNA-dependent RNA polymerase (RDRP) and a polyprotein that forms at least part of a capsid or coat protein. The RNA molecule can also contain an RNA sub-sequence that encodes an ENPP1 or ENPP3 polypeptides that are translated by the cellular components of a host cell. When the dsRP is transfected into a host cell the sub-sequence can be translated by the cellular machinery of the host cell to produce the ENPP1 or ENPP3 polypeptides.

In another aspect the disclosure provides a method of producing a protein product in a host cell. The method includes transfecting a host cell with a dsRP having a recombinant double-stranded RNA molecule (dsRNA) and a capsid or coat protein. The RNA molecule can encode an RNA-dependent RNA polymerase and a polyprotein that forms at least part of the capsid or coat protein, and the dsRP can be able to replicate in the host cell. The RNA molecule has at least one RNA sub-sequence that encodes ENPP1 or ENPP3 polypeptides that is translated by cellular components of the host cell.

In another aspect the disclosure provides an RNA molecule translatable by a host cell. The RNA molecule can be any RNA molecule that encodes the ENPP1 or ENPP3 polypeptides described herein. In one embodiment the RNA molecule encodes an RNA-dependent RNA polymerase and a polyprotein that forms at least part of a capsid or coat protein of a dsRP and, optionally, can have at least one sub-sequence of RNA that encodes an additional protein product.

Production of dsRP

A dsRP of the disclosure can also be produced by presenting to a host cell a plasmid or other DNA molecule encoding a dsRP of the disclosure or encoding the genes of the dsRP. The plasmid or DNA molecule containing nucleotide sequences encoding desired protein such as ENPP1 or ENPP3 polypeptide is then transfected into the host cell and the host cell begins producing the dsRP of the disclosure. The dsRP can also be produced in the host cell by presenting to the host cell an RNA molecule encoding the genes of the dsRP. The RNA molecule can be (+)-strand RNA.

Once the dsRP of the disclosure has been presented to the host cell (or a plasmid encoding the genes of the dsRP of the disclosure, or an RNA molecule encoding the genes of the dsRP), the dsRP will be produced within the host cell using the cellular components of the host cell. The dsRP of the disclosure is therefore self-sustaining within the host cell and is propagated within the host cell. The host cell can be any suitable host cell such as, for example, a eukaryotic cell, a mammalian cell, a fungal cell, a bacterial cell, an insect cell, or a yeast cell. The host cell can propagate a recombinant dsRP after a recombinant dsRNA molecule of the disclosure or a DNA molecule encoding a dsRP of the disclosure is presented to and taken up by the host cell.

Methods of Producing a dsRNA Virus or dsRP

The disclosure also provides methods of producing a dsRP of the disclosure. A double-stranded or single-stranded RNA or DNA molecule can be presented to a host cell. The amplification of the dsRNA molecules in the host cell utilizes the natural production and assembly processes already present in many types of host cells (e.g., yeast). The disclosure can thus be applied by presenting to a host cell a single-stranded or double-stranded RNA or DNA molecule of the disclosure, which is taken up by the host cell and is utilized to produce the recombinant dsRP and protein or peptide encoded by the RNA sub-sequence using the host cell's cellular components. The disclosure can also be applied by providing to the host cell a linear or circular DNA molecule (e.g., a plasmid or vector) containing one or more sequences coding for an RNA-dependent RNA polymerase, a polyprotein that forms at least part of the capsid or coat protein of the dsRP, and a sub-sequence encoding the protein of interest such as ENPP1 or ENPP3 polypeptides as disclosed herein.

The presentation of a dsRNA or ssRNA molecule of the disclosure can be performed in any suitable way such as, for example, by presenting an RNA molecule of the disclosure directly to the host cell as “naked” or unmodified single-stranded or double-stranded RNA. The RNA molecule can be transfected (or transformed) into a yeast, bacterial, or mammalian host cell by any suitable method, for example by electroporation, exposure of the host cell to calcium phosphate, or by the production of liposomes that fuse with the cell membrane and deposit the viral sequence inside. It can also be performed by a specific mechanism of direct introduction of dsRNA from killer viruses or heterologous dsRNA into the host cell. This step can be optimized using a reporter system, such as red fluorescent protein (RFP), or by targeting a specific constitutive gene transcript within the host cell genome. This can be done by using a target with an obvious phenotype or by monitoring by quantitative reverse transcriptase PCR (RT-PCR).

In some embodiments a DNA molecule (e.g., a plasmid or other vector) that encodes an RNA molecule of the disclosure is introduced into the host cell. The DNA molecule can contain a sequence coding for the RNA molecule of a dsRP of the disclosure. The DNA molecule can code for an entire genome of the dsRP, or a portion thereof. The DNA molecule can further code for the at least one sub-sequence of RNA that produces the additional (heterologous) protein product. The DNA sequence can also code for gag protein or gag-pol protein, and as well as any necessary or desirable promoters or other sequences supporting the expression and purpose of the molecule. The DNA molecule can be a linear DNA, a circular DNA, a plasmid, a yeast artificial chromosome, or may take another form convenient for the specific application.

In one embodiment the DNA molecule can further comprise T7 ends for producing concatamers and hairpin structures, thus allowing for propagation of the virus or dsRP sequence in the host cell. The DNA molecule can be transfected or transformed into the host cell and then, using the host cellular machinery, transcribed and thus provide the dsRNA molecule having the at least one sub-sequence of RNA to the host cell. The host cell can then produce the encoded desired ENPP1 or ENPP3 polypeptide. The dsRNA can be packaged in the same manner that a wild-type virus would be, using the host cell's metabolic processes and machinery. The ENPP1 or ENPP3 polypeptide is also produced using the host cell's metabolic processes and cellular components.

The patent, US 10266834 by Brown et al., the contents of which are incorporated by reference in their entirety herein, describes in detail the process by which dsRNA particles that encode polypeptides are generated, delivered and administered.

ENPP1 Coated Stents and ENPP3 Coated stents

Stents are typically elongated structures used to keep open lumens (e.g., openings in the body) found in various parts of the body so that the parts of the body containing those lumens may function properly. Stents are often used in the treatment of atherosclerosis, a disease of the vascular system in which arteries become partially, and sometimes completely, occluded with substances that may include lipids, cholesterol, calcium, and various types of cells, such as smooth muscle cells and platelets.

Stents located within any lumen in the body may not always prevent partial or complete restenosis. In particular, stents do not always prevent the re-narrowing of an artery following Percutaneous transluminal angioplasty (PTA). In some cases, the introduction and presence of the stent itself in the artery or vein can create regions of trauma or tissue injury such as, e.g., tears in the inner lining of the artery, called the endothelium requiring further surgeries post stent placement.

It is believed that such trauma or tissue injury can trigger migration of vascular smooth muscle cells, which are usually separated from the arterial lumen by the endothelium, into the arterial lumen, where they proliferate to create a mass of cells that may, in a matter of days or weeks, occlude the artery. Such re-occlusion, which is sometimes seen after PTA, is an example of restenosis. Coating a stent with therapeutic agent such as ENPP1 agent or ENPP3 agent is expected to prevent and/or reduce vascular smooth muscle cell proliferation which in return reduces the occurrence of or treats restenosis.

In some embodiments, the patient is need of surgery and/or has tissue injury due to the presence of a prior implanted non-eluting stent.

In some embodiments, the patient is need of surgery and/or has tissue injury due to the presence of a prior implanted eluting stent that elutes therapeutic agents other than ENPP1 agent or ENPP3 agent.

In some embodiments, the prior stent that had caused the tissue injury is removed and replaced with ENPP1 agent coated stent.

In some embodiments, the prior stent that had caused the tissue injury is removed and replaced with ENPP3 agent coated stent.

In some embodiments, the prior stent that had caused the tissue injury is not removed and the ENPP1 agent coated stent is implanted adjacent to the prior stent.

In some embodiments, the prior stent that had caused the tissue injury is not removed and the ENPP3 agent coated stent is implanted adjacent to the prior stent.

ENPP1 or ENPP3 coated stents are typically hollow, cylindrical structures made from struts or interconnected filaments. Stents are usually implanted at their site of use in the body by attaching them in a compressed state to a catheter that is directed through the body to the site of stent use. Vascular stents are frequently used in blood vessels to open the vessel and provide improved blood flow. The stent can be expanded to a size which enables it to keep the lumen open by supporting the walls of the lumen once it is positioned at the desired site. Vascular stents can be collapsed to reduce their diameter so that the stent can be guided through a patient's arteries or veins to reach the site of deployment. Stents are typically either coupled to the outside of the balloon for expansion by the expanding balloon or are self-expanding upon removal of a restraint such as a wire or sleeve maintaining the stent in its collapsed state.

Vascular stents are often made of metal to provide the strength necessary to support the occluded arterial walls. Two of the preferred metals are Nitinol alloys of nickel and titanium, and stainless steel. Other materials that can be used in fabricating stents are ceramics, polymers, and plastics. The polymer may be a polymer having no functional groups. Alternatively, the polymer may be one having functional groups, but none that are reactive with the ENPP1 agent or ENPP3 agent. The polymer may include a biodegradable polymer. For example, the polymer may include a polymer selected from the group consisting of polyhydroxy acids, polyanhydrides, polyphosphazenes, polyalkylene oxalates, biodegradable polyamides, polyorthoesters, polyphosphoesters, polyorthocarbonates, and blends or copolymers thereof. The polymer may also include a biostable polymer, alone or in combination with a biodegradable polymer. For example, the polymer may include a polymer selected from the group consisting of polyurethanes, silicones, polyacrylates, polyesters, polyalkylene oxides, polyalcohols, polyolefins, polyvinyl chlorides, cellulose and its derivatives, fluorinated polymers, biostable polyamides, and blends or copolymers thereof.

The effect of different stent designs on the drug distribution pattern has been scrutinized in experimental studies and also tested in clinical trials (*Hwang CW, Wu D, Edelman ER. 2001. Physiological transport forces govern drug distribution for stent-based delivery. Circulation, 104: 600–5; & Takebayashi H, Mintz GS, Carlier SG, et al. 2004. Nonuniform strut distribution correlates with more neointimal hyperplasia after Sirolimus-eluting stent implantation. Circulation, 110:3430–4*). Although a large number of stent designs have been developed to date, only the multicellular design is currently most commonly used; they can be categorized into “closed cell” and “open cell” configurations (*Rogers CDK. 2002. Drug-eluting stents: role of stent design, delivery vehicle, and drug selection. Rev Cardiovasc Med, 3(Suppl 5): S10–15.*). A closed cell stent has a uniform cell expansion and constant cell spacing when deployed in a curved vascular segment, which gives more uniform drug distribution (Rogers 2002). An open cell stent has a greater variation in the surface coverage between the inner and outer curvatures in the curved segment but gives better conformability to curved surface at the expense of less uniform drug distribution (Rogers 2002). The majority of current stents use a closed cell design. The optimal stent design for drug delivery would have a large stent surface area, a small cell gap, and minimal strut deformation after deployment while maintaining conformability, radial support, and flexibility to reach the complex coronary lesions. Several examples of the different geometrical stent structures are described in Paisal et al. (*Muhammad Sufyan Amir Paisal et al 2017 IOP Conf. Ser.: Mater. Sci. Eng. 165 012003*)

ENPP1 coated stents or ENPP3 coated stents are prepared by applying a coating composition comprising an effective amount of ENPP1 agent or ENPP3 agent respectively. The coating composition preferably includes an amount of the ENPP1 agent or ENPP3 agent that is sufficient to be therapeutically effective for inhibiting regrowth of plaque or inhibiting restenosis or preventing vascular smooth cell proliferation.

In one embodiment, the coating composition comprises from about 1 wt % to about 50 wt % ENPP1 polypeptide, based on the total weight of the coating composition. In another embodiment, the coating composition comprises from about 5 wt % to about 30 wt % ENPP1 polypeptide. In yet another embodiment, the coating composition comprises from about 10 wt % to about 20 wt % ENPP1 polypeptide.

In one embodiment, the coating composition comprises from about 1 wt % to about 50 wt % ENPP3 polypeptide, based on the total weight of the coating composition. In another

embodiment, the coating composition comprises from about 5 wt % to about 30 wt % ENPP3 polypeptide. In yet another embodiment, the coating composition comprises from about 10 wt % to about 20 wt % ENPP3 polypeptide.

In one embodiment, the coating composition comprises from about 1 µg/ml to about 10 mg/ml of ENPP1 polypeptide. In another embodiment, the coating composition comprises from about 100 µg/ml to 5mg/ml ENPP1 polypeptide. In yet another embodiment, the coating composition comprises from about 500 µg/ml to about 2 mg/ml ENPP1 polypeptide.

In a related embodiment, the ENPP1 polypeptide of the coating composition is ENPP1-Fc.

In a related embodiment, the ENPP1 polypeptide of the coating composition is ENPP1-Albumin.

In one embodiment, the coating composition comprises from about 1 µg/ml to about 10 mg/ml of ENPP3 polypeptide. In another embodiment, the coating composition comprises from about 100 µg/ml to 5mg/ml ENPP3 polypeptide. In yet another embodiment, the coating composition comprises from about 500 µg/ml to about 2 mg/ml ENPP3 polypeptide.

In a related embodiment, the ENPP3 polypeptide of the coating composition is ENPP3-Fc.

In a related embodiment, the ENPP3 polypeptide of the coating composition is ENPP3-Albumin.

In one embodiment, the coating composition comprises from about 1 ng/µl to about 1000 µg/µl of ENPP1 mRNA. In another embodiment, the coating composition comprises from about 100 ng/µl to 10µg/µl ENPP1 mRNA. In yet another embodiment, the coating composition comprises from about 50 ng/µl to about 5 µg/µl ENPP1 mRNA.

In one embodiment, the coating composition comprises from about 1 ng/µl to about 1000 µg/µl of ENPP1-Fc mRNA. In another embodiment, the coating composition comprises from about 100 ng/µl to 10µg/µl ENPP1 -Fc mRNA. In yet another embodiment, the coating composition comprises from about 50 ng/µl to about 5 µg/µl ENPP1-Fc mRNA.

In one embodiment, the coating composition comprises from about 1 ng/µl to about 1000 µg/µl of ENPP1-Albumin mRNA. In another embodiment, the coating composition comprises from about 100 ng/µl to 10µg/µl ENPP1-Albumin mRNA. In yet another

embodiment, the coating composition comprises from about 50 ng/ μ l to about 5 μ g/ μ l ENPP1-Albumin mRNA.

In one embodiment, the coating composition comprises from about 1ng/ μ l to about 1000 μ g/ μ l of ENPP3 mRNA. In another embodiment, the coating composition comprises from about 100 ng/ μ l to 5 μ g/ μ l ENPP3 mRNA. In yet another embodiment, the coating composition comprises from about 500 ng/ μ l to about 2 μ g/ μ l ENPP3 mRNA.

In one embodiment, the coating composition comprises from about 1ng/ μ l to about 1000 μ g/ μ l of ENPP3-Fc mRNA. In another embodiment, the coating composition comprises from about 100 ng/ μ l to 5 μ g/ μ l ENPP3-Fc mRNA. In yet another embodiment, the coating composition comprises from about 500 ng/ μ l to about 2 μ g/ μ l ENPP3-Fc mRNA.

In one embodiment, the coating composition comprises from about 1ng/ μ l to about 1000 μ g/ μ l of ENPP3-Albumin mRNA. In another embodiment, the coating composition comprises from about 100 ng/ μ l to 5 μ g/ μ l ENPP3-Albumin mRNA. In yet another embodiment, the coating composition comprises from about 500 ng/ μ l to about 2 μ g/ μ l ENPP3-Albumin mRNA.

Stents may be coated with a substance, such as a biodegradable or biostable polymer, to improve the biocompatibility of the stent, making it less likely to cause an allergic or other immunological response in a patient. A coating substance may also add to the strength of the stent. Some known coating substances include organic acids, their derivatives, and synthetic polymers that are either biodegradable or biostable. Biostable coating substances do not degrade in the body, biodegradable coating substances can degrade in the body.

The coating composition comprises an effective amount of carrier which helps in the coating process to ensure that the therapeutic molecules such as ENPP1 agent or ENPP3 agent adhere to the stent surface and also facilitate in eluting the therapeutic agent into the body at the site of stent placement. The carrier could be a liquid carrier or a solid carrier. The coating composition may alternatively comprise more than one solid compound in a solid carrier. The coating composition may further comprise both a liquid carrier and a solid carrier. In a still further aspect, the coating composition may also comprise more than one type of nonpolymeric or polymeric compound in the carrier and may further comprise both a polymeric material and a nonpolymeric material in a solid or liquid carrier.

In another embodiment, two or more types of biodegradable compounds (polymers or non-polymers) may be blended together to obtain a liquid carrier for use in the coating composition. The biodegradable compounds can be liquids before they are mixed together, e.g., forming a homogeneous solution, mixture, or suspension. Alternatively, some of the biodegradable compounds may be solids before they are mixed with other liquid biodegradable compounds. The solid biodegradable compounds preferably dissolve when they are mixed with the liquid biodegradable compounds, resulting in a liquid carrier composition containing the different biodegradable compounds.

In another embodiment, the biodegradable carrier component of the coating composition is a solid, which dissolves when mixed with the biologically active component and any other components included in the coating composition.

The carrier could be a polymeric carrier. Some polymeric carriers are synthetic polymers. Examples of synthetic polymers that serve as reservoir matrices include but not limited to poly-n-butyl methacrylate, polyethylene-vinyl acetate, poly (lactide-co- Σ -caprolactone) copolymer, Fibrin, cellulose, Phosphorylcholine. Some eluting stent comprise porous 300 μ m ceramic layer containing therapeutic molecule -loaded nanocavities. Examples of drug eluting stents, stent structures and stent designs can be found in *Drug-Eluting Stent: A Review and Update, Vasc Health Risk Manag. 2005 Dec; 1(4): 263–276* and *Modern Stents: Where Are We Going?, Rambam Maimonides Med J. 2020 Apr; 11(2): e0017*.

The carriers in the coating composition may be either biodegradable or biostable. Biodegradable polymers are often used in synthetic biodegradable sutures. These polymers include polyhydroxy acids. Polyhydroxy acids suitable for use in the present invention include poly-L-lactic acids, poly- DL-lactic acids, polyglycolic acids, polylactides including homopolymers and copolymers of lactide (including lactides made from all stereo isomers of lactic acids, such as D-,L-lactic acid and meso lactic acid), polylactones, polycaprolactones, polyglycolides, polyparadioxanone, poly 1,4-dioxepan- 2-one, poly 1,5-dioxepan-2-one, poly 6,6-dimethyl-1, 4-dioxan-2-one, polyhydroxyvalerate, polyhydroxybuterate, polytrimethylene carbonate polymers, and blends of the foregoing.

Polylactones suitable for use in the present invention include polycaprolactones such as poly(ϵ -caprolactone), polyvalerolactones such as poly(δ -valerolactone), and polybutyrolactones such as poly(butyrolactone). Other biodegradable polymers that can be

used are polyanhydrides, polyphosphazenes, biodegradable polyamides such as synthetic polypeptides such as polylysine and polyaspartic acid, polyalkylene oxalates, polyorthoesters, polyphosphoesters, and polyorthocarbonates. Copolymers and blends of any of the listed polymers may be used. Polymer names that are identical except for the presence or absence of brackets represent the same polymers.

Biostable polymers suitable for use in the present invention include, but are not limited to polyurethanes, silicones such as polyalkyl siloxanes such as polydimethyl siloxane and polybutyl methacrylate, polyesters such as poly(ethylene terephthalate), polyalkylene oxides such as polyethylene oxide or polyethylene glycol, polyalcohols such as polyvinyl alcohols and polyethylene glycols, polyolefins such as poly-5 ethylene, polypropylene, poly(ethylene-propylene) rubber and natural rubber, polyvinyl chloride, cellulose and modified cellulose derivatives such as rayon, rayon-triacetate, cellulose acetate, cellulose acetate butyrate, cellophane, cellulose nitrate, cellulose propionate, cellulose ethers such as carboxymethyl cellulose and hydroxyalkyl celluloses, fluorinated polymers such as polytetrafluoroethylene (Teflon), and bio stable polyamides such as Nylon 66 and polycaprolactam. Fixed animal tissues such as glutaraldehyde fixed bovine pericardium can also be used. Polyesters and polyamides can be either biodegradable or biostable. Ester and amide bonds are susceptible to hydrolysis, which can contribute to biodegradation.

In some cases, the coating composition further comprises an effective amount of a non-polymeric carrier. The non-polymeric carrier can include one or more of fatty acid, biocompatible oil, or wax. Examples of non-polymeric biodegradable carriers include liquid oleic acid, vitamin E, peanut oil, and cottonseed oil, which are liquids that are both hydrophobic and biocompatible. In some cases, the nonpolymeric or polymeric carrier, can be a liquid at room and body temperature. In some cases, the nonpolymeric or polymeric carrier can be a solid at room and body temperature, or a solid at room temperature and a liquid at body temperature.

In another embodiment, the polymer solution can be formed into a film and the film then applied to the stent. Any of a variety of conventional methods of forming films can be used. For example, the polymer, ENPP1 agent or ENPP3 agent and solvent are preferably mixed into solution and then poured onto a smooth, flat surface such that a coating film is formed after the solution is dried to remove the solvent. The film can then be cut to fit the

stent on which it is to be used. The film may then be mounted, such as by wrapping, on the outer surface of a stent.

In another embodiment, the coated stent is prepared by spraying the stent with the liquid carrier comprising the therapeutic agent such as ENPP1 agent or ENPP3 agent resulting in a coating of uniform thickness on the struts of the stent. In another embodiment, the stent may be dip coated or immersed in the coating solution comprising carrier and therapeutic agent, such that the solution completely coats the struts of the stent. Alternatively, the stent may be painted with the coating solution comprising carrier and therapeutic agent, such as with a paint brush. In each of these coating applications, the entirety of both the outer and inner surfaces of the stent are preferably coated, although only portions of either or both surfaces may be coated in some embodiments.

As discussed above, the coating composition comprises a bioactive component and a biodegradable carrier component. Preferably, the coating composition comprises from 0.1% to 100% by weight of a biologically active component and from 1% to 99% by weight of a biodegradable carrier component. More preferably, the coating composition comprises from 0.1% to 50% by weight of a biologically active component and from 50% to 99.9% by weight of a biodegradable carrier component. The coating composition can be prepared in a number of ways including by simply mixing the bioactive component and the carrier component together to form a mixture, e.g., a solution or suspension. Alternatively, the bioactive component and the carrier component together are mixed in a suitable solvent, the coating is applied to the stent, and the solvent is removed. Preferably the coating composition is applied to the stent in its expanded state.

In addition to stents, examples of other medical devices that can be coated in accordance with aspects of the inventions disclosed herein include catheters, heart valves, pacemaker leads, annuloplasty rings and other medical implants. In other specific embodiments, coated angioplasty balloons and other coated medical devices can also comprise one of the coating compositions disclosed herein. However, stents are preferred. The coating composition may be applied to the stent (or other medical device) by any number of ways, e.g, by spraying the coating composition onto the stent, by immersing the stent in the coating composition, or by painting the stent with the coating composition. Preferably, a stent is coated in its expanded (i.e., enlarged diameter) form so that a sufficient amount of the coating composition will be applied to coat the entire surface of the expanded stent. When the

stent is immersed in the coating composition, the excess coating composition on the surface of the stent may be removed, such as by brushing off the excess coating composition with a paint brush. In each of these coating applications, preferably both the outer and inner surfaces of the stent are coated.

The coating compositions described herein preferably remain on a stent, partially or in substantial part, after the stent has been introduced to the body, for at least several days, for several weeks and more preferably for several months thereby slowly releasing the therapeutic agents such as ENPP1 agent or ENPP3 agent into the blood stream.

Pharmaceutical Compositions and Formulations

The disclosure provides pharmaceutical compositions comprising a polypeptide of the disclosure within the methods described herein. Such a pharmaceutical composition is in a form suitable for administration to a subject, or the pharmaceutical composition may further comprise one or more pharmaceutically acceptable carriers, one or more additional ingredients, or some combination of these. The various components of the pharmaceutical composition may be present in the form of a physiologically acceptable salt, such as in combination with a physiologically acceptable cation or anion, as is well known in the art.

In an embodiment, the pharmaceutical compositions useful for practicing the method of the disclosure may be administered to deliver a dose of between 1 ng/kg/day and 100 mg/kg/day. In other embodiments, the pharmaceutical compositions useful for practicing the disclosure may be administered to deliver a dose of between 1 ng/kg/day and 500 mg/kg/day.

The relative amounts of the active ingredient, the pharmaceutically acceptable carrier, and any additional ingredients in a pharmaceutical composition of the disclosure will vary, depending upon the identity, size, and condition of the subject treated and further depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between about 0.1% and about 100% (w/w) active ingredient.

Pharmaceutical compositions that are useful in the methods of the disclosure may be suitably developed for inhalational, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intrathecal, intravenous or another route of administration. Other contemplated formulations include projected nanoparticles, liposomal preparations, resealed erythrocytes containing the active ingredient, and immunologically-

based formulations. The route(s) of administration is readily apparent to the skilled artisan and depends upon any number of factors including the type and severity of the disease being treated, the type and age of the veterinary or human patient being treated, and the like.

The formulations of the pharmaceutical compositions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient into association with a carrier or one or more other accessory ingredients, and then, if necessary or desirable, shaping or packaging the product into a desired single- or multi-dose unit.

As used herein, a "unit dose" is a discrete amount of the pharmaceutical composition comprising a predetermined amount of the active ingredient. The amount of the active ingredient is generally equal to the dosage of the active ingredient that would be administered to a subject or a convenient fraction of such a dosage such as, for example, one-half or one-third of such a dosage. The unit dosage form may be for a single daily dose or one of multiple daily doses (e.g., about 1 to 4 or more times per day). When multiple daily doses are used, the unit dosage form may be the same or different for each dose.

The regimen of administration may affect what constitutes an effective amount. For example, several divided dosages, as well as staggered dosages may be administered daily or sequentially, or the dose may be continuously infused, or may be a bolus injection. Further, the dosages of the therapeutic formulations may be proportionally increased or decreased as indicated by the exigencies of the therapeutic or prophylactic situation. In certain embodiments, administration of the compound of the disclosure to a subject elevates the subject's plasma PPI to a level that is close to normal, where a normal level of PPI in mammals is 1-3 μM . "Close to normal" refers to 0 to 1.2 μM or 0-40% below or above normal, 30 nM to 0.9 μM or 1-30% below or above normal, 0 to 0.6 μM or 0-20% below or above normal, or 0 to 0.3 μM or 0-10% below or above normal.

Administration of the compositions of the present disclosure to a patient, such as a mammal, such as a human, may be carried out using known procedures, at dosages and for periods of time effective to treat a disease or disorder in the patient. An effective amount of the therapeutic compound necessary to achieve a therapeutic effect may vary according to factors such as the activity of the particular compound employed; the time of administration; the rate of excretion of the compound; the duration of the treatment; other drugs, compounds or materials used in combination with the compound; the state of the disease or disorder, age,

sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well-known in the medical arts. Dosage regimens may be adjusted to provide the optimum therapeutic response. Dosage is determined based on the biological activity of the therapeutic compound which in turn depends on the half-life and the area under the plasma time of the therapeutic compound curve. The polypeptide according to the disclosure is administered at an appropriate time interval of every 2 days, or every 4 days, or every week or every month so as to achieve a continuous level of plasma PPI that is either close to the normal (1-3 μM) level or above (30-50% higher than) normal levels of PPI. Therapeutic dosage of the polypeptides of the disclosure may also be determined based on half-life or the rate at which the therapeutic polypeptide is cleared out of the body. The polypeptide according to the disclosure is administered at appropriate time intervals of either every 2 days, or every 4 days, every week or every month so as to achieve a constant level of enzymatic activity of ENPP1 or ENPP3 polypeptides.

For example, several divided doses may be administered daily, or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. A non-limiting example of an effective dose range for a therapeutic compound of the disclosure is from about 0.01 and 50 mg/kg of body weight/per day. In certain embodiments, the effective dose range for a therapeutic compound of the disclosure is from about 50 ng to 500 ng/kg, preferably 100 ng to 300 ng/kg of bodyweight. One of ordinary skill in the art would be able to study the relevant factors and make the determination regarding the effective amount of the therapeutic compound without undue experimentation.

The compound can be administered to a patient as frequently as several times daily, or it may be administered less frequently, such as once a day, once a week, once every two weeks, once a month, or even less frequently, such as once every several months or even once a year or less. It is understood that the amount of compound dosed per day may be administered, in non-limiting examples, every day, every other day, every 2 days, every 3 days, every 4 days, or every 5 days. For example, with every other day administration, a 5 mg per day dose may be initiated on Monday with a first subsequent 5 mg per day dose administered on Wednesday, a second subsequent 5 mg per day dose administered on Friday, and so on. The frequency of the dose is readily apparent to the skilled artisan and depends upon any number of factors, such as, but not limited to, the type and severity of the disease being treated, and the type and age of the patient. Actual dosage levels of the active ingredients in the pharmaceutical compositions of this disclosure may be varied so as to

obtain an amount of the active ingredient that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

A medical doctor, e.g., physician, having ordinary skill in the art may readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the disclosure employed in the pharmaceutical composition at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved.

In certain embodiments, the compositions of the disclosure are administered to the patient in dosages that range from one to five times per day or more. In other embodiments, the compositions of the disclosure are administered to the patient in range of dosages that include, but are not limited to, once every day, every two, days, every three days to once a week, and once every two weeks. The frequency of administration of the various combination compositions of the disclosure varies from subject to subject depending on many factors including, but not limited to, age, disease or disorder to be treated, gender, overall health, and other factors. Thus, the disclosure should not be construed to be limited to any particular dosage regime and the precise dosage and composition to be administered to any patient will be determined by the attending physician taking all other factors about the patient into account.

In certain embodiments, the present disclosure is directed to a packaged pharmaceutical composition comprising a container holding a therapeutically effective amount of a compound of the disclosure, alone or in combination with a second pharmaceutical agent; and instructions for using the compound to treat, prevent, or reduce one or more symptoms of a disease or disorder in a patient.

Routes of Administration

Routes of administration of any of the compositions of the disclosure include inhalational, oral, nasal, rectal, parenteral, sublingual, transdermal, transmucosal (e.g., sublingual, lingual, (trans)buccal, (trans)urethral, vaginal (e.g., trans- and perivaginally), (intra)nasal, and (trans)rectal), intravesical, intrapulmonary, intraduodenal, intragastrical, intrathecal, subcutaneous, intramuscular, intradermal, intra-arterial, intravenous, intrabronchial, inhalation, and topical administration.

Suitable compositions and dosage forms include, for example, tablets, capsules, caplets, pills, gel caps, troches, dispersions, suspensions, solutions, syrups, granules, beads, transdermal patches, gels, powders, pellets, magmas, lozenges, creams, pastes, plasters, lotions, discs, suppositories, liquid sprays for nasal or oral administration, dry powder or aerosolized formulations for inhalation, compositions and formulations for intravesical administration and the like. The formulations and compositions that would be useful in the present disclosure are not limited to the particular formulations and compositions that are described herein.

"Parenteral administration" of a pharmaceutical composition includes any route of administration characterized by physical breaching of a tissue of a subject and administration of the pharmaceutical composition through the breach in the tissue. Parenteral administration thus includes, but is not limited to, administration of a pharmaceutical composition by injection of the composition, by application of the composition through a surgical incision, by application of the composition through a tissue-penetrating non-surgical wound, and the like. In particular, parenteral administration is contemplated to include, but is not limited to, subcutaneous, intravenous, intraperitoneal, intramuscular, intrasternal injection, and kidney dialytic infusion techniques.

EXAMPLES

The present disclosure is further exemplified by the following examples. The examples are for illustrative purpose only and are not intended, nor should they be construed as limiting the disclosure in any manner.

Example 1: Efficacy of ENPP1-Fc Fusion Protein in In-Stent Restenosis Model

The efficacy of an ENPP1-Fc fusion protein was evaluated in large animal model of peripheral vascular injury – specifically, in-stent restenosis lesions in the peripheral vasculature of domestic (Yorkshire) swine. Therapeutic effects of the ENPP1-Fc fusion protein were assessed with respect to the ability to inhibit stenosis after angioplasty in previously injured and stented peripheral arteries of Yorkshire swine.

Four peripheral arterial sites were created for induction of neointimal response in each animal; one site was selected in each of four arteries (bilateral profunda and superficial femoral arteries).

All target sites were injured on Day 0 to create the in-stent restenosis model, 10 days prior to the first dose of ENPP1-Fc or a vehicle only control, and 14 days before repeat injury. The four peripheral artery sites were mapped using quantitative vascular angiography (QVA) in order to select the treatment site and correctly sized balloon and stent. The injury was created by overstretch of the artery with a standard angioplasty balloon catheter at a target 130% overstretch; three inflations were performed. Immediately following injury, a bare metal stent was deployed. Peripheral stents were self-expandable, targeting approximately a 120% overstretch.

ENPP1-Fc treatment occurred systemically starting on Day 10 and was dosed every 4 days subcutaneously until termination. On Day 14, all vessels were assessed by angiography and Optical Coherence Tomography (OCT). Then the previously injured and stented artery sites were subjected to a re-injury event consisting of overstretch of the artery with a single inflation of a standard angioplasty balloon catheter at the same pressure/diameter as the original pre-stent injury was done (130% of the baseline reference diameter). Following re-injury interventions, final post-procedural angiography and OCT were also recorded for select peripheral sites.

Four weeks following the re-injury event on Day 14, arteries underwent repeat imaging with angiography and endovascular imaging (OCT). The treated peripheral segments were explanted and stored in 10% neutral buffered formalin.

As shown in Figure 1, angiography revealed a pronounced narrowing of the profunda at day 42 relative to the morphology of the vessel at day 14 in animals given the vehicle control. By contrast, in animals treated with ENPP1-Fc little visible change in profunda morphology was observed between day 14 and day 42. Similarly, as measured by OCT, pronounced intimal thickening was observed within the profunda at day 42 relative to the morphology of the vessel at day 14 in animals treated with the vehicle control. By contrast, little visible intimal thickening was observed between day 14 and day 42 in the profunda of animals treated with ENPP1-Fc (Figure 2).

Tables 1 and 2 (below) summarizes the mean OCT values in all profunda arteries by treatment group.

Table 1.

Day 14 Re-Injury, Profunda	

	Lumen Area (mm ²)	Stent Area (mm ²)	Neointimal Thickness (mm)	Neointimal Area (mm ²)	% Area of Stenosis
ENPP1-Fc	12.10±1.09	14.59±1.24	0.19±0.04	2.49±0.52	17±3
Control	10.82±1.06	13.60±0.82	0.23±0.04	2.78±0.40	21±4

Table 2.

	Day 42 Termination, Profunda				
	Lumen Area (mm ²)	Stent Area (mm ²)	Neointimal Thickness (mm)	Neointimal Area (mm ²)	% Area of Stenosis
ENPP1-Fc	12.95±0.70	16.47±0.89	0.27±0.08	3.52±1.07	21±5
Control	9.51±2.24	14.60±1.40	0.45±0.16	5.10±1.34	35±11

As set forth in the Table, the profunda arteries of animals treated with ENPP1-Fc had a higher lumen area at day 42 compared to the vehicle control group. The stent area was similar between both groups. Neointimal thickness and neointimal area were also reduced at day 42 in animals treated with ENPP1-Fc relative to the vehicle control animals. In addition, animals treated with ENPP1-Fc had a markedly lower % area of stenosis as compared to the vehicle control group (see Figure 3). These data indicate that ENPP1 polypeptides are useful for, among other things, inhibiting the intimal thickening associated with injury of and/or to peripheral arteries.

Example 2: Efficacy of ENPP3-Fc Fusion Protein in In-Stent Restenosis Model

The efficacy of an ENPP3-Fc fusion protein is evaluated in large animal model of peripheral vascular injury – specifically, in-stent restenosis lesions in the peripheral vasculature of domestic (Yorkshire) swine. Therapeutic effects of the ENPP3-Fc fusion protein are assessed with respect to the ability to inhibit stenosis after angioplasty in previously injured and stented peripheral arteries of Yorkshire swine.

Four peripheral arterial sites are created for induction of neointimal response in each animal as described in Example 1. All target sites are injured on Day 0 to create the in-stent restenosis model, 10 days prior to the first dose of ENPP3-Fc or a vehicle only control, and 14 days before repeat injury. The four peripheral artery sites are mapped using quantitative vascular angiography (QVA) in order to select the treatment site and correctly sized balloon and stent. The injury is created by overstretch of the artery with a standard angioplasty balloon catheter at a target 130% overstretch; three inflations are performed. Immediately

following injury, a bare metal stent is deployed. Peripheral stents are self-expandable, targeting approximately a 120% overstretch.

ENPP3-Fc treatment is initiated systemically starting on Day 10 and is dosed every 4 days subcutaneously until termination. On Day 14, all vessels are assessed by angiography and Optical Coherence Tomography (OCT). Then the previously injured and stented artery sites are subjected to a re-injury event consisting of overstretch of the artery with a single inflation of a standard angioplasty balloon catheter at the same pressure/diameter as the original pre-stent injury (130% of the baseline reference diameter). Following re-injury interventions, final post-procedural angiography and OCT are recorded for select peripheral sites.

Four weeks following the re-injury event on Day 14, arteries underwent repeat imaging with angiography and endovascular imaging (OCT). The treated peripheral segments are explanted and stored in 10% neutral buffered formalin.

Without being bound to any one theory, it is expected that animals treated with ENPP3-Fc would exhibit lower % area of stenosis as compared to the vehicle control group. It is expected that ENPP3 polypeptides would be useful for, among other things, inhibiting the intimal thickening associated with injury of and/or to peripheral arteries.

EXAMPLE 3 – ENPP1 Eluting coated stent for the treatment of Atherosclerotic Peripheral Blood Vessels.

In this example the ability of ENPP1 polypeptides (ENPP1 or ENPP1-Fc or ENPP1-Albumin) coated stents to inhibit neointima formation and inflammation in peripheral arteries thereby reducing thrombosis and/or vessel occlusion.

Without being bound to any one theory, it is expected that inducing the overexpression of ENPP1 polypeptides (ENPP1 or ENPP1-Fc or ENPP1-Albumin) at the site of the implanted stent in the peripheral arteries would result in one or more (i) a decrease in platelet activation, (ii) a reduction in restenosis and inflammatory responses, and (iii) a decrease in VSMC proliferation, following stent implantation. This therapy is based on the delivery of ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) to the endothelial cells, which then in turn express the ENPP1 protein at the site of the stent implant after mRNA translation.

Production of ENPP1 mRNA

pcDNA 3.3 plasmid (Eurofins Genomics GmbH, Ebersberg, Germany) containing ENPP1 DNA templates is amplified using the HotStar HiFidelity Polymerase Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The PCR product (PCR cyclor: Eppendorf, Wesseling, Germany) is purified with the Qiaquick PCR Purification Kit (Qiagen). In vitro transcribed mRNA is generated with the MEGAscript1 T7 Kit (Ambion, Glasgow, Scotland) according to the manufacturer's instructions.

To modify the mRNA a 3'-0-Mem7 G(5')ppp(5')G RNA Cap Structure Analog (New England Biolabs, Frankfurt, Germany) is added to the reaction as well as pseudouridine-5'-triphosphate and 5-methylcytidine-5'-triphosphate (TriLink Biotech, San Diego, CA, USA), which are substituted for UTP and CTP, respectively. For RNase inhibition 1 µl of RNase inhibitor (Thermo Scientific, Waltham) is added per reaction. The in vitro transcribed mRNA is then purified with the RNeasy Kit (Qiagen). The purified mRNA is dephosphorylated using the Antarctic Phosphatase Kit (New England Biolabs) and once again purified with the RNeasy Kit (Qiagen). The same procedure is repeated to generate enhanced green fluorescent protein (eGFP) mRNA using eGFP DNA. (*Avci-Adali M, Behring A, Keller T, Krajewski S, Schlensak C, Wendel HP (2014) Optimized conditions for successful transfection of human endothelial cells with in vitro synthesized and modified mRNA for induction of protein expression. J Biol Eng 8: 8*).

The functionality of the generated ENPP1 mRNA is validated by measuring free phosphate after hydrolysis of ATP by transfected HEK293 cells. ENPP1 mRNA transfected HEK293 cells are incubated with 20 µM ATP (möLab, Langenfeld, Germany) or PBS as control for 10 min at 37°C on a shaking platform (Polymax 1040, Heidolph, Schwabach, Germany). The ATP substrate degrades over time in the presence of ENPP1, with the accumulation of the enzymatic product AMP. Using varying concentrations of ATP substrate, the initial rate velocities for ENPP1 are derived in the presence of ATP, and the data is fit to a curve to derive the enzymatic rate constants.

Stent Coating

In order to develop a bioactive stent coating, which allows local delivery of ENPP1mRNA and transfection of endothelial cells in vivo, the generated ENPP1 mRNA is

first coated on thermanox plastic slides. The stent coating is thus simulated using thermanox plastic slides (Nunc, Thermo scientific, USA). First, 100,000 HEK293 cells per well are seeded on a 12-well plate.

After 24 hours, 2 μ l Lipofectamin as well as 10 μ g ENPP1 mRNA are mixed with 50 μ l Opti-MEM and incubated at room temperature for 20 min. Meanwhile, 10 μ l from a polylactic-co-glycolic-acid (PLGA) (Evoniks, Darmstadt) stock solution (20 mg/ml) is diluted in 990 μ l ethyl acetate (final concentration 200 μ g/ml). Then 200 μ l of the PLGA solution are mixed with the transfection complexes.

The thermanox slides are coated with the solution in a step-by-step approach at room temperature. eGFP mRNA and sterilized water are used as controls. The HEK293 cells are supplied with a new medium before the dried slides are plated face down onto the cells. The cells are incubated with the slides at 37°C and 5% CO₂ for 24 hrs, 48 hrs and 72 hrs and then analyzed using a FACScan cytometer.

The expression of ENPP1 of HEK293 cells is measured using flow cytometry. The ENPP1 coated thermanox slide exposed cells and control cells are stained with anti-ENPP1-fluorescein isothiocyanate (FITC) antibody. Flow cytometric analysis of the HEK293 cells after incubation with the ENPP1mRNA/PLGA covered thermanox slides are expected to show that the ENPP1 mRNA is released from the PLGA coating, whereby increase in ENPP1 expression is expected to be detectable after 24 hours, 48 hours and 72 hours post exposure to slides.

Compared to control HEK293 cells, (which were exposed thermanox slides coated with Lipofectamine alone) 0.5-1 μ g of the ENPP1 mRNA is expected to be sufficient to induce increase of the ENPP1 protein expression in HEK cells exposed to ENPP1 mRNA coated thermanox slides even after 24 hours of exposure.

Without being bound to any one theory, it is proposed herein that the ENPP1 expressed at the site of the stent implant is expected to prevent intimal proliferation and reduce platelet occlusion in peripheral arteries.

EXAMPLE 4 – Preparation and implantation of ENPP1 coated stent for the treatment of Atherosclerotic Peripheral Blood Vessels

In this example, a juvenile pig animal model is used for implanting the ENPP1-coated stent to determine the efficacy of an ENPP1 coated stent to inhibit neointima formation, restenosis and inflammation. An ENPP1 agent coated stent is prepared and then implanted in peripheral artery. Four peripheral arterial sites are created for induction of neointimal response in each animal; one site was selected in each of four arteries (bilateral profunda and superficial femoral arteries) as described in Example 1.

Preparation of ENPP1 coated stent

Any stent is amenable to be coated with ENPP1 agent. Common examples of commercial sources that sell stents for use include Abbot, Boston Scientific, Medtronic, Alvimedica, Lepu Medical Technology, Cordis, Balton or Biotronik. Peripheral arterial stents are shorter in length (12-18 mm) with a diameter range from 5-8 mm are commonly used for placement in iliac and femoral arteries. Henry et al. describes in detail the different types of stent lengths and diameters available for peripheral arteries (*Henry et al., Tex Heart Inst J. 2000; 27(2): 119–126.*)

For example, a plain stent such as a bare metal stent can be converted to ENPP1 coated eluting stent by placing a polymeric film comprising ENPP1 mRNA inside the stent or by spraying a polymeric or nonpolymeric solution comprising ENPP1 mRNA or ENPP1 polypeptide on to the stent surface.

Some examples of ENPP1 polymeric film are shown below, the ENPP1 polymeric film can be placed inside stents to create ENPP1 coated eluting stents. Optionally nonpolymeric carrier such as Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil can be added to the solution improve the stability of ENPP1 agent in the polymeric film

- (a) ENPP1 agent coating composition (A) – 10 mg PCL (poly caprolactone) polymer and 100 µg ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) are dissolved in sterile double distilled water at room temperature. The solution is poured onto a glass plate and the solvent is allowed to evaporate for 12-24 hours. After almost complete removal of the solvent, the ENPP1-loaded PCL film is removed from the glass plate and is cut to 1.5 cm by 1.5 cm size which is then further trimmed to fit the size of the stent. The ENPP1 mRNA (or ENPP1-Fc

mRNA or ENPP1-Albumin mRNA) comprising polymeric film is then mounted on the stainless stent. The same process can be repeated for preparing a stent coated with a vector expressing ENPP1 polypeptide (ENPP1 or ENPP1-Fc or ENPP1-Albumin) by using 50 µg of vector DNA.

- (b) ENPP1 agent coating composition (B) – 10 mg EVA (ethylene-vinyl acetate) polymer and 100 µg ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) are dissolved in sterile double distilled water at room temperature. The solution is poured onto a glass plate and the solvent is allowed to evaporate for 12-24 hours. After almost complete removal of the solvent, the ENPP1-mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) loaded EVA film is removed from the glass plate and was cut to 1.5 cm by 1.5 cm size. The ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) comprising polymeric film is then mounted on the stainless stent. The same process can be repeated for preparing a stent coated with a vector expressing ENPP1 polypeptide (ENPP1 or ENPP1-Fc or ENPP1-Albumin) by using 50 µg of vector DNA.

Some examples of ENPP1 comprising spray solutions are shown below, the spray solutions can be applied onto stents to create ENPP1 coated eluting stents. Optionally nonpolymeric carrier such as Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil can be added to the spray solution improve the stability of ENPP1 agent.

- (c) ENPP1 agent coating composition (C)– 10 mg PCL (poly caprolactone) polymer and 100 µg ENPP1 mRNA is dissolved in sterile double distilled water at room temperature. 100 µl polymeric PCL solution comprising the ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) is sprayed onto a stent (6 mmx20 mm) using a semi-automated nebulizer apparatus. The nebulizer spray system provides means of rotating and traversing the length of the stent at a controlled rate. The traversing component of the apparatus contained a glass nebulizer system that applies nebulized polycaprolactone solution to the stent at a rate of 3 ml per minute. Once applied, the polymer coating is "reflowed" by application of 60° C heated air for approximately 5 seconds. The process of reflowing the polymer provides better adherence to the stent surface. The same process can be

repeated for preparing a stent coated with a vector expressing ENPP1 polypeptide (ENPP1 or ENPP1-Fc or ENPP1-Albumin) by using 50 µg of vector DNA.

- (d) ENPP1 agent coating composition (D)-A 1% solution of uncured two-part silicone rubber is dissolved in trichloroethylene and then sprayed on to the stent using a nebulizer spray system as described above in (C). The coated stent is dried at room temperature for 15 minutes to allow the trichloroethylene to evaporate. The coated stent comprising silicone is heated in a vacuum oven for a period of four hours in order to crosslink the silicone coating. The coated stents are removed from the oven and allowed to cool for a period of 1 hour. 100 µg ENPP1 mRNA is dissolved in sterile double distilled water at room temperature. A volume of 100 µl of ENPP1 comprising spray solution is applied to the silicone coating of each stent in dropwise fashion. The crosslinked silicone absorbs the solution, where the solvent subsequently evaporates at room temperature, leaving behind the ENPP1 mRNA (or ENPP1-Fc mRNA or ENPP1-Albumin mRNA) entrapped within the silicone. The same process can be repeated for preparing a stent coated with a vector expressing ENPP1 polypeptide (ENPP1 or ENPP1-Fc or ENPP1-Albumin) by using 50 µg of vector DNA. The solvent subsequently evaporates at room temperature, leaving behind the ENPP1 encoding vector entrapped within the silicone.
- (e) ENPP1 agent coating composition (E)-10 mg PCL (poly caprolactone) polymer and ENPP1 polypeptide (any one of ENPP1 or ENPP1-Fc or ENPP1-albumin) is dissolved in sterile double distilled water at room temperature to reach an ENPP1 polypeptide concentration of 10 mg/ml. 100µl polymeric PCL solution comprising the ENPP1 polypeptide (10 mg/ml) is sprayed onto a stent as described in (C)
- (f) ENPP1 agent coating composition (F)- The coated stent comprising silicone are prepared as discussed in (d). The coated stents are removed from the oven and allowed to cool for a period of 1 hour. ENPP1 polypeptide (ENPP1 or ENPP1-Fc or ENPP1-Albumin) is dissolved in a sterile double distilled water at room temperature to reach an ENPP1 polypeptide concentration of 10 mg/ml. A volume of 100 µl of ENPP1 comprising spray solution (10 mg/ml) is applied to the silicone coating of each stent in dropwise fashion. The crosslinked silicone absorbs the solution, where the solvent subsequently evaporates at room temperature, leaving behind the ENPP1 mRNA entrapped within the silicone.

Animal Model

Thirty 4-to-5-month-old juvenile pigs with the weight of 25–35 kg are procured from commercial sources. Thirty stainless steel vents are obtained from one or more commercial sources such as Abbot, Boston Scientific, Medtronic, Alvimedica, Lepu Medical Technology, Cordis, Balton or Biotronik. Thirty stainless steel stents thus obtained are coated with ENPP1 mRNA following the protocol shown above for coating. Thirty bare metal stents (BMSs) are obtained from Abbott to be used as control set. The ENPP1 coated stent is then sterilized using ethylene oxide, compressed, and mounted on a balloon angioplasty catheter. It is then deployed at a site in an artery using standard balloon angioplasty techniques. Same is done for the control set using bare metal stents.

All target sites are injured on Day 0 to create the in-stent restenosis model. The four peripheral artery sites are mapped using quantitative vascular angiography (QVA) as described in Example. The injury is created as described in Example 1.

The stents are randomly assigned and placed in the peripheral (bilateral profunda and superficial femoral) arteries (one stent per artery) of 30 pigs, one coated stent per pig. The pigs are then maintained on 100 mg aspirin per day. On Day 14, all vessels are assessed by angiography and Optical Coherence Tomography (OCT). Then the previously injured and stented artery sites were subjected to a re-injury event consisting of overstretch of the artery with a single inflation of a standard angioplasty balloon catheter at the same pressure/diameter as the original pre-stent injury was done (130% of the baseline reference diameter). Following re-injury interventions, final post-procedural angiography and OCT are recorded for select peripheral sites. Four weeks following the re-injury event on Day 14, arteries underwent repeat imaging with angiography and endovascular imaging (OCT). The treated peripheral segments are explanted and stored in 10% neutral buffered formalin.

Lumen area, Stent area, Neointimal thickness, Neointimal area and % of Stenosis is calculated for pigs with ENPP1 coated stents and pigs with bare metal stents. It is expected that the profunda arteries of animals treated with ENPP1-Fc coated stents would have a higher lumen area at compared to the vehicle control group treated with bare metal stents. The stent area is expected to be similar between both groups. Neointimal thickness and neointimal area are expected to be reduced in animals treated with ENPP1-Fc coated stents relative to the vehicle control animals with bare metal stents. In addition, animals treated with

ENPP1-Fc are expected to have a markedly lower % area of stenosis as compared to the vehicle control group.

Thus, in situ administration of ENPP1 agent by using ENPP1 coated stents is expected to prevent and effectively treat myointimal proliferation and/or restenosis at the site of injury in peripheral arteries.

EXAMPLE 5 – Preparation and implantation of ENPP3 coated stent for the treatment of Atherosclerotic Peripheral Blood Vessels

In this example, a juvenile pig animal model is used for implanting the ENPP3-coated stent to determine the efficacy of an ENPP3 coated stent to inhibit neointima formation, restenosis and inflammation. An ENPP3 agent coated stent is prepared and then implanted in peripheral artery. Four peripheral arterial sites are created for induction of neointimal response in each animal; one site was selected in each of four arteries (bilateral profunda and superficial femoral arteries) as described in Example 1.

Preparation of ENPP3 coated stent

Any stent is amenable to be coated with ENPP3 agent. Common examples of commercial sources that sell stents for use include Abbot, Boston Scientific, Medtronic, Alvimedica, Lepu Medical Technology, Cordis, Balton or Biotronik. Peripheral arterial stents are shorter in length (12-18 mm) with a diameter range from 5-8 mm are commonly used for placement in iliac and femoral arteries. Henry et al. describes in detail the different types of stent lengths and diameters available for peripheral arteries (*Henry et al., Tex Heart Inst J. 2000; 27(2): 119–126.*)

For example, a plain stent such as a bare metal stent can be converted to ENPP3 coated eluting stent by placing a polymeric film comprising ENPP3 mRNA inside the stent or by spraying a polymeric or nonpolymeric solution comprising ENPP3 mRNA or ENPP3 polypeptide on to the stent surface.

Some examples of ENPP3 polymeric film are shown below, the ENPP3 polymeric film can be placed inside stents to create ENPP3 coated eluting stents. Optionally nonpolymeric carrier such as Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid,

peanut oil and cottonseed oil can be added to the solution improve the stability of ENPP1 agent in the polymeric film

- (g) ENPP3 agent coating composition (A) – 10 mg PCL (poly caprolactone) polymer and 100 µg ENPP1 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) are dissolved in sterile double distilled water at room temperature. The solution is poured onto a glass plate and the solvent is allowed to evaporate for 12-24 hours. After almost complete removal of the solvent, the ENPP3-loaded PCL film is removed from the glass plate and is cut to 1.5 cm by 1.5 cm size which is then further trimmed to fit the size of the stent. The ENPP3 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) comprising polymeric film is then mounted on the stainless stent. The same process can be repeated for preparing a stent coated with a vector expressing ENPP1 polypeptide (ENPP3 or ENPP3-Fc or ENPP3-Albumin) by using 50 µg of vector DNA.
- (h) ENPP3 agent coating composition (B) – 10 mg EVA (ethylene-vinyl acetate) polymer and 100 µg ENPP3 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) are dissolved in sterile double distilled water at room temperature. The solution is poured onto a glass plate and the solvent is allowed to evaporate for 12-24 hours. After almost complete removal of the solvent, the ENPP3-mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) loaded EVA film is removed from the glass plate and was cut to 1.5 cm by 1.5 cm size. The ENPP3 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) comprising polymeric film is then mounted on the stainless stent. The same process can be repeated for preparing a stent coated with a vector expressing ENPP3 polypeptide (ENPP3 or ENPP3-Fc or ENPP3-Albumin) by using 50 µg of vector DNA.

Some examples of ENPP3 comprising spray solutions are shown below, the spray solutions can be applied onto stents to create ENPP3 coated eluting stents. Optionally nonpolymeric carrier such as Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil can be added to the spray solution improve the stability of ENPP3 agent.

- (i) ENPP3 agent coating composition (C)- 10 mg PCL (poly caprolactone) polymer and 100 µg ENPP3 mRNA is dissolved in sterile double distilled water at room

temperature. 100 μ l polymeric PCL solution comprising the ENPP3 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) is sprayed onto a stent (6 mmx20 mm) using a semi-automated nebulizer apparatus. The nebulizer spray system provides means of rotating and traversing the length of the stent at a controlled rate. The traversing component of the apparatus contained a glass nebulizer system that applies nebulized polycaprolactone solution to the stent at a rate of 3 ml per minute. Once applied, the polymer coating is "reflowed" by application of 60° C heated air for approximately 5 seconds. The process of reflowing the polymer provides better adherence to the stent surface. The same process can be repeated for preparing a stent coated with a vector expressing ENPP3 polypeptide (ENPP3 or ENPP3-Fc or ENPP3-Albumin) by using 50 μ g of vector DNA.

- (j) ENPP3 agent coating composition (D)-A 1% solution of uncured two-part silicone rubber is dissolved in trichloroethylene and then sprayed on to the stent using a nebulizer spray system as described above in (C). The coated stent is dried at room temperature for 15 minutes to allow the trichloroethylene to evaporate. The coated stent comprising silicone is heated in a vacuum oven for a period of four hours in order to crosslink the silicone coating. The coated stents are removed from the oven and allowed to cool for a period of 1 hour. 100 μ g ENPP3 mRNA is dissolved in sterile double distilled water at room temperature. A volume of 100 μ l of ENPP3 comprising spray solution is applied to the silicone coating of each stent in dropwise fashion. The crosslinked silicone absorbs the solution, where the solvent subsequently evaporates at room temperature, leaving behind the ENPP3 mRNA (or ENPP3-Fc mRNA or ENPP3-Albumin mRNA) entrapped within the silicone. The same process can be repeated for preparing a stent coated with a vector expressing ENPP3 polypeptide (ENPP3 or ENPP3-Fc or ENPP3-Albumin) by using 50 μ g of vector DNA. The solvent subsequently evaporates at room temperature, leaving behind the ENPP3 encoding vector entrapped within the silicone.
- (k) ENPP3 agent coating composition (E)-10 mg PCL (poly caprolactone) polymer and ENPP3 polypeptide (any one of ENPP3 or ENPP3-Fc or ENPP3-albumin) is dissolved in sterile double distilled water at room temperature to reach an ENPP3 polypeptide concentration of 10 mg/ml. 100 μ l polymeric PCL solution comprising the ENPP3 polypeptide (10 mg/ml) is sprayed onto a stent as described in (C)

- (1) ENPP3 agent coating composition (F)- The coated stent comprising silicone are prepared as discussed in (d). The coated stents are removed from the oven and allowed to cool for a period of 1 hour. ENPP3 polypeptide (ENPP3 or ENPP3-Fc or ENPP3-Albumin) is dissolved in a sterile double distilled water at room temperature to reach an ENPP3 polypeptide concentration of 10 mg/ml. A volume of 100 μ l of ENPP3 comprising spray solution (10 mg/ml) is applied to the silicone coating of each stent in dropwise fashion. The crosslinked silicone absorbs the solution, where the solvent subsequently evaporates at room temperature, leaving behind the ENPP3 mRNA entrapped within the silicone.

Animal Model

Thirty 4-to-5-month-old juvenile pigs with the weight of 25–35 kg are procured from commercial sources. Thirty stainless steel vents are obtained from one or more commercial sources such as Abbot, Boston Scientific, Medtronic, Alvimedica, Lepu Medical Technology, Cordis, Balton or Biotronik. Thirty stainless steel stents thus obtained are coated with ENPP1 mRNA following the protocol shown above for coating. Thirty bare metal stents (BMSs) are obtained from Abbott to be used as control set. The ENPP3 coated stent is then sterilized using ethylene oxide, compressed, and mounted on a balloon angioplasty catheter. It is then deployed at a site in an artery using standard balloon angioplasty techniques. Same is done for the control set using bare metal stents.

All target sites are injured on Day 0 to create the in-stent restenosis model. The four peripheral artery sites are mapped using quantitative vascular angiography (QVA) as described in Example. The injury is created as described in Example 1.

The stents are randomly assigned and placed in the peripheral (bilateral profunda and superficial femoral) arteries (one stent per artery) of 30 pigs, one coated stent per pig. The pigs are then maintained on 100 mg aspirin per day. On Day 14, all vessels are assessed by angiography and Optical Coherence Tomography (OCT). Then the previously injured and stented artery sites were subjected to a re-injury event consisting of overstretch of the artery with a single inflation of a standard angioplasty balloon catheter at the same pressure/diameter as the original pre-stent injury was done (130% of the baseline reference diameter). Following re-injury interventions, final post-procedural angiography and OCT are recorded for select peripheral sites. Four weeks following the re-injury event on Day 14,

arteries underwent repeat imaging with angiography and endovascular imaging (OCT). The treated peripheral segments are explanted and stored in 10% neutral buffered formalin.

Lumen area, Stent area, Neointimal thickness, Neointimal area and % of Stenosis is calculated for pigs with ENPP3 coated stents and pigs with bare metal stents. It is expected that the profunda arteries of animals treated with ENPP3-Fc coated stents would have a higher lumen area at compared to the vehicle control group treated with bare metal stents. The stent area is expected to be similar between both groups. Neointimal thickness and neointimal area are expected to be reduced in animals treated with ENPP3-Fc coated stents relative to the vehicle control animals with bare metal stents. In addition, animals treated with ENPP3-Fc are expected to have a markedly lower % area of stenosis as compared to the vehicle control group.

Thus, in situ administration of ENPP3 agent by using ENPP3 coated stents is expected to prevent and effectively treat myointimal proliferation and/or restenosis at the site of injury in peripheral arteries.

INCORPORATION BY REFERENCE

The disclosure of each and every U.S. and foreign patent and pending patent application and publication referred to herein is specifically incorporated herein by reference in its entirety, as are the contents of Sequence Listing and Figures.

EQUIVALENTS

Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents of the specific embodiments described herein. Such equivalents are intended to be encompassed by the following claims. Any combination of the embodiments disclosed in the any plurality of the dependent claims or Examples is contemplated to be within the scope of the disclosure.

OTHER EMBODIMENTS

From the foregoing description, it will be apparent that variations and modifications may be made to the disclosure described herein to adopt it to various usages and conditions, including the use of different signal sequences to express functional variants of ENPP1 or ENPP3 or combinations thereof in different viral vectors having different promoters or enhancers or different cell types known in art to treat any diseases characterized by the presence of pathological calcification or ossification are within the scope according to the disclosure. Other embodiments according to the disclosure are within the following claims.

Recitation of a listing of elements in any definition of a variable herein includes definitions of that variable as any single element or combination (or sub combination) of listed elements. Recitation of an embodiment herein includes that embodiment as any single embodiment or in combination with any other embodiments or portions thereof.

All publications and patent applications mentioned in the specification are indicative of the level of skill of those skilled in the art to which this disclosure pertains. All publications and patent applications are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

Other embodiments are within the following claims.

What is claimed is:

1. A method for treating a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby treat said peripheral artery disease in said subject.
2. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.
3. The method of claim 1 or 2, wherein the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.
4. A method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.
5. The method of any one of claims 1-4, wherein the subject has common femoral artery disease.
6. The method of any one of claims 1-4, wherein the subject has femoral-popliteal disease.
7. The method of any one of claims 1-4, wherein the subject has tibial-peroneal disease.
8. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who requires surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

9. The method of claim 8, wherein the agent is administered prior to, during and/or after said surgery.
10. The method of claims 8 or 9, wherein the surgery comprises placement of a stent.
11. The method of any one of claims 1-10, wherein the subject does not have a deficiency of ENPP1.
12. The method of any one of claims 1-11, wherein the ENPP1 agent comprises an ENPP1 polypeptide.
13. The method of any one of claims 1-11, wherein the ENPP1 agent comprises a nucleic acid encoding an ENPP1 polypeptide.
14. The method of any one of claims 1-11, wherein the ENPP1 agent comprises a viral vector comprising a nucleic acid encoding an ENPP1 polypeptide.
15. The method of any one of claims 12-14, wherein the ENPP1 polypeptide comprises the extracellular domain of ENPP1.
16. The method of any one of claims 12-14, wherein the ENPP1 polypeptide comprises the catalytic domain of ENPP1.
17. The method of any one of claims 12-14, wherein the ENPP1 polypeptide comprises amino acids 99 to 925 of SEQ ID NO:1.
18. The method of any one of claims 12-14, wherein the ENPP1 polypeptide comprises a heterologous protein.
19. The method of claim 18, wherein the heterologous protein increases the circulating half-life of the ENPP1 polypeptide in mammal.
20. The method of claim 18 or 19, wherein the heterologous protein is an Fc region of an immunoglobulin molecule.

21. The method of claim 20, wherein the immunoglobulin molecule is an IgG1 molecule.
22. The method of claim 18 or 19, wherein the heterologous protein is an albumin molecule.
23. The method of any one of claims 18-22, wherein the heterologous protein is carboxy-terminal to the ENPP1 polypeptide.
24. The method of any one of claims 18-23, wherein the ENPP1 agent comprises a linker.
25. The method of claim 24, wherein the linker separates the ENPP1 polypeptide and the heterologous protein.
26. The method of claim 24 or 25, wherein the linker comprises the following amino acid sequence: (GGGS)_n, wherein n is an integer from 1 to 10.
27. The method according to any one of claims 1-26, wherein the ENPP1 agent is administered to the subject subcutaneously.
28. The method according to any one of claims 1-26, wherein the ENPP1 agent is administered to the subject intravenously.
29. The method according to any one of claims 1-28, wherein the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.
30. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery.
31. The method of claim 30, wherein the agent is administered prior to, during and/or after stent placement.

32. A method for treating a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby treat said peripheral artery disease in said subject.

33. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

34. The method of claim 32 or 33, wherein the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

35. A method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

36. The method of any one of claims 32-35, wherein the subject has common femoral artery disease.

37. The method of any one of claims 32-35, wherein the subject has femoral-popliteal disease.

38. The method of any one of claims 32-35, wherein the subject has tibial-peroneal disease.

39. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who requires surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: administering to the subject an effective amount of an ENPP1 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

40. The method of claim 39, wherein the agent is administered prior to, during and/or after said surgery.
41. The method of claims 39 or 40, wherein the surgery comprises placement of a stent.
42. The method of any one of claims 32-41, wherein the subject does not have a deficiency of ENPP1.
43. The method of any one of claims 32-42, wherein the ENPP3 agent comprises an ENPP3 polypeptide.
44. The method of any one of claims 32-42, wherein the ENPP3 agent comprises a nucleic acid encoding an ENPP3 polypeptide.
45. The method of any one of claims 32-42, wherein the ENPP3 agent comprises a viral vector comprising a nucleic acid encoding an ENPP3 polypeptide.
46. The method of any one of claims 32-45, wherein the ENPP3 polypeptide comprises the extracellular domain of ENPP3.
47. The method of any one of claims 32-45, wherein the ENPP3 polypeptide comprises the catalytic domain of ENPP3.
48. The method of any one of claims 32-45, wherein the ENPP3 polypeptide comprises amino acids 49-875 of SEQ ID NO:7.
49. The method of any one of claims 32-45, wherein the ENPP3 polypeptide comprises a heterologous protein.
50. The method of claim 49, wherein the heterologous protein increases the circulating half-life of the ENPP3 polypeptide in mammal.
51. The method of claim 49 or 50, wherein the heterologous protein is an Fc region of an immunoglobulin molecule.

52. The method of claim 51, wherein the immunoglobulin molecule is an IgG1 molecule.
53. The method of claim 49 or 50, wherein the heterologous protein is an albumin molecule.
54. The method of any one of claims 49-53, wherein the heterologous protein is carboxy-terminal to the ENPP3 polypeptide.
55. The method of any one of claims 49-53, wherein the ENPP3 agent comprises a linker.
56. The method of claim 55, wherein the linker separates the ENPP3 polypeptide and the heterologous protein.
57. The method of claim 55 or 56, wherein the linker comprises the following amino acid sequence: (GGGS)_n, wherein n is an integer from 1 to 10.
58. The method according to any one of claims 32-57, wherein the ENPP3 agent is administered to the subject subcutaneously.
59. The method according to any one of claims 32-57, wherein the ENPP3 agent is administered to the subject intravenously.
60. The method according to any one of claims 32-59, wherein the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.
61. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who undergoes stent placement in said peripheral artery, the method comprising: administering to the subject an effective amount of an ENPP3 agent to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery.
62. The method of claim 30, wherein the ENPP3 agent is administered prior to, during and/or after stent placement.

63. A coated stent comprising:

a vascular stent; and

a coating on the stent, the coating comprising an ENPP1 agent; and

a carrier for said ENPP1 agent,

wherein said coating is configured to release said ENPP1 agent from the stent at a rate of 1-10 µg/ml per day.

64. The coated stent of claim 63, said ENPP1 agent in an amount between 1 wt % and 50 wt %, based on a total weight of the coating.

65. The coated stent of claim 64 wherein said ENPP1 agent is selected from a group consisting of: ENPP1, ENPP1-Fc, ENPP1-Albumin, and ENPP1 mRNA.

66. The coated stent of claim 63, wherein the carrier is non-reactive with said ENPP1 agent.

67. The coated stent of claim 63, wherein the carrier comprises a polymeric carrier that is physically bound to said ENPP1 agent.

68. The coated stent of claim 63, wherein the carrier comprises a polymeric carrier that is chemically bound to said ENPP1 agent.

69. The coated stent of claim 63, wherein the carrier comprises a polymeric biodegradable carrier.

70. The coated stent of claim 63 wherein the carrier comprises a nonpolymeric carrier.

71. The coated stent of claim 70, wherein the nonpolymeric carrier is selected from a group consisting of: Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil.

72. The coated stent of claim 63, wherein the carrier is liquid at body temperature.

73. The coated stent of claim 63, wherein the carrier is solid at body temperature.

74. A coated stent comprising:

a vascular stent; and

a coating on the stent, the coating comprising an ENPP3 agent; and

a carrier for said ENPP3 agent,

wherein said coating is configured to release said ENPP3 agent from the stent at a rate of 1-10 $\mu\text{g/ml}$ per day.

75. The coated stent of claim 74, said ENPP3 agent in an amount between 1 wt % and 50 wt %, based on a total weight of the coating.

76. The coated stent of claim 75, wherein said ENPP3 agent is selected from a group consisting of: ENPP3, ENPP3-Fc, ENPP3-Albumin, and ENPP3 mRNA.

77. The coated stent of claim 74, wherein the carrier is non-reactive with said ENPP3 agent.

78. The coated stent of claim 74, wherein the carrier comprises a polymeric carrier that is physically bound to said ENPP3 agent.

79. The coated stent of claim 74, wherein the carrier comprises a polymeric carrier that is chemically bound to said ENPP3 agent.

80. The coated stent of claim 74, wherein the carrier comprises a polymeric biodegradable carrier.

81. The coated stent of claim 74, wherein the carrier comprises a nonpolymeric carrier.

82. The coated stent of claim 74, wherein the nonpolymeric carrier is selected from a group consisting of: Vitamin E, Vitamin E acetate, Vitamin E succinate, oleic acid, peanut oil and cottonseed oil.

83. The coated stent of claim 74, wherein the carrier is liquid at body temperature.

84. The coated stent of claim 74, wherein the carrier is solid at body temperature.

85. A method for treating a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby treat said peripheral artery disease in said subject.

86. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said

subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

87. The method of claim 85 or 86, wherein the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

88. A method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

89. The method of any one of claims 85-88, wherein the subject has common femoral artery disease.

90. The method of any one of claims 85-88, wherein the subject has femoral-popliteal disease.

91. The method of any one of claims 85-88, wherein the subject has tibial-peroneal disease.

92. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who has a condition requiring surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP1 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

93. The method of claim 92, wherein the agent is administered prior to, during and/or after said surgery.

94. The method of claims 92 or 93, wherein the condition requiring surgery is due to a prior placement of a non-eluting arterial stent in said artery.

95. The method of claims 92 or 93, wherein the condition requiring is due to a prior placement of an eluting arterial stent in said artery which elutes therapeutic agents other than said ENPP1 agent.

96. The method of any one of claims 85-95, wherein the subject does not have a deficiency of ENPP1.
97. The method of any one of claims 85-96, wherein the ENPP1 agent comprises an ENPP1 polypeptide.
98. The method of any one of claims 85-96, wherein the ENPP1 agent comprises a nucleic acid encoding an ENPP1 polypeptide.
99. The method of any one of claims 85-96, wherein the ENPP1 agent comprises a viral vector comprising a nucleic acid encoding an ENPP1 polypeptide.
100. The method of any one of claims 97-99, wherein the ENPP1 polypeptide comprises the extracellular domain of ENPP1.
101. The method of any one of claims 97-99, wherein the ENPP1 polypeptide comprises the catalytic domain of ENPP1.
102. The method of any one of claims 97-99, wherein the ENPP1 polypeptide comprises amino acids 99 to 925 of SEQ ID NO:1.
103. The method of any one of claims 97-99, wherein the ENPP1 polypeptide comprises a heterologous protein.
104. The method of claim 103, wherein the heterologous protein increases the circulating half-life of the ENPP1 polypeptide in mammal.
105. The method of claim 103 or 104, wherein the heterologous protein is an Fc region of an immunoglobulin molecule.
106. The method of claim 105, wherein the immunoglobulin molecule is an IgG1 molecule.
107. The method of claim 103 or 104, wherein the heterologous protein is an albumin molecule.
108. The method of any one of claims 103-107, wherein the heterologous protein is carboxy-terminal to the ENPP1 polypeptide.
109. The method of any one of claims 103-108, wherein the ENPP1 agent comprises a linker.

110. The method of claim 109, wherein the linker separates the ENPP1 polypeptide and the heterologous protein.

111. The method of claim 109 or 110, wherein the linker comprises the following amino acid sequence: (GGGGS)_n, wherein n is an integer from 1 to 10.

112. The method according to any one of claims 85-111, wherein the ENPP1 agent is administered to the subject subcutaneously.

113. The method according to any one of claims 85-111, wherein the ENPP1 agent is administered to the subject intravenously.

114. The method according to any one of claims 85-113, wherein the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

115. A method for treating a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby treat said peripheral artery disease in said subject.

116. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject having peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby reduce and/or prevent progression of said vascular smooth muscle cell proliferation in said peripheral artery of said subject.

117. The method of claim 115 or 116, wherein the subject has stage III, stage IV or stage IV, grade III peripheral artery disease.

118. A method for inhibiting or slowing progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in a subject, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP1 agent in an amount effective to thereby inhibit and/or slow progression of Stage III peripheral artery disease to Stage IV peripheral artery disease in said subject.

119. The method of any one of claims 115-118, wherein the subject has common femoral artery disease.

120. The method of any one of claims 115-118, wherein the subject has femoral-popliteal disease.

121. The method of any one of claims 115-118 wherein the subject has tibial-peroneal disease.

122. A method for reducing and/or preventing progression of vascular smooth muscle cell proliferation in a peripheral artery of a subject who has a condition requiring surgery on said peripheral artery, wherein the subject has peripheral artery disease, the method comprising: implanting an arterial stent coated with an ENPP3 agent into an artery of said subject, wherein said implanted stent is configured to release said ENPP3 agent in an amount effective to thereby reduce and/or prevent progression of vascular smooth muscle cell proliferation in said peripheral artery at a surgical site of said peripheral artery in said subject.

123. The method of claim 122, wherein the agent is administered prior to, during and/or after said surgery.

124. The method of claims 122 or 123, wherein the condition requiring surgery is due to a prior placement of a non-eluting arterial stent in said artery.

125. The method of claims 122 or 123, wherein the condition requiring is due to a prior placement of an eluting arterial stent in said artery which elutes therapeutic agents other than said ENPP3 agent.

126. The method of any one of claims 115-125, wherein the subject does not have a deficiency of ENPP1.

127. The method of any one of claims 115-126, wherein the ENPP1 agent comprises an ENPP3 polypeptide.

128. The method of any one of claims 115-126, wherein the ENPP3 agent comprises a nucleic acid encoding an ENPP1 polypeptide.

129. The method of any one of claims 115-126, wherein the ENPP3 agent comprises a viral vector comprising a nucleic acid encoding an ENPP3 polypeptide.

130. The method of any one of claims 127-129, wherein the ENPP3 polypeptide comprises the extracellular domain of ENPP3.

131. The method of any one of claims 127-129, wherein the ENPP3 polypeptide comprises the catalytic domain of ENPP3.

132. The method of any one of claims 127-129, wherein the ENPP3 polypeptide comprises amino acids 49-875 of SEQ ID NO:7.

133. The method of any one of claims 127-129, wherein the ENPP3 polypeptide comprises a heterologous protein.

134. The method of claim 133, wherein the heterologous protein increases the circulating half-life of the ENPP3 polypeptide in mammal.

135. The method of claim 133 or 134, wherein the heterologous protein is an Fc region of an immunoglobulin molecule.

136. The method of claim 135, wherein the immunoglobulin molecule is an IgG1 molecule.

137. The method of claim 133 or 134, wherein the heterologous protein is an albumin molecule.

138. The method of any one of claims 133-137, wherein the heterologous protein is carboxy-terminal to the ENPP3 polypeptide.

139. The method of any one of claims 133-138, wherein the ENPP3 agent comprises a linker.

140. The method of claim 139, wherein the linker separates the ENPP3 polypeptide and the heterologous protein.

141. The method of claim 139 or 140, wherein the linker comprises the following amino acid sequence: (GGGGS)_n, wherein n is an integer from 1 to 10.

142. The method according to any one of claims 115-141, wherein the ENPP3 agent is administered to the subject subcutaneously.

143. The method according to any one of claims 115-141, wherein the ENPP3 agent is administered to the subject intravenously.

144. The method according to any one of claims 115-143, wherein the subject: is a tobacco user, has hypertension, has elevated cholesterol or triglyceride levels, is a diabetic, has renal disease, or is obese.

145. The method of any of the aforesaid claims, wherein the ENPP1 agent comprises ENPP1 variants that retain enzymatic activity.

146. The method of any of the aforesaid claims, wherein the ENPP3 agent comprises ENPP3 variants that retain enzymatic activity.

147. The coated stent of any one of claims 63-73, wherein the ENPP1 agent comprises ENPP1 variants that retain enzymatic activity.

148. The coated stent of any one of claims 74-84, wherein the ENPP3 agent comprises ENPP3 variants that retain enzymatic activity.

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FIGURE 1

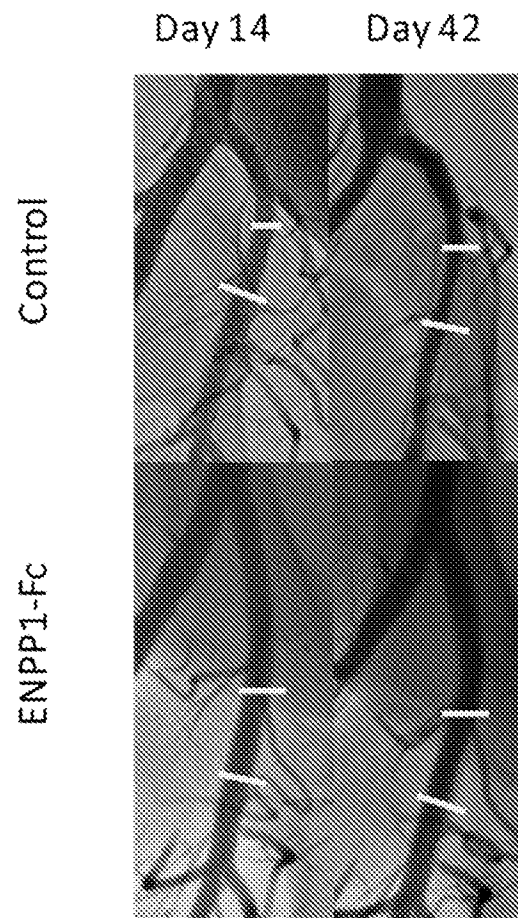
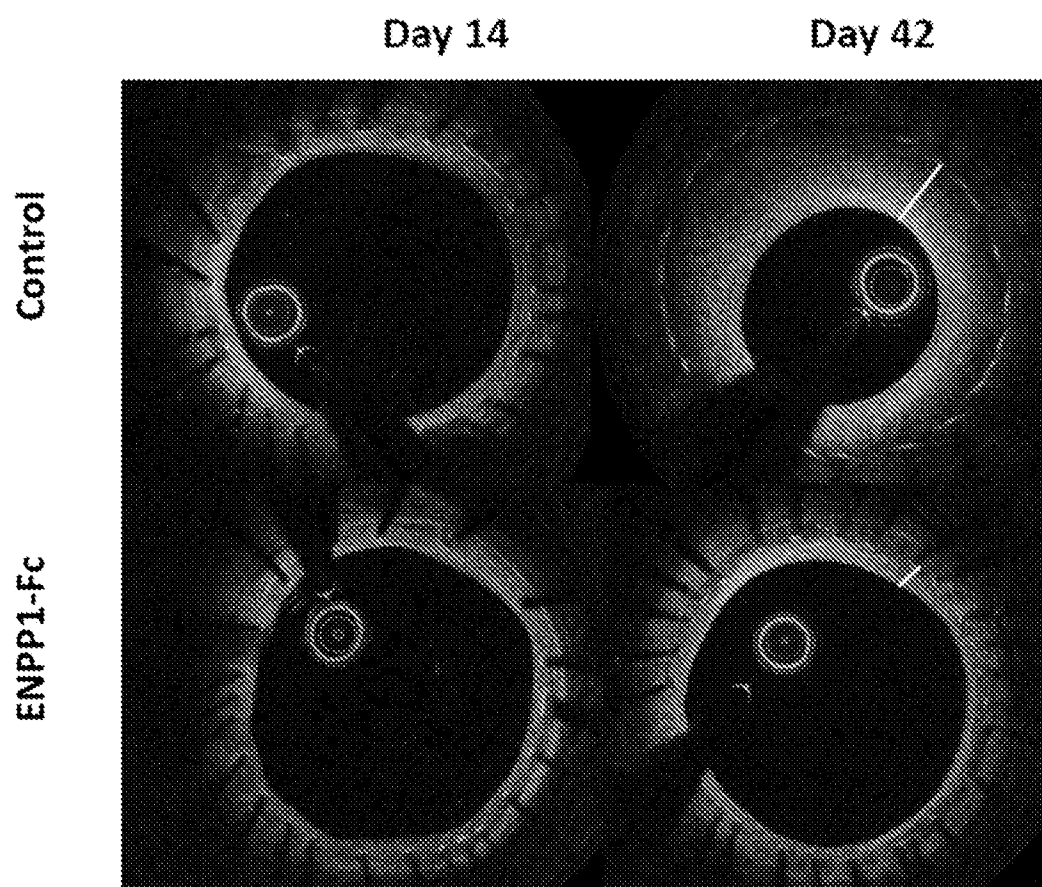
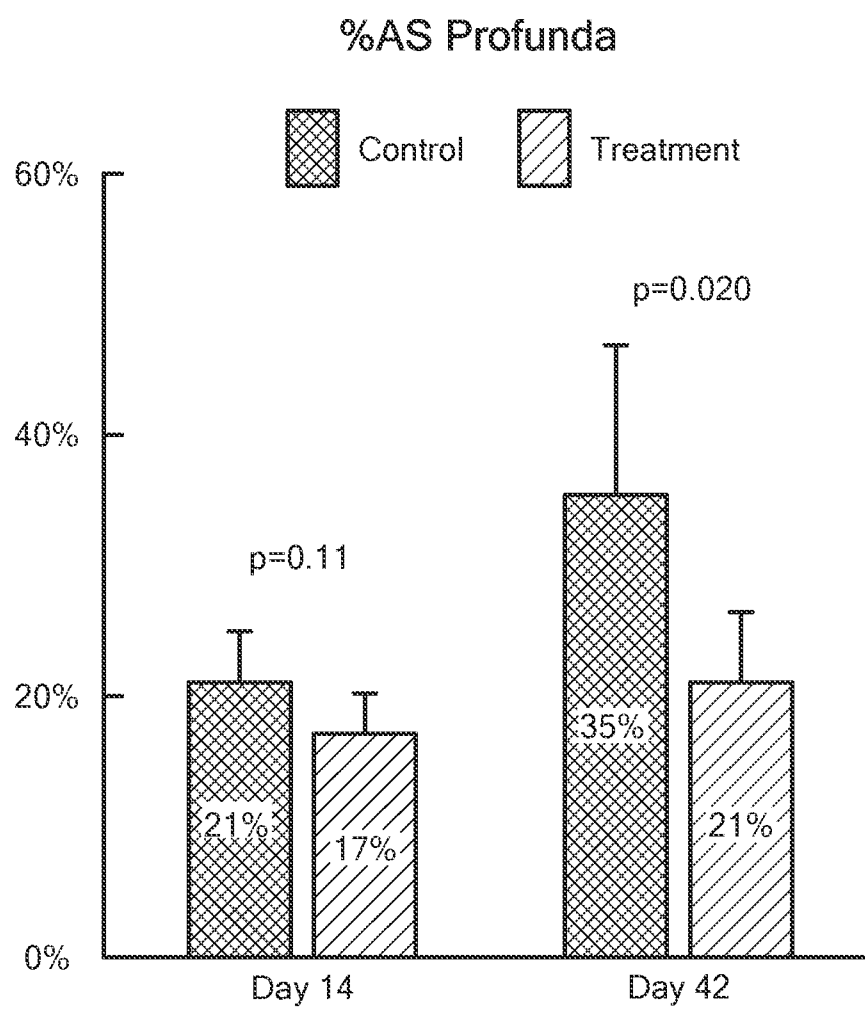


FIGURE 2



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FIGURE 3

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FIGURE 4A

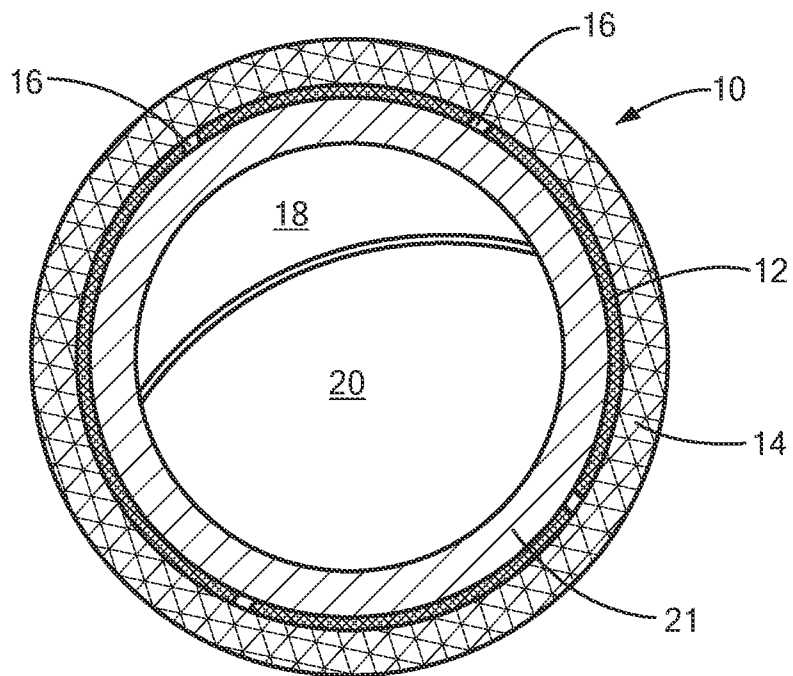
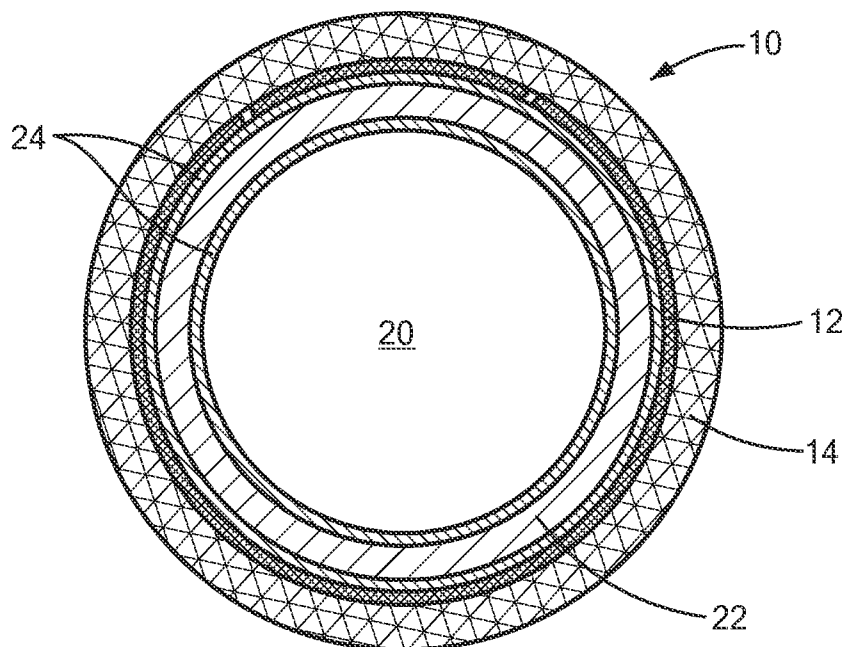


FIGURE 4B



SEQUENCE LISTING

<110> Inozyme Pharma, Inc.
 Westfaelische Wilhelms-Universitaet Muenster
 Thompson, David
 Rutsch, Frank
 Nitschke, Yvonne

 <120> COMPOSITIONS AND METHODS FOR TREATING PERIPHERAL ARTERY DISEASE

 <130> 4427-10202

 <140> Not Yet Assigned
 <141> 2021-05-27

 <150> US 63/030,840
 <151> 2020-05-27

 <160> 72

 <170> PatentIn version 3.5

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Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
 35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
 50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Val Leu Ser Leu
 65 70 75 80

Val Leu Ser Val Cys Val Leu Thr Thr Ile Leu Gly Cys Ile Phe Gly
 85 90 95

Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg Cys
100 105 110

Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val Glu
115 120 125

Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro Glu
130 135 140

His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu Thr
145 150 155 160

Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp Cys
165 170 175

Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val Glu
180 185 190

Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe Glu
195 200 205

Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu Tyr
210 215 220

Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys Lys
225 230 235 240

Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys Thr
245 250 255

Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser His
260 265 270

Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser Phe
275 280 285

Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly Glu
290 295 300

Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr Phe
305 310 315 320

Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp Ile
325 330 335

Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu Ala
340 345 350

Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe Tyr
355 360 365

Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly Pro
370 375 380

Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met Val
385 390 395 400

Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys Leu
405 410 415

Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys Lys
420 425 430

Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile Lys
435 440 445

Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro Asp
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Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser Cys
465 470 475 480

Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu Pro
485 490 495

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Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg Lys
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Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn Met
530 535 540

Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile Glu
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Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu
565 570 575

Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn
580 585 590

His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu Val
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His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn Leu
610 615 620

Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln Thr
625 630 635 640

Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu Thr
645 650 655

Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile Cys
660 665 670

Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile Leu
675 680 685

Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe Ser
690 695 700

Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro Leu
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Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys Val Ser
725 730 735

Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly Ile
740 745 750

Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln Ser
755 760 765

Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys Tyr
770 775 780

Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe Asp
785 790 795 800

Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln Lys
805 810 815

Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe Phe
820 825 830

Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His Cys
835 840 845

Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp Asn
850 855 860

Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu Glu
865 870 875 880

Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile Thr
885 890 895

Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile Leu
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<223> Cleavage point of the signal sequence

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35 40 45

Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu
50 55 60

Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg
65 70 75 80

Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly
85 90 95

Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp
100 105 110

Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly
115 120 125

Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala
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Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu
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Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr
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Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu
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Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala
195 200 205

Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys
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Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly
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Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro
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Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile
260 265 270

Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His
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Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr
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Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly
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Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg
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Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser
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Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn
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Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val

370

375

380

Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu
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Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe
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Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu
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Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu
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Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser
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Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly
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Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys
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Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His
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Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr
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Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser
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Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile
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Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys
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Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser
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Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr
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Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg
690 695 700

Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val
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Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His
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Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu
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His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr
770 775 780

Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val
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Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His

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810

815

Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp
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Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp Leu
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Ile Asn Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
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Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
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Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
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Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
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Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
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Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
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Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
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Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
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Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu
50 55 60

Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg
65 70 75 80

Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly
85 90 95

Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp
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Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala
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Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu
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Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr
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Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu
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Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala
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Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys
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Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro
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Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly
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Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser
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Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn
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Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser
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Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys
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Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp
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Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His
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Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr
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Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp
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Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser
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Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile
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Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys
645 650 655

Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser
660 665 670

Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr
675 680 685

Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg
690 695 700

Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val
705 710 715 720

Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg
725 730 735

Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His
740 745 750

Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu
755 760 765

His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr
770 775 780

Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val
785 790 795 800

Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His
805 810 815

Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp
820 825 830

Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp Leu
835 840 845

Ile Asn Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly
850 855 860

Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu
865 870 875 880

Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu
885 890 895

Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu
900 905 910

His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val
915 920 925

Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe
930 935 940

Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu
945 950 955 960

Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
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Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro
980 985 990

Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe
995 1000 1005

Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe
1010 1015 1020

Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile
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1040 1045 1050

Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val
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Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg
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Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro
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Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr
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Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
1115 1120 1125

Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala
1130 1135 1140

Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu
1145 1150 1155

Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro
1160 1165 1170

Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
1175 1180 1185

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Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu
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Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln
1265 1270 1275

Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser
1280 1285 1290

Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly
1295 1300 1305

Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val
1310 1315 1320

Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His
1325 1330 1335

Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly
1340 1345 1350

Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp
1355 1360 1365

Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe
1370 1375 1380

His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys
1385 1390 1395

Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala
1400 1405 1410

Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
1415 1420 1425

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
1430 1435 1440

Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
1445 1450 1455

Arg Ser Trp Ser His Pro Gln Phe Glu Lys
1460 1465

<210> 4
<211> 1594
<212> PRT
<213> Artificial Sequence

<220>
<223> Azurocidin-ENPP1

<220>
<221> SIGNAL
<222> (19)..(20)
<223> Cleavage point of the signal sequence

<400> 4

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala Ser
1 5 10 15

Ser Arg Ala Ala Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly
20 25 30

Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys
35 40 45

Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu
50 55 60

Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg
65 70 75 80

Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly
85 90 95

Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp
100 105 110

Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly
115 120 125

Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala
130 135 140

Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu
145 150 155 160

Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr
165 170 175

Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu
180 185 190

Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala
195 200 205

Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys
210 215 220

Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly
225 230 235 240

Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro
245 250 255

Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile
260 265 270

Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His
275 280 285

Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr
290 295 300

Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly
305 310 315 320

Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg
325 330 335

Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser
340 345 350

Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn
355 360 365

Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val
370 375 380

Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu
385 390 395 400

Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe
405 410 415

Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu
420 425 430

Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu
435 440 445

Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser
450 455 460

Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly
465 470 475 480

Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys
485 490 495

Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser
500 505 510

Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys
515 520 525

Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp
530 535 540

Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe
545 550 555 560

Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His
565 570 575

Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr
580 585 590

Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp
595 600 605

Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser
610 615 620

Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile
625 630 635 640

Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys
645 650 655

Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser
660 665 670

Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr
675 680 685

Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg
690 695 700

Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val
705 710 715 720

Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg
725 730 735

Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His
740 745 750

Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Ala Pro
755 760 765

Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg Cys Phe Glu Arg
770 775 780

Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val Glu Leu Gly Asn
785 790 795 800

Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro Glu His Ile Trp
805 810 815

Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu Thr Arg Ser Leu
820 825 830

Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp Cys Cys Ile Asn
835 840 845

Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val Glu Glu Pro Cys
850 855 860

Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe Glu Thr Pro Pro
865 870 875 880

Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu Tyr Leu His Thr
885 890 895

Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys Lys Cys Gly Thr
900 905 910

Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys Thr Phe Pro Asn
915 920 925

His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly Ile Ile
930 935 940

Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser Phe Ser Leu Lys
945 950 955 960

Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly Glu Pro Ile Trp
965 970 975

Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr Phe Phe Trp Pro
980 985 990

Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp Ile Tyr Lys Met
995 1000 1005

Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu Ala Val Leu
1010 1015 1020

Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe Tyr Thr
1025 1030 1035

Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly Pro
1040 1045 1050

Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met
1055 1060 1065

Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg
1070 1075 1080

Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly
1085 1090 1095

Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val
1100 1105 1110

Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro
1115 1120 1125

Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile
1130 1135 1140

Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro
1145 1150 1155

Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser
1160 1165 1170

Asp Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln
1175 1180 1185

Leu Ala Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe
1190 1195 1200

His Gly Ser Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val
1205 1210 1215

Gly Tyr Gly Pro Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe
1220 1225 1230

Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu
1235 1240 1245

Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His Leu
1250 1255 1260

Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu Val His
1265 1270 1275

Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn Leu
1280 1285 1290

Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln
1295 1300 1305

Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His
1310 1315 1320

Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn
1325 1330 1335

Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser
1340 1345 1350

Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg
1355 1360 1365

Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln
1370 1375 1380

Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr
1385 1390 1395

Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln
1400 1405 1410

Leu Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr
1415 1420 1425

Thr Asn Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg
1430 1435 1440

Tyr Phe His Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn
1445 1450 1455

Gly Val Asn Val Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp
1460 1465 1470

Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln Lys Arg Arg Val
1475 1480 1485

Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe Phe Ile Val
1490 1495 1500

Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His Cys Glu
1505 1510 1515

Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp Asn
1520 1525 1530

Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu
1535 1540 1545

Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His
1550 1555 1560

Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser
1565 1570 1575

Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu
1580 1585 1590

Asp

<210> 5
<211> 888
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP2 Amino Acid Sequence - Wild Type

<400> 5

Met Ala Arg Arg Ser Ser Phe Gln Ser Cys Gln Ile Ile Ser Leu Phe
1 5 10 15

Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala His Arg
20 25 30

Ile Lys Arg Ala Glu Gly Trp Glu Glu Gly Pro Pro Thr Val Leu Ser
35 40 45

Asp Ser Pro Trp Thr Asn Ile Ser Gly Ser Cys Lys Gly Arg Cys Phe
50 55 60

Glu Leu Gln Glu Ala Gly Pro Pro Asp Cys Arg Cys Asp Asn Leu Cys
65 70 75 80

Lys Ser Tyr Thr Ser Cys Cys His Asp Phe Asp Glu Leu Cys Leu Lys
85 90 95

Thr Ala Arg Gly Trp Glu Cys Thr Lys Asp Arg Cys Gly Glu Val Arg
100 105 110

Asn Glu Glu Asn Ala Cys His Cys Ser Glu Asp Cys Leu Ala Arg Gly
115 120 125

Asp Cys Cys Thr Asn Tyr Gln Val Val Cys Lys Gly Glu Ser His Trp
130 135 140

Val Asp Asp Asp Cys Glu Glu Ile Lys Ala Ala Glu Cys Pro Ala Gly
145 150 155 160

Phe Val Arg Pro Pro Leu Ile Ile Phe Ser Val Asp Gly Phe Arg Ala
165 170 175

Ser Tyr Met Lys Lys Gly Ser Lys Val Met Pro Asn Ile Glu Lys Leu
180 185 190

Arg Ser Cys Gly Thr His Ser Pro Tyr Met Arg Pro Val Tyr Pro Thr
195 200 205

Lys Thr Phe Pro Asn Leu Tyr Thr Leu Ala Thr Gly Leu Tyr Pro Glu
210 215 220

Ser His Gly Ile Val Gly Asn Ser Met Tyr Asp Pro Val Phe Asp Ala
225 230 235 240

Thr Phe His Leu Arg Gly Arg Glu Lys Phe Asn His Arg Trp Trp Gly
245 250 255

Gly Gln Pro Leu Trp Ile Thr Ala Thr Lys Gln Gly Val Lys Ala Gly
260 265 270

Thr Phe Phe Trp Ser Val Val Ile Pro His Glu Arg Arg Ile Leu Thr
275 280 285

Ile Leu Gln Trp Leu Thr Leu Pro Asp His Glu Arg Pro Ser Val Tyr
290 295 300

Ala Phe Tyr Ser Glu Gln Pro Asp Phe Ser Gly His Lys Tyr Gly Pro
305 310 315 320

Phe Gly Pro Glu Met Thr Asn Pro Leu Arg Glu Ile Asp Lys Ile Val
325 330 335

Gly Gln Leu Met Asp Gly Leu Lys Gln Leu Lys Leu His Arg Cys Val
340 345 350

Asn Val Ile Phe Val Gly Asp His Gly Met Glu Asp Val Thr Cys Asp
355 360 365

Arg Thr Glu Phe Leu Ser Asn Tyr Leu Thr Asn Val Asp Asp Ile Thr
370 375 380

Leu Val Pro Gly Thr Leu Gly Arg Ile Arg Ser Lys Phe Ser Asn Asn
385 390 395 400

Ala Lys Tyr Asp Pro Lys Ala Ile Ile Ala Asn Leu Thr Cys Lys Lys
405 410 415

Pro Asp Gln His Phe Lys Pro Tyr Leu Lys Gln His Leu Pro Lys Arg
420 425 430

Leu His Tyr Ala Asn Asn Arg Arg Ile Glu Asp Ile His Leu Leu Val
435 440 445

Glu Arg Arg Trp His Val Ala Arg Lys Pro Leu Asp Val Tyr Lys Lys
450 455 460

Pro Ser Gly Lys Cys Phe Phe Gln Gly Asp His Gly Phe Asp Asn Lys
465 470 475 480

Val Asn Ser Met Gln Thr Val Phe Val Gly Tyr Gly Ser Thr Phe Lys
485 490 495

Tyr Lys Thr Lys Val Pro Pro Phe Glu Asn Ile Glu Leu Tyr Asn Val
500 505 510

Met Cys Asp Leu Leu Gly Leu Lys Pro Ala Pro Asn Asn Gly Thr His
515 520 525

Gly Ser Leu Asn His Leu Leu Arg Thr Asn Thr Phe Arg Pro Thr Met
530 535 540

Pro Glu Glu Val Thr Arg Pro Asn Tyr Pro Gly Ile Met Tyr Leu Gln
545 550 555 560

Ser Asp Phe Asp Leu Gly Cys Thr Cys Asp Asp Lys Val Glu Pro Lys
565 570 575

Asn Lys Leu Asp Glu Leu Asn Lys Arg Leu His Thr Lys Gly Ser Thr
580 585 590

Glu Ala Glu Thr Arg Lys Phe Arg Gly Ser Arg Asn Glu Asn Lys Glu
595 600 605

Asn Ile Asn Gly Asn Phe Glu Pro Arg Lys Glu Arg His Leu Leu Tyr
610 615 620

Gly Arg Pro Ala Val Leu Tyr Arg Thr Arg Tyr Asp Ile Leu Tyr His
625 630 635 640

Thr Asp Phe Glu Ser Gly Tyr Ser Glu Ile Phe Leu Met Pro Leu Trp
645 650 655

Thr Ser Tyr Thr Val Ser Lys Gln Ala Glu Val Ser Ser Val Pro Asp
660 665 670

His Leu Thr Ser Cys Val Arg Pro Asp Val Arg Val Ser Pro Ser Phe
675 680 685

Ser Gln Asn Cys Leu Ala Tyr Lys Asn Asp Lys Gln Met Ser Tyr Gly
690 695 700

Phe Leu Phe Pro Pro Tyr Leu Ser Ser Ser Pro Glu Ala Lys Tyr Asp
705 710 715 720

Ala Phe Leu Val Thr Asn Met Val Pro Met Tyr Pro Ala Phe Lys Arg
725 730 735

Val Trp Asn Tyr Phe Gln Arg Val Leu Val Lys Lys Tyr Ala Ser Glu
740 745 750

Arg Asn Gly Val Asn Val Ile Ser Gly Pro Ile Phe Asp Tyr Asp Tyr
755 760 765

Asp Gly Leu His Asp Thr Glu Asp Lys Ile Lys Gln Tyr Val Glu Gly
770 775 780

Ser Ser Ile Pro Val Pro Thr His Tyr Tyr Ser Ile Ile Thr Ser Cys
785 790 795 800

Leu Asp Phe Thr Gln Pro Ala Asp Lys Cys Asp Gly Pro Leu Ser Val
805 810 815

Ser Ser Phe Ile Leu Pro His Arg Pro Asp Asn Glu Glu Ser Cys Asn
820 825 830

Ser Ser Glu Asp Glu Ser Lys Trp Val Glu Glu Leu Met Lys Met His
835 840 845

Thr Ala Arg Val Arg Asp Ile Glu His Leu Thr Ser Leu Asp Phe Phe
850 855 860

Arg Lys Thr Ser Arg Ser Tyr Pro Glu Ile Leu Thr Leu Lys Thr Tyr
865 870 875 880

Leu His Thr Tyr Glu Ser Glu Ile
885

<210> 6

<211> 827

<212> PRT

<213> Artificial Sequence

<220>

<223> Extracellular Domain of ENPP3

<400> 6

Glu Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala Ser Phe Arg
1 5 10 15

Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp Arg Gly Asp
20 25 30

Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr Arg Ile Trp
35 40 45

Met Cys Asn Lys Phe Arg Cys Gly Glu Thr Arg Leu Glu Ala Ser Leu
50 55 60

Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys Ala Asp
65 70 75 80

Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu Asn Cys
85 90 95

Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu Pro Pro
100 105 110

Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu Tyr Thr
115 120 125

Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys Gly Ile
130 135 140

His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe Pro Asn
145 150 155 160

His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly Ile Ile
165 170 175

Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser Leu Ser
180 185 190

Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro Met Trp
195 200 205

Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe Trp Pro
210 215 220

Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr Met Pro
225 230 235 240

Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu Leu Lys
245 250 255

Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr Met Tyr
260 265 270

Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val Ser Ala
275 280 285

Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe Gly Met Leu
290 295 300

Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn Ile Ile
305 310 315 320

Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys Met Glu
325 330 335

Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met Tyr Glu
340 345 350

Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His Asp Phe Phe
355 360 365

Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg Lys Pro
370 375 380

Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro Lys Arg Leu
385 390 395 400

His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu Phe Val Asp
405 410 415

Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn Cys Gly Gly
420 425 430

Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala Ile Phe
435 440 445

Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu Pro Phe
450 455 460

Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg Ile Gln
465 470 475 480

Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His Leu Leu Lys
485 490 495

Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys Phe Ser
500 505 510

Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp Cys Phe
515 520 525

Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn Gln Met
530 535 540

Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val Asn Leu
545 550 555 560

Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp His Cys Leu
565 570 575

Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met Arg Met
580 585 590

Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr Ser Pro
595 600 605

Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg Val Pro
610 615 620

Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys Asn Ile
625 630 635 640

Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser Asp Ser
645 650 655

Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr Glu Glu
660 665 670

Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile Lys His
675 680 685

Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile Phe Asp
690 695 700

Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His
705 710 715 720

Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu
725 730 735

Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp
740 745 750

Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu
755 760 765

Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe
770 775 780

Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr Gly Leu
785 790 795 800

Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu Gln Leu
805 810 815

Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile
820 825

<210> 7
<211> 875

<212> PRT
<213> Artificial Sequence

<220>
<223> NPP3 Amino Acid Sequence

<400> 7

Met Glu Ser Thr Leu Thr Leu Ala Thr Glu Gln Pro Val Lys Lys Asn
1 5 10 15

Thr Leu Lys Lys Tyr Lys Ile Ala Cys Ile Val Leu Leu Ala Leu Leu
20 25 30

Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys Leu
35 40 45

Glu Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala Ser Phe Arg
50 55 60

Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp Arg Gly Asp
65 70 75 80

Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr Arg Ile Trp
85 90 95

Met Cys Asn Lys Phe Arg Cys Gly Glu Thr Arg Leu Glu Ala Ser Leu
100 105 110

Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys Ala Asp
115 120 125

Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu Asn Cys
130 135 140

Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu Pro Pro
145 150 155 160

Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu Tyr Thr
165 170 175

Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys Gly Ile
180 185 190

His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe Pro Asn
195 200 205

His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly Ile Ile
210 215 220

Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser Leu Ser
225 230 235 240

Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro Met Trp
245 250 255

Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe Trp Pro
260 265 270

Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr Met Pro
275 280 285

Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu Leu Lys
290 295 300

Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr Met Tyr
305 310 315 320

Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val Ser Ala
325 330 335

Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe Gly Met Leu
340 345 350

Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn Ile Ile
355 360 365

Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys Met Glu
370 375 380

Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met Tyr Glu
385 390 395 400

Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His Asp Phe Phe
405 410 415

Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg Lys Pro
420 425 430

Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro Lys Arg Leu
435 440 445

His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu Phe Val Asp
450 455 460

Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn Cys Gly Gly
465 470 475 480

Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala Ile Phe
485 490 495

Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu Pro Phe
500 505 510

Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg Ile Gln
515 520 525

Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His Leu Leu Lys
530 535 540

Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys Phe Ser
545 550 555 560

Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp Cys Phe
565 570 575

Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn Gln Met
580 585 590

Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val Asn Leu
595 600 605

Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp His Cys Leu
610 615 620

Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met Arg Met
625 630 635 640

Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr Ser Pro
645 650 655

Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg Val Pro
660 665 670

Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys Asn Ile
675 680 685

Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser Asp Ser
690 695 700

Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr Glu Glu
705 710 715 720

Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile Lys His
725 730 735

Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile Phe Asp
740 745 750

Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His
755 760 765

Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu
770 775 780

Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp
785 790 795 800

Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu
805 810 815

Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe
820 825 830

Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr Gly Leu
835 840 845

Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu Gln Leu
850 855 860

Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile
865 870 875

<210> 8
<211> 1073
<212> PRT
<213> Artificial Sequence

<220>
<223> Azurocidin-ENPP3-FC

<220>
<221> SIGNAL
<222> (19)..(20)
<223> Cleavage point of the signal sequence

<220>
<221> MISC_FEATURE
<222> (847)..(1074)
<223> Indicate Fc sequence

<220>
<221> MISC_FEATURE
<222> (848)..(1074)
<223> Indicate Fc sequence

<400> 8

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala Ser
1 5 10 15

Ser Arg Ala Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Thr Arg Leu Glu
65 70 75 80

Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys
85 90 95

Cys Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu
100 105 110

Glu Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp
115 120 125

Leu Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr
130 135 140

Leu Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr
145 150 155 160

Cys Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr
165 170 175

Phe Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His
180 185 190

Gly Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe
195 200 205

Ser Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln
210 215 220

Pro Met Asn Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr
225 230 235 240

Phe Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile
245 250 255

Tyr Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr
260 265 270

Leu Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr
275 280 285

Thr Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro
290 295 300

Val Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe
305 310 315 320

Gly Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val
325 330 335

Asn Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn
340 345 350

Lys Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr
355 360 365

Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His
370 375 380

Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys
385 390 395 400

Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro
405 410 415

Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu
420 425 430

Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn
435 440 445

Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu
450 455 460

Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val
465 470 475 480

Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu
485 490 495

Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His
500 505 510

Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser
515 520 525

Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu
530 535 540

Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val
545 550 555 560

Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys
565 570 575

Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp
580 585 590

His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala
595 600 605

Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp
610 615 620

Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val
625 630 635 640

Arg Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp
645 650 655

Lys Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr
660 665 670

Ser Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met
675 680 685

Tyr Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu
690 695 700

Ile Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro
705 710 715 720

Ile Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile
725 730 735

Thr Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe
740 745 750

Val Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys
755 760 765

Pro Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr
770 775 780

Asn Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu
785 790 795 800

Glu Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu
805 810 815

Thr Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile
820 825 830

Leu Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Asp Lys
835 840 845

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
850 855 860

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
865 870 875 880

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
885 890 895

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
900 905 910

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
915 920 925

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
930 935 940

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
945 950 955 960

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
965 970 975

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
980 985 990

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
995 1000 1005

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
1010 1015 1020

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
1025 1030 1035

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
1040 1045 1050

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
1055 1060 1065

Leu Ser Pro Gly Lys
1070

<210> 9
<211> 1464
<212> PRT
<213> Artificial Sequence

<220>
<223> Azurocidin-ENPP3-Albumin

<220>
<221> SIGNAL
<222> (19)..(20)
<223> Cleavage point of the signal sequence

<220>

<221> MISC_FEATURE

<222> (848)..(1465)

<223> Indicate Albumin sequence

<400> 9

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala Ser
1 5 10 15

Ser Arg Ala Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Thr Arg Leu Glu
65 70 75 80

Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys
85 90 95

Cys Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu
100 105 110

Glu Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp
115 120 125

Leu Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr
130 135 140

Leu Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr
145 150 155 160

Cys Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr
165 170 175

Phe Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His
180 185 190

Gly Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe
195 200 205

Ser Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln
210 215 220

Pro Met Asn Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr
225 230 235 240

Phe Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile
245 250 255

Tyr Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr
260 265 270

Leu Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr
275 280 285

Thr Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro
290 295 300

Val Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe
305 310 315 320

Gly Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val
325 330 335

Asn Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn
340 345 350

Lys Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr
355 360 365

Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His
370 375 380

Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys
385 390 395 400

Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro

405

410

415

Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu
 420 425 430

Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn
 435 440 445

Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu
 450 455 460

Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val
 465 470 475 480

Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu
 485 490 495

Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His
 500 505 510

Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser
 515 520 525

Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu
 530 535 540

Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val
 545 550 555 560

Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys
 565 570 575

Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp
 580 585 590

His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala
 595 600 605

Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp
 610 615 620

Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val
625 630 635 640

Arg Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp
645 650 655

Lys Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr
660 665 670

Ser Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met
675 680 685

Tyr Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu
690 695 700

Ile Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro
705 710 715 720

Ile Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile
725 730 735

Thr Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe
740 745 750

Val Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys
755 760 765

Pro Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr
770 775 780

Asn Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu
785 790 795 800

Glu Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu
805 810 815

Thr Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile
820 825 830

Leu Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Met Lys

835

840

845

Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala Phe Ser
 850 855 860

Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala His Arg
 865 870 875 880

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
 885 890 895

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
 900 905 910

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
 915 920 925

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
 930 935 940

Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
 945 950 955 960

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
 965 970 975

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
 980 985 990

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
 995 1000 1005

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
 1010 1015 1020

Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys
 1025 1030 1035

Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp
 1040 1045 1050

Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met
1055 1060 1065

Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
1070 1075 1080

Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe
1085 1090 1095

Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys
1100 1105 1110

Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
1115 1120 1125

Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser
1130 1135 1140

Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His
1145 1150 1155

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro
1160 1165 1170

Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn
1175 1180 1185

Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu
1190 1195 1200

Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg
1205 1210 1215

Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu
1220 1225 1230

Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln
1235 1240 1245

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp

1250						1255						1260			
Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	
1265						1270					1275				
Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	
1280						1285					1290				
Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	
1295						1300					1305				
Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	
1310						1315					1320				
Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	
1325						1330					1335				
Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	
1340						1345					1350				
Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	
1355						1360					1365				
Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	
1370						1375					1380				
Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	
1385						1390					1395				
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	
1400						1405					1410				
Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	
1415						1420					1425				
Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	
1430						1435					1440				
Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Arg	Ser	Trp	Ser	
1445						1450					1455				

His Pro Gln Phe Glu Lys
1460

<210> 10
<211> 846
<212> PRT
<213> Artificial Sequence

<220>
<223> Azurocidin-ENPP3

<220>
<221> SIGNAL
<222> (19)..(20)
<223> Cleavage point of the signal sequence

<400> 10

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala Ser
1 5 10 15

Ser Arg Ala Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Thr Arg Leu Glu
65 70 75 80

Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys
85 90 95

Cys Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu
100 105 110

Glu Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp
115 120 125

Leu Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr

130

135

140

Leu Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr
 145 150 155 160

Cys Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr
 165 170 175

Phe Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His
 180 185 190

Gly Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe
 195 200 205

Ser Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln
 210 215 220

Pro Met Asn Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr
 225 230 235 240

Phe Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile
 245 250 255

Tyr Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr
 260 265 270

Leu Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr
 275 280 285

Thr Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro
 290 295 300

Val Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe
 305 310 315 320

Gly Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val
 325 330 335

Asn Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn
 340 345 350

Lys Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr
355 360 365

Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His
370 375 380

Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys
385 390 395 400

Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro
405 410 415

Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu
420 425 430

Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn
435 440 445

Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu
450 455 460

Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val
465 470 475 480

Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu
485 490 495

Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His
500 505 510

Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser
515 520 525

Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu
530 535 540

Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val
545 550 555 560

Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys

565

570

575

Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp
 580 585 590

His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala
 595 600 605

Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp
 610 615 620

Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val
 625 630 635 640

Arg Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp
 645 650 655

Lys Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr
 660 665 670

Ser Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met
 675 680 685

Tyr Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu
 690 695 700

Ile Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro
 705 710 715 720

Ile Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile
 725 730 735

Thr Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe
 740 745 750

Val Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys
 755 760 765

Pro Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr
 770 775 780

Asn Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu
785 790 795 800

Glu Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu
805 810 815

Thr Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile
820 825 830

Leu Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile
835 840 845

<210> 11
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP4 Amino Acid Sequence - Wild Type

<400> 11

Met Lys Leu Leu Val Ile Leu Leu Phe Ser Gly Leu Ile Thr Gly Phe
1 5 10 15

Arg Ser Asp Ser Ser Ser Ser Leu Pro Pro Lys Leu Leu Leu Val Ser
20 25 30

Phe Asp Gly Phe Arg Ala Asp Tyr Leu Lys Asn Tyr Glu Phe Pro His
35 40 45

Leu Gln Asn Phe Ile Lys Glu Gly Val Leu Val Glu His Val Lys Asn
50 55 60

Val Phe Ile Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly
65 70 75 80

Leu Tyr Glu Glu Ser His Gly Ile Val Ala Asn Ser Met Tyr Asp Ala
85 90 95

Val Thr Lys Lys His Phe Ser Asp Ser Asn Asp Lys Asp Pro Phe Trp
100 105 110

Trp Asn Glu Ala Val Pro Ile Trp Val Thr Asn Gln Leu Gln Glu Asn
115 120 125

Arg Ser Ser Ala Ala Ala Met Trp Pro Gly Thr Asp Val Pro Ile His
130 135 140

Asp Thr Ile Ser Ser Tyr Phe Met Asn Tyr Asn Ser Ser Val Ser Phe
145 150 155 160

Glu Glu Arg Leu Asn Asn Ile Thr Met Trp Leu Asn Asn Ser Asn Pro
165 170 175

Pro Val Thr Phe Ala Thr Leu Tyr Trp Glu Glu Pro Asp Ala Ser Gly
180 185 190

His Lys Tyr Gly Pro Glu Asp Lys Glu Asn Met Ser Arg Val Leu Lys
195 200 205

Lys Ile Asp Asp Leu Ile Gly Asp Leu Val Gln Arg Leu Lys Met Leu
210 215 220

Gly Leu Trp Glu Asn Leu Asn Val Ile Ile Thr Ser Asp His Gly Met
225 230 235 240

Thr Gln Cys Ser Gln Asp Arg Leu Ile Asn Leu Asp Ser Cys Ile Asp
245 250 255

His Ser Tyr Tyr Thr Leu Ile Asp Leu Ser Pro Val Ala Ala Ile Leu
260 265 270

Pro Lys Ile Asn Arg Thr Glu Val Tyr Asn Lys Leu Lys Asn Cys Ser
275 280 285

Pro His Met Asn Val Tyr Leu Lys Glu Asp Ile Pro Asn Arg Phe Tyr
290 295 300

Tyr Gln His Asn Asp Arg Ile Gln Pro Ile Ile Leu Val Ala Asp Glu
305 310 315 320

Gly Trp Thr Ile Val Leu Asn Glu Ser Ser Gln Lys Leu Gly Asp His

325

330

335

Gly Tyr Asp Asn Ser Leu Pro Ser Met His Pro Phe Leu Ala Ala His
 340 345 350

Gly Pro Ala Phe His Lys Gly Tyr Lys His Ser Thr Ile Asn Ile Val
 355 360 365

Asp Ile Tyr Pro Met Met Cys His Ile Leu Gly Leu Lys Pro His Pro
 370 375 380

Asn Asn Gly Thr Phe Gly His Thr Lys Cys Leu Leu Val Asp Gln Trp
 385 390 395 400

Cys Ile Asn Leu Pro Glu Ala Ile Ala Ile Val Ile Gly Ser Leu Leu
 405 410 415

Val Leu Thr Met Leu Thr Cys Leu Ile Ile Ile Met Gln Asn Arg Leu
 420 425 430

Ser Val Pro Arg Pro Phe Ser Arg Leu Gln Leu Gln Glu Asp Asp Asp
 435 440 445

Asp Pro Leu Ile Gly
 450

<210> 12
 <211> 850
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ENPP51 Amino Acid Sequence

<220>
 <221> SIGNAL
 <222> (24)..(25)
 <223> Cleavage point of the signal sequence

<220>
 <221> SIGNAL
 <222> (24)..(25)
 <223> Cleavage point of the signal peptide sequence

<400> 12

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Leu Gln Pro Ser Cys Ala Lys Glu Val Lys
20 25 30

Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Ser Asn Cys Arg Cys
35 40 45

Asp Ala Ala Cys Val Ser Leu Gly Asn Cys Cys Leu Asp Phe Gln Glu
50 55 60

Thr Cys Val Glu Pro Thr His Ile Trp Thr Cys Asn Lys Phe Arg Cys
65 70 75 80

Gly Glu Lys Arg Leu Ser Arg Phe Val Cys Ser Cys Ala Asp Asp Cys
85 90 95

Lys Thr His Asn Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Asp
100 105 110

Lys Lys Ser Trp Val Glu Glu Thr Cys Glu Ser Ile Asp Thr Pro Glu
115 120 125

Cys Pro Ala Glu Phe Glu Ser Pro Pro Thr Leu Leu Phe Ser Leu Asp
130 135 140

Gly Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val
145 150 155 160

Ile Ser Lys Leu Lys Asn Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro
165 170 175

Met Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly
180 185 190

Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro
195 200 205

Lys Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro
210 215 220

Leu Trp Tyr Lys Gly Gln Pro Ile Trp Val Thr Ala Asn His Gln Glu
225 230 235 240

Val Lys Ser Gly Thr Tyr Phe Trp Pro Gly Ser Asp Val Glu Ile Asp
245 250 255

Gly Ile Leu Pro Asp Ile Tyr Lys Val Tyr Asn Gly Ser Val Pro Phe
260 265 270

Glu Glu Arg Ile Leu Ala Val Leu Glu Trp Leu Gln Leu Pro Ser His
275 280 285

Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser
290 295 300

Gly His Ser His Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln
305 310 315 320

Lys Val Asp Arg Leu Val Gly Met Leu Met Asp Gly Leu Lys Asp Leu
325 330 335

Gly Leu Asp Lys Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met
340 345 350

Glu Gln Gly Ser Cys Lys Lys Tyr Val Tyr Leu Asn Lys Tyr Leu Gly
355 360 365

Asp Val Asn Asn Val Lys Val Val Tyr Gly Pro Ala Ala Arg Leu Arg
370 375 380

Pro Thr Asp Val Pro Glu Thr Tyr Tyr Ser Phe Asn Tyr Glu Ala Leu
385 390 395 400

Ala Lys Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Arg Pro Tyr
405 410 415

Leu Lys Pro Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg
420 425 430

Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu
435 440 445

Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp
450 455 460

Asn Leu Phe Ser Asn Met Gln Ala Leu Phe Ile Gly Tyr Gly Pro Ala
465 470 475 480

Phe Lys His Gly Ala Glu Val Asp Ser Phe Glu Asn Ile Glu Val Tyr
485 490 495

Asn Leu Met Cys Asp Leu Leu Gly Leu Ile Pro Ala Pro Asn Asn Gly
500 505 510

Ser His Gly Ser Leu Asn His Leu Leu Lys Lys Pro Ile Tyr Asn Pro
515 520 525

Ser His Pro Lys Glu Glu Gly Phe Leu Ser Gln Cys Pro Ile Lys Ser
530 535 540

Thr Ser Asn Asp Leu Gly Cys Thr Cys Asp Pro Trp Ile Val Pro Ile
545 550 555 560

Lys Asp Phe Glu Lys Gln Leu Asn Leu Thr Thr Glu Asp Val Asp Asp
565 570 575

Ile Tyr His Met Thr Val Pro Tyr Gly Arg Pro Arg Ile Leu Leu Lys
580 585 590

Gln His Arg Val Cys Leu Leu Gln Gln Gln Gln Phe Leu Thr Gly Tyr
595 600 605

Ser Leu Asp Leu Leu Met Pro Leu Trp Ala Ser Tyr Thr Phe Leu Ser
610 615 620

Asn Asp Gln Phe Ser Arg Asp Asp Phe Ser Asn Cys Leu Tyr Gln Asp
625 630 635 640

Leu Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Tyr Tyr Lys Ser
645 650 655

Asn Ser Lys Leu Ser Tyr Gly Phe Leu Thr Pro Pro Arg Leu Asn Arg
660 665 670

Val Ser Asn His Ile Tyr Ser Glu Ala Leu Leu Thr Ser Asn Ile Val
675 680 685

Pro Met Tyr Gln Ser Phe Gln Val Ile Trp His Tyr Leu His Asp Thr
690 695 700

Leu Leu Gln Arg Tyr Ala His Glu Arg Asn Gly Ile Asn Val Val Ser
705 710 715 720

Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Tyr Asp Ser Leu Glu
725 730 735

Ile Leu Lys Gln Asn Ser Arg Val Ile Arg Ser Gln Glu Ile Leu Ile
740 745 750

Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Gln Leu Ser Glu
755 760 765

Thr Pro Leu Glu Cys Ser Ala Leu Glu Ser Ser Ala Tyr Ile Leu Pro
770 775 780

His Arg Pro Asp Asn Ile Glu Ser Cys Thr His Gly Lys Arg Glu Ser
785 790 795 800

Ser Trp Val Glu Glu Leu Leu Thr Leu His Arg Ala Arg Val Thr Asp
805 810 815

Val Glu Leu Ile Thr Gly Leu Ser Phe Tyr Gln Asp Arg Gln Glu Ser
820 825 830

Val Ser Glu Leu Leu Arg Leu Lys Thr His Leu Pro Ile Phe Ser Gln
835 840 845

Glu Asp
850

<210> 13
<211> 1474
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP51 - ALB Amino Acid Sequence

<220>
<221> SIGNAL
<222> (24)..(25)
<223> Cleavage point of the signal sequence

<220>
<221> SIGNAL
<222> (24)..(25)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (857)..(1474)
<223> Indicate Albumin sequence

<400> 13

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Leu Gln Pro Ser Cys Ala Lys Glu Val Lys
20 25 30

Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Ser Asn Cys Arg Cys
35 40 45

Asp Ala Ala Cys Val Ser Leu Gly Asn Cys Cys Leu Asp Phe Gln Glu
50 55 60

Thr Cys Val Glu Pro Thr His Ile Trp Thr Cys Asn Lys Phe Arg Cys
65 70 75 80

Gly Glu Lys Arg Leu Ser Arg Phe Val Cys Ser Cys Ala Asp Asp Cys
85 90 95

Lys Thr His Asn Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Asp
100 105 110

Lys Lys Ser Trp Val Glu Glu Thr Cys Glu Ser Ile Asp Thr Pro Glu
115 120 125

Cys Pro Ala Glu Phe Glu Ser Pro Pro Thr Leu Leu Phe Ser Leu Asp
130 135 140

Gly Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val
145 150 155 160

Ile Ser Lys Leu Lys Asn Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro
165 170 175

Met Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly
180 185 190

Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro
195 200 205

Lys Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro
210 215 220

Leu Trp Tyr Lys Gly Gln Pro Ile Trp Val Thr Ala Asn His Gln Glu
225 230 235 240

Val Lys Ser Gly Thr Tyr Phe Trp Pro Gly Ser Asp Val Glu Ile Asp
245 250 255

Gly Ile Leu Pro Asp Ile Tyr Lys Val Tyr Asn Gly Ser Val Pro Phe
260 265 270

Glu Glu Arg Ile Leu Ala Val Leu Glu Trp Leu Gln Leu Pro Ser His
275 280 285

Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser
290 295 300

Gly His Ser His Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln
305 310 315 320

Lys Val Asp Arg Leu Val Gly Met Leu Met Asp Gly Leu Lys Asp Leu
325 330 335

Gly Leu Asp Lys Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met
340 345 350

Glu Gln Gly Ser Cys Lys Lys Tyr Val Tyr Leu Asn Lys Tyr Leu Gly
355 360 365

Asp Val Asn Asn Val Lys Val Val Tyr Gly Pro Ala Ala Arg Leu Arg
370 375 380

Pro Thr Asp Val Pro Glu Thr Tyr Tyr Ser Phe Asn Tyr Glu Ala Leu
385 390 395 400

Ala Lys Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Arg Pro Tyr
405 410 415

Leu Lys Pro Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg
420 425 430

Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu
435 440 445

Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp
450 455 460

Asn Leu Phe Ser Asn Met Gln Ala Leu Phe Ile Gly Tyr Gly Pro Ala
465 470 475 480

Phe Lys His Gly Ala Glu Val Asp Ser Phe Glu Asn Ile Glu Val Tyr
485 490 495

Asn Leu Met Cys Asp Leu Leu Gly Leu Ile Pro Ala Pro Asn Asn Gly
500 505 510

Ser His Gly Ser Leu Asn His Leu Leu Lys Lys Pro Ile Tyr Asn Pro
515 520 525

Ser His Pro Lys Glu Glu Gly Phe Leu Ser Gln Cys Pro Ile Lys Ser
530 535 540

Thr Ser Asn Asp Leu Gly Cys Thr Cys Asp Pro Trp Ile Val Pro Ile
545 550 555 560

Lys Asp Phe Glu Lys Gln Leu Asn Leu Thr Thr Glu Asp Val Asp Asp
565 570 575

Ile Tyr His Met Thr Val Pro Tyr Gly Arg Pro Arg Ile Leu Leu Lys
580 585 590

Gln His Arg Val Cys Leu Leu Gln Gln Gln Gln Phe Leu Thr Gly Tyr
595 600 605

Ser Leu Asp Leu Leu Met Pro Leu Trp Ala Ser Tyr Thr Phe Leu Ser
610 615 620

Asn Asp Gln Phe Ser Arg Asp Asp Phe Ser Asn Cys Leu Tyr Gln Asp
625 630 635 640

Leu Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Tyr Tyr Lys Ser
645 650 655

Asn Ser Lys Leu Ser Tyr Gly Phe Leu Thr Pro Pro Arg Leu Asn Arg
660 665 670

Val Ser Asn His Ile Tyr Ser Glu Ala Leu Leu Thr Ser Asn Ile Val
675 680 685

Pro Met Tyr Gln Ser Phe Gln Val Ile Trp His Tyr Leu His Asp Thr
690 695 700

Leu Leu Gln Arg Tyr Ala His Glu Arg Asn Gly Ile Asn Val Val Ser
705 710 715 720

Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Tyr Asp Ser Leu Glu
725 730 735

Ile Leu Lys Gln Asn Ser Arg Val Ile Arg Ser Gln Glu Ile Leu Ile
740 745 750

Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Gln Leu Ser Glu
755 760 765

Thr Pro Leu Glu Cys Ser Ala Leu Glu Ser Ser Ala Tyr Ile Leu Pro
770 775 780

His Arg Pro Asp Asn Ile Glu Ser Cys Thr His Gly Lys Arg Glu Ser
785 790 795 800

Ser Trp Val Glu Glu Leu Leu Thr Leu His Arg Ala Arg Val Thr Asp
805 810 815

Val Glu Leu Ile Thr Gly Leu Ser Phe Tyr Gln Asp Arg Gln Glu Ser
820 825 830

Val Ser Glu Leu Leu Arg Leu Lys Thr His Leu Pro Ile Phe Ser Gln
835 840 845

Glu Asp Gly Gly Ser Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu
850 855 860

Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg
865 870 875 880

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
885 890 895

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
900 905 910

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
915 920 925

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
930 935 940

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
945 950 955 960

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
965 970 975

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
980 985 990

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
995 1000 1005

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
1010 1015 1020

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
1025 1030 1035

Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp
1040 1045 1050

Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys
1055 1060 1065

Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met
1070 1075 1080

Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
1085 1090 1095

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys
1100 1105 1110

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
1115 1120 1125

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr
1130 1135 1140

Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys
1145 1150 1155

Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val
1160 1165 1170

Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp
1175 1180 1185

Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys
1190 1195 1200

Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His
1205 1210 1215

Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr
1220 1225 1230

Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala
1235 1240 1245

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu
1250 1255 1260

Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu
1265 1270 1275

Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln
1280 1285 1290

Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg
1295 1300 1305

Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp
1310 1315 1320

Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
1325 1330 1335

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
1340 1345 1350

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
1355 1360 1365

Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys
1370 1375 1380

Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu
1385 1390 1395

Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val
1400 1405 1410

Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met
1415 1420 1425

Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp
1430 1435 1440

Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg
1445 1450 1455

Cys Lys Asp Ala Leu Ala Arg Ser Trp Ser His Pro Gln Phe Glu
1460 1465 1470

Lys

<210> 14
<211> 1074
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP5-NPP3-Fc sequence

<220>
<221> SIGNAL
<222> (22)..(23)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (848)..(1074)

<400> 14

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe
20 25 30

Asp Ala Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys
35 40 45

Lys Asp Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu
50 55 60

Ser Thr Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu
65 70 75 80

Glu Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp
85 90 95

Cys Cys Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu
100 105 110

Glu Glu Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe
115 120 125

Asp Leu Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu
130 135 140

Tyr Leu Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys
145 150 155 160

Thr Cys Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys
165 170 175

Thr Phe Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser
180 185 190

His Gly Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn
195 200 205

Phe Ser Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly
210 215 220

Gln Pro Met Trp Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr
225 230 235 240

Tyr Phe Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser
245 250 255

Ile Tyr Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser
260 265 270

Thr Leu Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe
275 280 285

Tyr Thr Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly
290 295 300

Pro Val Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala
305 310 315 320

Phe Gly Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys
325 330 335

Val Asn Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys
340 345 350

Asn Lys Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe
355 360 365

Tyr Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro
370 375 380

His Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser
385 390 395 400

Cys Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu
405 410 415

Pro Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His
420 425 430

Leu Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr
435 440 445

Asn Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met
450 455 460

Glu Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu
465 470 475 480

Val Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu
485 490 495

Leu Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn
500 505 510

His Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val
515 520 525

Ser Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser
530 535 540

Leu Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln
545 550 555 560

Val Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val
565 570 575

Lys Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val
580 585 590

Asp His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys
595 600 605

Ala Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly
610 615 620

Asp Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp
625 630 635 640

Val Arg Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala
645 650 655

Asp Lys Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg
660 665 670

Thr Ser Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro
675 680 685

Met Tyr Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu
690 695 700

Leu Ile Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly
705 710 715 720

Pro Ile Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu
725 730 735

Ile Thr Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr
740 745 750

Phe Val Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn
755 760 765

Cys Pro Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro
770 775 780

Thr Asn Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val
785 790 795 800

Glu Glu Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu
805 810 815

Leu Thr Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu
820 825 830

Ile Leu Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Asp
835 840 845

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
850 855 860

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
865 870 875 880

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
885 890 895

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
900 905 910

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
915 920 925

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
930 935 940

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
945 950 955 960

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
965 970 975

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
980 985 990

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
995 1000 1005

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
1010 1015 1020

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
1025 1030 1035

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
1040 1045 1050

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
1055 1060 1065

Ser Leu Ser Pro Gly Lys
1070

<210> 15
<211> 1469

<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP5-NPP3-Albumin sequence

<220>
<221> SIGNAL
<222> (22)..(23)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (848)..(1469)

<400> 15

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe
20 25 30

Asp Ala Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys
35 40 45

Lys Asp Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu
50 55 60

Ser Thr Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu
65 70 75 80

Glu Ala Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp
85 90 95

Cys Cys Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu
100 105 110

Glu Glu Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe
115 120 125

Asp Leu Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu
130 135 140

Tyr Leu Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys
145 150 155 160

Thr Cys Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys
165 170 175

Thr Phe Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser
180 185 190

His Gly Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn
195 200 205

Phe Ser Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly
210 215 220

Gln Pro Met Trp Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr
225 230 235 240

Tyr Phe Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser
245 250 255

Ile Tyr Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser
260 265 270

Thr Leu Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe
275 280 285

Tyr Thr Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly
290 295 300

Pro Val Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala
305 310 315 320

Phe Gly Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys
325 330 335

Val Asn Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys
340 345 350

Asn Lys Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe
355 360 365

Tyr Met Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro
370 375 380

His Asp Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser
385 390 395 400

Cys Arg Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu
405 410 415

Pro Lys Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His
420 425 430

Leu Phe Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr
435 440 445

Asn Cys Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met
450 455 460

Glu Ala Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu
465 470 475 480

Val Glu Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu
485 490 495

Leu Arg Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn
500 505 510

His Leu Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val
515 520 525

Ser Lys Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser
530 535 540

Leu Asp Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln
545 550 555 560

Val Asn Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val
565 570 575

Lys Val Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val
580 585 590

Asp His Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys
595 600 605

Ala Met Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly
610 615 620

Asp Thr Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp
625 630 635 640

Val Arg Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala
645 650 655

Asp Lys Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg
660 665 670

Thr Ser Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro
675 680 685

Met Tyr Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu
690 695 700

Leu Ile Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly
705 710 715 720

Pro Ile Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu
725 730 735

Ile Thr Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr
740 745 750

Phe Val Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn
755 760 765

Cys Pro Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro
770 775 780

Thr Asn Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val
785 790 795 800

Glu Glu Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu
805 810 815

Leu Thr Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu
820 825 830

Ile Leu Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Gly
835 840 845

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Lys Trp
850 855 860

Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg
865 870 875 880

Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr
885 890 895

Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe
900 905 910

Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val
915 920 925

Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
930 935 940

Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
945 950 955 960

Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys
965 970 975

Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
980 985 990

Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met
995 1000 1005

Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
1010 1015 1020

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
1025 1030 1035

Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys
1040 1045 1050

Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp
1055 1060 1065

Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met
1070 1075 1080

Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
1085 1090 1095

Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe
1100 1105 1110

Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys
1115 1120 1125

Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
1130 1135 1140

Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser
1145 1150 1155

Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His
1160 1165 1170

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro
1175 1180 1185

Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn
1190 1195 1200

Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu
1205 1210 1215

Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg
1220 1225 1230

Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu
1235 1240 1245

Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln
1250 1255 1260

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp
1265 1270 1275

Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu
1280 1285 1290

Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu
1295 1300 1305

Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys
1310 1315 1320

Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu
1325 1330 1335

Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro
1340 1345 1350

Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu
1355 1360 1365

Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val
1370 1375 1380

Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile
1385 1390 1395

Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala
1400 1405 1410

Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln
1415 1420 1425

Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys
1430 1435 1440

Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro
1445 1450 1455

Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
1460 1465

<210> 16
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP5 Protein Export Signal Sequence

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> X can be any amino acid

<400> 16

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Xaa
20

<210> 17
<211> 1079
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP51-Fc

<220>
<221> SIGNAL
<222> (22)..(23)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (853)..(1079)
<223> Indicate Fc sequence

<400> 17

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser Gly Leu Lys Pro Ser Cys Ala Lys Glu Val
20 25 30

Lys Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg
35 40 45

Cys Asp Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln
50 55 60

Glu Thr Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg
65 70 75 80

Cys Gly Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp
85 90 95

Cys Lys Asp Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln
100 105 110

Gly Glu Lys Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro
115 120 125

Gln Cys Pro Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu
130 135 140

Asp Gly Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro
145 150 155 160

Val Ile Ser Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg
165 170 175

Pro Val Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr
180 185 190

Gly Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp
195 200 205

Pro Lys Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn
210 215 220

Pro Glu Trp Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln
225 230 235 240

Gly Leu Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile
245 250 255

Asn Gly Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro
260 265 270

Phe Glu Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys
275 280 285

Asp Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser
290 295 300

Ser Gly His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu
305 310 315 320

Gln Arg Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu
325 330 335

Leu Asn Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly
340 345 350

Met Glu Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu
355 360 365

Gly Asp Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu
370 375 380

Arg Pro Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly
385 390 395 400

Ile Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro

405

410

415

Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp
 420 425 430

Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala
 435 440 445

Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser
 450 455 460

Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro
 465 470 475 480

Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val
 485 490 495

Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn
 500 505 510

Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr
 515 520 525

Pro Lys His Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr
 530 535 540

Arg Asn Pro Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu
 545 550 555 560

Pro Ile Glu Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu
 565 570 575

Lys Ile Ile Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu
 580 585 590

Gln Lys Glu Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser
 595 600 605

Gly Tyr Ser Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val
 610 615 620

Asp Arg Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr
625 630 635 640

Gln Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr
645 650 655

Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu
660 665 670

Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn
675 680 685

Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His
690 695 700

Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val
705 710 715 720

Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser
725 730 735

Leu Glu Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile
740 745 750

Leu Ile Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr
755 760 765

Ser Gln Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile
770 775 780

Leu Pro His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His
785 790 795 800

Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile
805 810 815

Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys
820 825 830

Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe

835

840

845

Ser Gln Glu Asp Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
 850 855 860

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
 865 870 875 880

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
 885 890 895

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
 900 905 910

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
 915 920 925

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
 930 935 940

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
 945 950 955 960

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
 965 970 975

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
 980 985 990

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
 995 1000 1005

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 1010 1015 1020

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
 1025 1030 1035

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 1040 1045 1050

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 1055 1060 1065

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 1070 1075

<210> 18
 <211> 1082
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ENPP71-Fc Amino Acid Sequence

<220>
 <221> SIGNAL
 <222> (22)..(23)
 <223> Cleavage point of the signal peptide sequence

<220>
 <221> MISC_FEATURE
 <222> (856)..(1082)
 <223> Indicate Fc sequence

<400> 18

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
 1 5 10 15

Ala Pro Gly Ala Gly Ala Gly Leu Lys Pro Ser Cys Ala Lys Glu Val
 20 25 30

Lys Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg
 35 40 45

Cys Asp Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln
 50 55 60

Glu Thr Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg
 65 70 75 80

Cys Gly Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp
 85 90 95

Cys Lys Asp Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln
100 105 110

Gly Glu Lys Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro
115 120 125

Gln Cys Pro Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu
130 135 140

Asp Gly Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro
145 150 155 160

Val Ile Ser Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg
165 170 175

Pro Val Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr
180 185 190

Gly Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp
195 200 205

Pro Lys Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn
210 215 220

Pro Glu Trp Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln
225 230 235 240

Gly Leu Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile
245 250 255

Asn Gly Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro
260 265 270

Phe Glu Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys
275 280 285

Asp Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser
290 295 300

Ser Gly His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu
305 310 315 320

Gln Arg Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu
325 330 335

Leu Asn Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly
340 345 350

Met Glu Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu
355 360 365

Gly Asp Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu
370 375 380

Arg Pro Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly
385 390 395 400

Ile Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro
405 410 415

Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp
420 425 430

Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala
435 440 445

Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser
450 455 460

Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro
465 470 475 480

Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val
485 490 495

Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn
500 505 510

Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr
515 520 525

Pro Lys His Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr
530 535 540

Arg Asn Pro Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu
545 550 555 560

Pro Ile Glu Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu
565 570 575

Lys Ile Ile Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu
580 585 590

Gln Lys Glu Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser
595 600 605

Gly Tyr Ser Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val
610 615 620

Asp Arg Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr
625 630 635 640

Gln Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr
645 650 655

Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu
660 665 670

Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn
675 680 685

Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His
690 695 700

Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val
705 710 715 720

Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser
725 730 735

Leu Glu Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile
740 745 750

Leu Ile Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr
755 760 765

Ser Gln Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile
770 775 780

Leu Pro His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His
785 790 795 800

Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile
805 810 815

Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys
820 825 830

Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe
835 840 845

Ser Gln Glu Asp Leu Ile Asn Asp Lys Thr His Thr Cys Pro Pro Cys
850 855 860

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
865 870 875 880

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
885 890 895

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
900 905 910

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
915 920 925

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
930 935 940

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
945 950 955 960

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
965 970 975

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
980 985 990

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
995 1000 1005

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
1010 1015 1020

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
1025 1030 1035

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
1040 1045 1050

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
1055 1060 1065

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
1070 1075 1080

<210> 19
<211> 849
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP71 (lacking NPP1 N-Terminus GLK) Amino Acid Sequence

<220>
<221> SIGNAL
<222> (22)..(23)
<223> Cleavage point of the signal peptide sequence

<400> 19

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Ala Pro Ser Cys Ala Lys Glu Val Lys Ser Cys
20 25 30

Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala
35 40 45

Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys
50 55 60

Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu
65 70 75 80

Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp
85 90 95

Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys
100 105 110

Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro
115 120 125

Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe
130 135 140

Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser
145 150 155 160

Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr
165 170 175

Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr
180 185 190

Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met
195 200 205

Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp
210 215 220

Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys
225 230 235 240

Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile
245 250 255

Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu
260 265 270

Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg
275 280 285

Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His
290 295 300

Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val
305 310 315 320

Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu
325 330 335

His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln
340 345 350

Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val
355 360 365

Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser
370 375 380

Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg
385 390 395 400

Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys
405 410 415

His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu
420 425 430

Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro
435 440 445

Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val
450 455 460

Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys
465 470 475 480

His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu
485 490 495

Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His
500 505 510

Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His
515 520 525

Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro
530 535 540

Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu
545 550 555 560

Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile
565 570 575

Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu
580 585 590

Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser
595 600 605

Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn
610 615 620

Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe
625 630 635 640

Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn
645 650 655

Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn
660 665 670

Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro
675 680 685

Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu
690 695 700

Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly
705 710 715 720

Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn
725 730 735

Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro
740 745 750

Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr
755 760 765

Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His
770 775 780

Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser
785 790 795 800

Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val
805 810 815

Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val
820 825 830

Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu
835 840 845

Asp

<210> 20

<211> 1079

<212> PRT

<213> Artificial Sequence

<220>

<223> ENPP71 (lacking NPP1 N-Terminus GLK) - Fc Amino Acid Sequence

<220>

<221> SIGNAL

<222> (22)..(23)

<223> Cleavage point of the signal peptide sequence

<220>

<221> MISC_FEATURE

<222> (854)..(1079)

<223> Indicate Fc sequence

<400> 20

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Ala Pro Ser Cys Ala Lys Glu Val Lys Ser Cys
20 25 30

Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala
35 40 45

Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys
50 55 60

Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu
65 70 75 80

Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp
85 90 95

Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys
100 105 110

Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro
115 120 125

Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe
130 135 140

Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser
145 150 155 160

Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr
165 170 175

Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr
180 185 190

Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met
195 200 205

Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp
210 215 220

Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys
225 230 235 240

Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile
245 250 255

Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu
260 265 270

Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg
275 280 285

Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His
290 295 300

Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val
305 310 315 320

Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu
325 330 335

His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln
340 345 350

Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val
355 360 365

Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser

370

375

380

Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg
 385 390 395 400

Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys
 405 410 415

His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu
 420 425 430

Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro
 435 440 445

Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val
 450 455 460

Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys
 465 470 475 480

His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu
 485 490 495

Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His
 500 505 510

Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His
 515 520 525

Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro
 530 535 540

Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu
 545 550 555 560

Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile
 565 570 575

Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu
 580 585 590

Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser
595 600 605

Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn
610 615 620

Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe
625 630 635 640

Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn
645 650 655

Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn
660 665 670

Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro
675 680 685

Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu
690 695 700

Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly
705 710 715 720

Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn
725 730 735

Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro
740 745 750

Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr
755 760 765

Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His
770 775 780

Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser
785 790 795 800

Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val

805																810				815			
Glu	His	Ile	Thr	Gly	Leu	Ser	Phe	Tyr	Gln	Gln	Arg	Lys	Glu	Pro	Val								
			820				825						830										
Ser	Asp	Ile	Leu	Lys	Leu	Lys	Thr	His	Leu	Pro	Thr	Phe	Ser	Gln	Glu								
			835				840						845										
Asp	Leu	Ile	Asn	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro								
			850				855						860										
Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys								
			865				870						875										
Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val								
			885							890			895										
Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp								
			900				905						910										
Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr								
			915				920						925										
Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp								
			930				935						940										
Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu								
			945				950						955										
Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg								
			965							970			975										
Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys								
			980							985			990										
Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp								
			995				1000						1005										
Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr									
			1010				1015						1020										

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
1025 1030 1035

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
1040 1045 1050

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
1055 1060 1065

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
1070 1075

<210> 21
<211> 1474
<212> PRT
<213> Artificial Sequence

<220>
<223> - ENPP71 (lacking NPP1 N-Terminus GLK) - ALB Amino Acid Sequence

<220>
<221> SIGNAL
<222> (22)..(23)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (857)..(1474)

<220>
<221> MISC_FEATURE
<222> (857)..(1474)
<223> Indicate Albumin sequence

<400> 21

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Ala Pro Ser Cys Ala Lys Glu Val Lys Ser Cys
20 25 30

Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala
35 40 45

Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys
50 55 60

Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu
65 70 75 80

Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp
85 90 95

Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys
100 105 110

Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro
115 120 125

Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe
130 135 140

Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser
145 150 155 160

Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr
165 170 175

Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr
180 185 190

Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met
195 200 205

Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp
210 215 220

Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys
225 230 235 240

Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile
245 250 255

Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu
260 265 270

Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg
275 280 285

Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His
290 295 300

Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val
305 310 315 320

Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu
325 330 335

His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln
340 345 350

Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val
355 360 365

Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser
370 375 380

Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg
385 390 395 400

Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys
405 410 415

His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu
420 425 430

Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro
435 440 445

Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val
450 455 460

Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys
465 470 475 480

His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu
485 490 495

Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His
500 505 510

Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His
515 520 525

Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro
530 535 540

Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu
545 550 555 560

Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile
565 570 575

Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu
580 585 590

Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser
595 600 605

Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn
610 615 620

Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe
625 630 635 640

Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn
645 650 655

Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn
660 665 670

Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro
675 680 685

Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu
690 695 700

Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly
705 710 715 720

Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn
725 730 735

Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro
740 745 750

Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr
755 760 765

Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His
770 775 780

Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser
785 790 795 800

Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val
805 810 815

Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val
820 825 830

Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu
835 840 845

Asp Arg Ser Gly Ser Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu
850 855 860

Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg
865 870 875 880

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
885 890 895

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
900 905 910

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
915 920 925

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
930 935 940

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
945 950 955 960

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
965 970 975

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
980 985 990

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
995 1000 1005

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
1010 1015 1020

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
1025 1030 1035

Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp
1040 1045 1050

Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys
1055 1060 1065

Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met
1070 1075 1080

Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
1085 1090 1095

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys
1100 1105 1110

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
1115 1120 1125

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr
1130 1135 1140

Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys
1145 1150 1155

Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val
1160 1165 1170

Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp
1175 1180 1185

Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys
1190 1195 1200

Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His
1205 1210 1215

Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr
1220 1225 1230

Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala
1235 1240 1245

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu
1250 1255 1260

Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu
1265 1270 1275

Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln
1280 1285 1290

Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg
1295 1300 1305

Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp
1310 1315 1320

Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
1325 1330 1335

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
1340 1345 1350

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
1355 1360 1365

Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys
1370 1375 1380

Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu
1385 1390 1395

Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val
1400 1405 1410

Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met
1415 1420 1425

Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp
1430 1435 1440

Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg
1445 1450 1455

Cys Lys Asp Ala Leu Ala Arg Ser Trp Ser His Pro Gln Phe Glu
1460 1465 1470

Lys

<210> 22

<211> 1072

<212> PRT

<213> Artificial Sequence

<220>

<223> ENPP7-NPP3-Fc sequence

<220>

<221> SIGNAL
<222> (20)..(21)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (846)..(1072)
<223> Indicate Fc sequence

<400> 22

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu Glu Ala
65 70 75 80

Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys
85 90 95

Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu
100 105 110

Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu
115 120 125

Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu
130 135 140

Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys
145 150 155 160

Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe
165 170 175

Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly
180 185 190

Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser
195 200 205

Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro
210 215 220

Met Trp Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe
225 230 235 240

Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr
245 250 255

Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu
260 265 270

Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr
275 280 285

Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val
290 295 300

Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe Gly
305 310 315 320

Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn
325 330 335

Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys
340 345 350

Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met
355 360 365

Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His Asp
370 375 380

Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg

385		390		395		400									
Lys	Pro	Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys
			405						410				415		
Arg	Leu	His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe
			420				425						430		
Val	Asp	Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys
		435					440					445			
Gly	Gly	Gly	Asn	His	Gly	Tyr	Asn	Asn	Glu	Phe	Arg	Ser	Met	Glu	Ala
	450					455					460				
Ile	Phe	Leu	Ala	His	Gly	Pro	Ser	Phe	Lys	Glu	Lys	Thr	Glu	Val	Glu
465					470					475					480
Pro	Phe	Glu	Asn	Ile	Glu	Val	Tyr	Asn	Leu	Met	Cys	Asp	Leu	Leu	Arg
			485						490					495	
Ile	Gln	Pro	Ala	Pro	Asn	Asn	Gly	Thr	His	Gly	Ser	Leu	Asn	His	Leu
			500					505					510		
Leu	Lys	Val	Pro	Phe	Tyr	Glu	Pro	Ser	His	Ala	Glu	Glu	Val	Ser	Lys
		515						520				525			
Phe	Ser	Val	Cys	Gly	Phe	Ala	Asn	Pro	Leu	Pro	Thr	Glu	Ser	Leu	Asp
	530					535					540				
Cys	Phe	Cys	Pro	His	Leu	Gln	Asn	Ser	Thr	Gln	Leu	Glu	Gln	Val	Asn
545					550					555					560
Gln	Met	Leu	Asn	Leu	Thr	Gln	Glu	Glu	Ile	Thr	Ala	Thr	Val	Lys	Val
			565						570					575	
Asn	Leu	Pro	Phe	Gly	Arg	Pro	Arg	Val	Leu	Gln	Lys	Asn	Val	Asp	His
			580					585					590		
Cys	Leu	Leu	Tyr	His	Arg	Glu	Tyr	Val	Ser	Gly	Phe	Gly	Lys	Ala	Met
		595					600					605			

Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr
610 615 620

Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg
625 630 635 640

Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys
645 650 655

Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser
660 665 670

Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr
675 680 685

Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile
690 695 700

Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile
705 710 715 720

Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr
725 730 735

Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val
740 745 750

Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro
755 760 765

Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn
770 775 780

Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu
785 790 795 800

Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr
805 810 815

Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu

820

825

830

Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Asp Lys Thr
835 840 845

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
850 855 860

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
865 870 875 880

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
885 890 895

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
900 905 910

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
915 920 925

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
930 935 940

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
945 950 955 960

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
965 970 975

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
980 985 990

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
995 1000 1005

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
1010 1015 1020

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
1025 1030 1035

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
1040 1045 1050

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
1055 1060 1065

Ser Pro Gly Lys
1070

<210> 23
<211> 1396
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP71-Albumin

<220>
<221> SIGNAL
<222> (23)..(24)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (857)..(1396)
<223> Indicate Fc sequence

<400> 23

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser
20 25 30

Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp
35 40 45

Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr
50 55 60

Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly
65 70 75 80

Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys
85 90 95

Asp Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu
100 105 110

Lys Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys
115 120 125

Pro Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly
130 135 140

Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile
145 150 155 160

Ser Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val
165 170 175

Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu
180 185 190

Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys
195 200 205

Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu
210 215 220

Trp Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu
225 230 235 240

Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly
245 250 255

Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu
260 265 270

Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu
275 280 285

Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly
290 295 300

His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg
305 310 315 320

Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn
325 330 335

Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu
340 345 350

Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp
355 360 365

Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro
370 375 380

Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala
385 390 395 400

Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu
405 410 415

Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile
420 425 430

Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn
435 440 445

Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn
450 455 460

Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe
465 470 475 480

Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn
485 490 495

Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr
500 505 510

His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys
515 520 525

His Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn
530 535 540

Pro Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile
545 550 555 560

Glu Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile
565 570 575

Ile Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys
580 585 590

Glu Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr
595 600 605

Ser Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg
610 615 620

Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp
625 630 635 640

Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn
645 650 655

Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys
660 665 670

Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val
675 680 685

Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr
690 695 700

Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser
705 710 715 720

Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu
725 730 735

Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile
740 745 750

Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln
755 760 765

Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro
770 775 780

His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His Asp Ser
785 790 795 800

Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp
805 810 815

Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro
820 825 830

Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln
835 840 845

Glu Asp Gly Gly Ser Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu
850 855 860

Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg
865 870 875 880

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
885 890 895

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
900 905 910

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
915 920 925

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
930 935 940

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
945 950 955 960

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
965 970 975

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
980 985 990

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
995 1000 1005

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
1010 1015 1020

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
1025 1030 1035

Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp
1040 1045 1050

Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys
1055 1060 1065

Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met
1070 1075 1080

Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
1085 1090 1095

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys
1100 1105 1110

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
1115 1120 1125

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr
1130 1135 1140

Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys
1145 1150 1155

Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val
1160 1165 1170

Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp
1175 1180 1185

Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys
1190 1195 1200

Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His
1205 1210 1215

Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr
1220 1225 1230

Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala
1235 1240 1245

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu
1250 1255 1260

Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu
1265 1270 1275

Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln
1280 1285 1290

Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg
1295 1300 1305

Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp
1310 1315 1320

Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
1325 1330 1335

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
1340 1345 1350

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
1355 1360 1365

Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys
1370 1375 1380

Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu
1385 1390 1395

<210> 24
<211> 1467
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP7-NPP3-Albumin

<220>
<221> SIGNAL
<222> (20)..(21)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (860)..(1467)
<223> Indicate Albumin sequence

<400> 24

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu Glu Ala
65 70 75 80

Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys

85

90

95

Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu
 100 105 110

Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu
 115 120 125

Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu
 130 135 140

Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys
 145 150 155 160

Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe
 165 170 175

Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly
 180 185 190

Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser
 195 200 205

Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro
 210 215 220

Met Trp Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe
 225 230 235 240

Trp Pro Gly Ser Glu Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr
 245 250 255

Met Pro Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu
 260 265 270

Leu Lys Trp Leu Asp Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr
 275 280 285

Met Tyr Phe Glu Glu Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val
 290 295 300

Ser Ala Arg Val Ile Lys Ala Leu Gln Val Val Asp His Ala Phe Gly
305 310 315 320

Met Leu Met Glu Gly Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn
325 330 335

Ile Ile Leu Leu Ala Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys
340 345 350

Met Glu Tyr Met Thr Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met
355 360 365

Tyr Glu Gly Pro Ala Pro Arg Ile Arg Ala His Asn Ile Pro His Asp
370 375 380

Phe Phe Ser Phe Asn Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg
385 390 395 400

Lys Pro Asp Gln His Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro Lys
405 410 415

Arg Leu His Tyr Ala Lys Asn Val Arg Ile Asp Lys Val His Leu Phe
420 425 430

Val Asp Gln Gln Trp Leu Ala Val Arg Ser Lys Ser Asn Thr Asn Cys
435 440 445

Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala
450 455 460

Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu
465 470 475 480

Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg
485 490 495

Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His Leu
500 505 510

Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys

515

520

525

Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp
 530 535 540

Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn
 545 550 555 560

Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val
 565 570 575

Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp His
 580 585 590

Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met
 595 600 605

Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr
 610 615 620

Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg
 625 630 635 640

Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys
 645 650 655

Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser
 660 665 670

Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr
 675 680 685

Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile
 690 695 700

Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile
 705 710 715 720

Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr
 725 730 735

Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val
740 745 750

Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro
755 760 765

Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn
770 775 780

Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu
785 790 795 800

Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr
805 810 815

Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu
820 825 830

Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Gly Gly Gly
835 840 845

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Lys Trp Val Thr
850 855 860

Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val
865 870 875 880

Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp
885 890 895

Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln
900 905 910

Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu
915 920 925

Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn
930 935 940

Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile

945		950		955		960
Pro Asn Leu Arg	Glu Asn Tyr Gly	Glu Leu Ala Asp	Cys Cys Thr Lys			
	965	970	975			
Gln Glu Pro Glu	Arg Asn Glu Cys	Phe Leu Gln His	Lys Asp Asp Asn			
	980	985	990			
Pro Ser Leu Pro	Pro Phe Glu Arg	Pro Glu Ala Glu	Ala Met Cys Thr			
	995	1000	1005			
Ser Phe Lys Glu	Asn Pro Thr Thr	Phe Met Gly His	Tyr Leu His			
	1010	1015	1020			
Glu Val Ala Arg	Arg His Pro Tyr	Phe Tyr Ala Pro	Glu Leu Leu			
	1025	1030	1035			
Tyr Tyr Ala Glu	Gln Tyr Asn Glu	Ile Leu Thr Gln	Cys Cys Ala			
	1040	1045	1050			
Glu Ala Asp Lys	Glu Ser Cys Leu	Thr Pro Lys Leu	Asp Gly Val			
	1055	1060	1065			
Lys Glu Lys Ala	Leu Val Ser Ser	Val Arg Gln Arg	Met Lys Cys			
	1070	1075	1080			
Ser Ser Met Gln	Lys Phe Gly Glu	Arg Ala Phe Lys	Ala Trp Ala			
	1085	1090	1095			
Val Ala Arg Leu	Ser Gln Thr Phe	Pro Asn Ala Asp	Phe Ala Glu			
	1100	1105	1110			
Ile Thr Lys Leu	Ala Thr Asp Leu	Thr Lys Val Asn	Lys Glu Cys			
	1115	1120	1125			
Cys His Gly Asp	Leu Leu Glu Cys	Ala Asp Asp Arg	Ala Glu Leu			
	1130	1135	1140			
Ala Lys Tyr Met	Cys Glu Asn Gln	Ala Thr Ile Ser	Ser Lys Leu			
	1145	1150	1155			

Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu
1160 1165 1170

Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile
1175 1180 1185

Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala
1190 1195 1200

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser
1205 1210 1215

Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala
1220 1225 1230

Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn
1235 1240 1245

Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu
1250 1255 1260

Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr
1265 1270 1275

Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg
1280 1285 1290

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu
1295 1300 1305

Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu
1310 1315 1320

Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala
1325 1330 1335

Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser
1340 1345 1350

Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg

1355

1360

1365

Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys
 1370 1375 1380

Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr
 1385 1390 1395

Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala
 1400 1405 1410

Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys
 1415 1420 1425

Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys
 1430 1435 1440

Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu
 1445 1450 1455

Val Thr Arg Cys Lys Asp Ala Leu Ala
 1460 1465

<210> 25

<211> 1507

<212> PRT

<213> Artificial Sequence

<220>

<223> ENPP7-ENPP3-Albumin

<220>

<221> SIGNAL

<222> (20)..(21)

<223> Cleavage point of the signal peptide sequence

<220>

<221> MISC_FEATURE

<222> (900)..(1507)

<400> 25

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
 1 5 10 15

Ala Pro Gly Ala Lys Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala
20 25 30

Ser Phe Arg Gly Leu Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp
35 40 45

Arg Gly Asp Cys Cys Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr
50 55 60

Arg Ile Trp Met Cys Asn Lys Phe Arg Cys Gly Glu Arg Leu Glu Ala
65 70 75 80

Ser Leu Cys Ser Cys Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys
85 90 95

Ala Asp Tyr Lys Ser Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu
100 105 110

Asn Cys Asp Thr Ala Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu
115 120 125

Pro Pro Val Ile Leu Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu
130 135 140

Tyr Thr Trp Asp Thr Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys
145 150 155 160

Gly Ile His Ser Lys Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe
165 170 175

Pro Asn His Tyr Thr Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly
180 185 190

Ile Ile Asp Asn Asn Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser
195 200 205

Leu Ser Ser Lys Glu Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro
210 215 220

Met Trp Leu Thr Ala Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe

225					230						235					240
Trp	Pro	Gly	Ser	Glu	Val	Ala	Ile	Asn	Gly	Ser	Phe	Pro	Ser	Ile	Tyr	
				245					250					255		
Met	Pro	Tyr	Asn	Gly	Ser	Val	Pro	Phe	Glu	Glu	Arg	Ile	Ser	Thr	Leu	
			260					265					270			
Leu	Lys	Trp	Leu	Asp	Leu	Pro	Lys	Ala	Glu	Arg	Pro	Arg	Phe	Tyr	Thr	
		275					280					285				
Met	Tyr	Phe	Glu	Glu	Pro	Asp	Ser	Ser	Gly	His	Ala	Gly	Gly	Pro	Val	
	290					295					300					
Ser	Ala	Arg	Val	Ile	Lys	Ala	Leu	Gln	Val	Val	Asp	His	Ala	Phe	Gly	
305					310					315					320	
Met	Leu	Met	Glu	Gly	Leu	Lys	Gln	Arg	Asn	Leu	His	Asn	Cys	Val	Asn	
				325					330					335		
Ile	Ile	Leu	Leu	Ala	Asp	His	Gly	Met	Asp	Gln	Thr	Tyr	Cys	Asn	Lys	
			340					345					350			
Met	Glu	Tyr	Met	Thr	Asp	Tyr	Phe	Pro	Arg	Ile	Asn	Phe	Phe	Tyr	Met	
		355					360					365				
Tyr	Glu	Gly	Pro	Ala	Pro	Arg	Ile	Arg	Ala	His	Asn	Ile	Pro	His	Asp	
	370					375					380					
Phe	Phe	Ser	Phe	Asn	Ser	Glu	Glu	Ile	Val	Arg	Asn	Leu	Ser	Cys	Arg	
385					390					395					400	
Lys	Pro	Asp	Gln	His	Phe	Lys	Pro	Tyr	Leu	Thr	Pro	Asp	Leu	Pro	Lys	
			405						410					415		
Arg	Leu	His	Tyr	Ala	Lys	Asn	Val	Arg	Ile	Asp	Lys	Val	His	Leu	Phe	
			420					425					430			
Val	Asp	Gln	Gln	Trp	Leu	Ala	Val	Arg	Ser	Lys	Ser	Asn	Thr	Asn	Cys	
		435					440					445				

Gly Gly Gly Asn His Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala
450 455 460

Ile Phe Leu Ala His Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu
465 470 475 480

Pro Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg
485 490 495

Ile Gln Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn His Leu
500 505 510

Leu Lys Val Pro Phe Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys
515 520 525

Phe Ser Val Cys Gly Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp
530 535 540

Cys Phe Cys Pro His Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn
545 550 555 560

Gln Met Leu Asn Leu Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val
565 570 575

Asn Leu Pro Phe Gly Arg Pro Arg Val Leu Gln Lys Asn Val Asp His
580 585 590

Cys Leu Leu Tyr His Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met
595 600 605

Arg Met Pro Met Trp Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr
610 615 620

Ser Pro Leu Pro Pro Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg
625 630 635 640

Val Pro Pro Ser Glu Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys
645 650 655

Asn Ile Thr His Gly Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser

660

665

670

Asp Ser Gln Tyr Asp Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr
 675 680 685

Glu Glu Phe Arg Lys Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile
 690 695 700

Lys His Ala Thr Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile
 705 710 715 720

Phe Asp Tyr Asn Tyr Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr
 725 730 735

Lys His Leu Ala Asn Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val
 740 745 750

Val Leu Thr Ser Cys Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro
 755 760 765

Gly Trp Leu Asp Val Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn
 770 775 780

Val Glu Ser Cys Pro Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu
 785 790 795 800

Arg Phe Thr Ala His Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr
 805 810 815

Gly Leu Asp Phe Tyr Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu
 820 825 830

Gln Leu Lys Thr Tyr Leu Pro Thr Phe Glu Thr Thr Ile Asp Lys Thr
 835 840 845

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 850 855 860

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 865 870 875 880

Thr Pro Glu Val Thr Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
885 890 895

Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser
900 905 910

Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser
915 920 925

Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly
930 935 940

Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp
945 950 955 960

Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys
965 970 975

Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu
980 985 990

Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly
995 1000 1005

Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu
1010 1015 1020

Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe
1025 1030 1035

Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn
1040 1045 1050

Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg
1055 1060 1065

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln
1070 1075 1080

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu

1085						1090						1095			
Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	
	1100					1105					1110				
Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	
	1115					1120					1125				
Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	
	1130					1135					1140				
Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala	
	1145					1150					1155				
Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	
	1160					1165					1170				
Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	
	1175					1180					1185				
Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	
	1190					1195					1200				
Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	
	1205					1210					1215				
Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	
	1220					1225					1230				
Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	
	1235					1240					1245				
Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	
	1250					1255					1260				
Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	
	1265					1270					1275				
Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	
	1280					1285					1290				

Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys
1295 1300 1305

Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu
1310 1315 1320

Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala
1325 1330 1335

Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu
1340 1345 1350

Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg
1355 1360 1365

Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val
1370 1375 1380

Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys
1385 1390 1395

Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
1400 1405 1410

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu
1415 1420 1425

Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu
1430 1435 1440

Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His
1445 1450 1455

Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp
1460 1465 1470

Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp
1475 1480 1485

Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys

1490

1495

1500

Asp Ala Leu Ala
1505

<210> 26

<211> 852

<212> PRT

<213> Artificial Sequence

<220>

<223> ENPP71 Amino Acid Sequence

<220>

<221> SIGNAL

<222> (22)..(23)

<223> Cleavage point of the signal peptide sequence

<400> 26

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Ala Gly Leu Lys Pro Ser Cys Ala Lys Glu Val
20 25 30

Lys Ser Cys Lys Gly Arg Cys Phe Glu Arg Thr Phe Gly Asn Cys Arg
35 40 45

Cys Asp Ala Ala Cys Val Glu Leu Gly Asn Cys Cys Leu Asp Tyr Gln
50 55 60

Glu Thr Cys Ile Glu Pro Glu His Ile Trp Thr Cys Asn Lys Phe Arg
65 70 75 80

Cys Gly Glu Lys Arg Leu Thr Arg Ser Leu Cys Ala Cys Ser Asp Asp
85 90 95

Cys Lys Asp Lys Gly Asp Cys Cys Ile Asn Tyr Ser Ser Val Cys Gln
100 105 110

Gly Glu Lys Ser Trp Val Glu Glu Pro Cys Glu Ser Ile Asn Glu Pro
115 120 125

Gln Cys Pro Ala Gly Phe Glu Thr Pro Pro Thr Leu Leu Phe Ser Leu
130 135 140

Asp Gly Phe Arg Ala Glu Tyr Leu His Thr Trp Gly Gly Leu Leu Pro
145 150 155 160

Val Ile Ser Lys Leu Lys Lys Cys Gly Thr Tyr Thr Lys Asn Met Arg
165 170 175

Pro Val Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Ser Ile Val Thr
180 185 190

Gly Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Lys Met Tyr Asp
195 200 205

Pro Lys Met Asn Ala Ser Phe Ser Leu Lys Ser Lys Glu Lys Phe Asn
210 215 220

Pro Glu Trp Tyr Lys Gly Glu Pro Ile Trp Val Thr Ala Lys Tyr Gln
225 230 235 240

Gly Leu Lys Ser Gly Thr Phe Phe Trp Pro Gly Ser Asp Val Glu Ile
245 250 255

Asn Gly Ile Phe Pro Asp Ile Tyr Lys Met Tyr Asn Gly Ser Val Pro
260 265 270

Phe Glu Glu Arg Ile Leu Ala Val Leu Gln Trp Leu Gln Leu Pro Lys
275 280 285

Asp Glu Arg Pro His Phe Tyr Thr Leu Tyr Leu Glu Glu Pro Asp Ser
290 295 300

Ser Gly His Ser Tyr Gly Pro Val Ser Ser Glu Val Ile Lys Ala Leu
305 310 315 320

Gln Arg Val Asp Gly Met Val Gly Met Leu Met Asp Gly Leu Lys Glu
325 330 335

Leu Asn Leu His Arg Cys Leu Asn Leu Ile Leu Ile Ser Asp His Gly

340

345

350

Met Glu Gln Gly Ser Cys Lys Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu
 355 360 365

Gly Asp Val Lys Asn Ile Lys Val Ile Tyr Gly Pro Ala Ala Arg Leu
 370 375 380

Arg Pro Ser Asp Val Pro Asp Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly
 385 390 395 400

Ile Ala Arg Asn Leu Ser Cys Arg Glu Pro Asn Gln His Phe Lys Pro
 405 410 415

Tyr Leu Lys His Phe Leu Pro Lys Arg Leu His Phe Ala Lys Ser Asp
 420 425 430

Arg Ile Glu Pro Leu Thr Phe Tyr Leu Asp Pro Gln Trp Gln Leu Ala
 435 440 445

Leu Asn Pro Ser Glu Arg Lys Tyr Cys Gly Ser Gly Phe His Gly Ser
 450 455 460

Asp Asn Val Phe Ser Asn Met Gln Ala Leu Phe Val Gly Tyr Gly Pro
 465 470 475 480

Gly Phe Lys His Gly Ile Glu Ala Asp Thr Phe Glu Asn Ile Glu Val
 485 490 495

Tyr Asn Leu Met Cys Asp Leu Leu Asn Leu Thr Pro Ala Pro Asn Asn
 500 505 510

Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Asn Pro Val Tyr Thr
 515 520 525

Pro Lys His Pro Lys Glu Val His Pro Leu Val Gln Cys Pro Phe Thr
 530 535 540

Arg Asn Pro Arg Asp Asn Leu Gly Cys Ser Cys Asn Pro Ser Ile Leu
 545 550 555 560

Pro Ile Glu Asp Phe Gln Thr Gln Phe Asn Leu Thr Val Ala Glu Glu
565 570 575

Lys Ile Ile Lys His Glu Thr Leu Pro Tyr Gly Arg Pro Arg Val Leu
580 585 590

Gln Lys Glu Asn Thr Ile Cys Leu Leu Ser Gln His Gln Phe Met Ser
595 600 605

Gly Tyr Ser Gln Asp Ile Leu Met Pro Leu Trp Thr Ser Tyr Thr Val
610 615 620

Asp Arg Asn Asp Ser Phe Ser Thr Glu Asp Phe Ser Asn Cys Leu Tyr
625 630 635 640

Gln Asp Phe Arg Ile Pro Leu Ser Pro Val His Lys Cys Ser Phe Tyr
645 650 655

Lys Asn Asn Thr Lys Val Ser Tyr Gly Phe Leu Ser Pro Pro Gln Leu
660 665 670

Asn Lys Asn Ser Ser Gly Ile Tyr Ser Glu Ala Leu Leu Thr Thr Asn
675 680 685

Ile Val Pro Met Tyr Gln Ser Phe Gln Val Ile Trp Arg Tyr Phe His
690 695 700

Asp Thr Leu Leu Arg Lys Tyr Ala Glu Glu Arg Asn Gly Val Asn Val
705 710 715 720

Val Ser Gly Pro Val Phe Asp Phe Asp Tyr Asp Gly Arg Cys Asp Ser
725 730 735

Leu Glu Asn Leu Arg Gln Lys Arg Arg Val Ile Arg Asn Gln Glu Ile
740 745 750

Leu Ile Pro Thr His Phe Phe Ile Val Leu Thr Ser Cys Lys Asp Thr
755 760 765

Ser Gln Thr Pro Leu His Cys Glu Asn Leu Asp Thr Leu Ala Phe Ile

770

775

780

Leu Pro His Arg Thr Asp Asn Ser Glu Ser Cys Val His Gly Lys His
785 790 795 800

Asp Ser Ser Trp Val Glu Glu Leu Leu Met Leu His Arg Ala Arg Ile
805 810 815

Thr Asp Val Glu His Ile Thr Gly Leu Ser Phe Tyr Gln Gln Arg Lys
820 825 830

Glu Pro Val Ser Asp Ile Leu Lys Leu Lys Thr His Leu Pro Thr Phe
835 840 845

Ser Gln Glu Asp
850

<210> 27
<211> 925
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP121 Amino Acid Sequence

<220>
<221> SIGNAL
<222> (92)..(93)
<223> Cleavage point of the signal peptide sequence

<400> 27

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala Gly
85 90 95

Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg Cys
100 105 110

Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val Glu
115 120 125

Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro Glu
130 135 140

His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu Thr
145 150 155 160

Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp Cys
165 170 175

Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val Glu
180 185 190

Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe Glu
195 200 205

Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu Tyr
210 215 220

Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys Lys
225 230 235 240

Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys Thr
245 250 255

Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser His
260 265 270

Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser Phe

275

280

285

Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly Glu
 290 295 300

Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr Phe
 305 310 315 320

Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp Ile
 325 330 335

Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu Ala
 340 345 350

Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe Tyr
 355 360 365

Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly Pro
 370 375 380

Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met Val
 385 390 395 400

Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys Leu
 405 410 415

Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys Lys
 420 425 430

Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile Lys
 435 440 445

Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro Asp
 450 455 460

Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser Cys
 465 470 475 480

Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu Pro
 485 490 495

Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu Thr Phe
500 505 510

Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg Lys
515 520 525

Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn Met
530 535 540

Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile Glu
545 550 555 560

Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu
565 570 575

Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn
580 585 590

His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu Val
595 600 605

His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn Leu
610 615 620

Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln Thr
625 630 635 640

Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu Thr
645 650 655

Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile Cys
660 665 670

Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile Leu
675 680 685

Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe Ser
690 695 700

Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro Leu

705					710						715					720
Ser	Pro	Val	His	Lys	Cys	Ser	Phe	Tyr	Lys	Asn	Asn	Thr	Lys	Val	Ser	
				725					730					735		
Tyr	Gly	Phe	Leu	Ser	Pro	Pro	Gln	Leu	Asn	Lys	Asn	Ser	Ser	Gly	Ile	
			740					745					750			
Tyr	Ser	Glu	Ala	Leu	Leu	Thr	Thr	Asn	Ile	Val	Pro	Met	Tyr	Gln	Ser	
		755					760					765				
Phe	Gln	Val	Ile	Trp	Arg	Tyr	Phe	His	Asp	Thr	Leu	Leu	Arg	Lys	Tyr	
	770					775					780					
Ala	Glu	Glu	Arg	Asn	Gly	Val	Asn	Val	Val	Ser	Gly	Pro	Val	Phe	Asp	
785					790					795					800	
Phe	Asp	Tyr	Asp	Gly	Arg	Cys	Asp	Ser	Leu	Glu	Asn	Leu	Arg	Gln	Lys	
				805					810					815		
Arg	Arg	Val	Ile	Arg	Asn	Gln	Glu	Ile	Leu	Ile	Pro	Thr	His	Phe	Phe	
			820					825					830			
Ile	Val	Leu	Thr	Ser	Cys	Lys	Asp	Thr	Ser	Gln	Thr	Pro	Leu	His	Cys	
		835					840					845				
Glu	Asn	Leu	Asp	Thr	Leu	Ala	Phe	Ile	Leu	Pro	His	Arg	Thr	Asp	Asn	
	850					855					860					
Ser	Glu	Ser	Cys	Val	His	Gly	Lys	His	Asp	Ser	Ser	Trp	Val	Glu	Glu	
865					870					875					880	
Leu	Leu	Met	Leu	His	Arg	Ala	Arg	Ile	Thr	Asp	Val	Glu	His	Ile	Thr	
				885					890					895		
Gly	Leu	Ser	Phe	Tyr	Gln	Gln	Arg	Lys	Glu	Pro	Val	Ser	Asp	Ile	Leu	
			900					905					910			
Lys	Leu	Lys	Thr	His	Leu	Pro	Thr	Phe	Ser	Gln	Glu	Asp				
		915					920					925				

<210> 28
<211> 1155
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP121-Fc Amino Acid Sequence

<220>
<221> SIGNAL
<222> (92)..(93)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (929)..(1155)
<223> Indicate Fc sequence

<400> 28

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala Gly
85 90 95

Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg Cys
100 105 110

Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val Glu
115 120 125

Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro Glu
130 135 140

His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu Thr
145 150 155 160

Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp Cys
165 170 175

Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val Glu
180 185 190

Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe Glu
195 200 205

Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu Tyr
210 215 220

Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys Lys
225 230 235 240

Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys Thr
245 250 255

Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser His
260 265 270

Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser Phe
275 280 285

Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly Glu
290 295 300

Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr Phe
305 310 315 320

Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp Ile
325 330 335

Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu Ala
340 345 350

Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe Tyr
355 360 365

Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly Pro
370 375 380

Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met Val
385 390 395 400

Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys Leu
405 410 415

Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys Lys
420 425 430

Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile Lys
435 440 445

Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro Asp
450 455 460

Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser Cys
465 470 475 480

Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu Pro
485 490 495

Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu Thr Phe
500 505 510

Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg Lys
515 520 525

Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn Met
530 535 540

Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile Glu
545 550 555 560

Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu
565 570 575

Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn
580 585 590

His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu Val
595 600 605

His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn Leu
610 615 620

Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln Thr
625 630 635 640

Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu Thr
645 650 655

Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile Cys
660 665 670

Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile Leu
675 680 685

Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe Ser
690 695 700

Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro Leu
705 710 715 720

Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys Val Ser
725 730 735

Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly Ile
740 745 750

Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln Ser
755 760 765

Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys Tyr
770 775 780

Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe Asp
785 790 795 800

Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln Lys
805 810 815

Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe Phe
820 825 830

Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His Cys
835 840 845

Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp Asn
850 855 860

Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu Glu
865 870 875 880

Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile Thr
885 890 895

Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile Leu
900 905 910

Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp Leu Ile Asn
915 920 925

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
930 935 940

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
945 950 955 960

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
965 970 975

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
980 985 990

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
995 1000 1005

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
1010 1015 1020

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
1025 1030 1035

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
1040 1045 1050

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
1055 1060 1065

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
1070 1075 1080

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
1085 1090 1095

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
1100 1105 1110

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
1115 1120 1125

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
1130 1135 1140

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
1145 1150 1155

<210> 29

<211> 1550

<212> PRT

<213> Artificial Sequence

<220>

<223> ENPP121-ALB Amino Acid Sequence

<220>

<221> SIGNAL
<222> (92)..(93)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (933)..(1550)
<223> Indicate Albumin sequence

<400> 29

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala Gly
85 90 95

Leu Lys Pro Ser Cys Ala Lys Glu Val Lys Ser Cys Lys Gly Arg Cys
100 105 110

Phe Glu Arg Thr Phe Gly Asn Cys Arg Cys Asp Ala Ala Cys Val Glu
115 120 125

Leu Gly Asn Cys Cys Leu Asp Tyr Gln Glu Thr Cys Ile Glu Pro Glu
130 135 140

His Ile Trp Thr Cys Asn Lys Phe Arg Cys Gly Glu Lys Arg Leu Thr
145 150 155 160

Arg Ser Leu Cys Ala Cys Ser Asp Asp Cys Lys Asp Lys Gly Asp Cys
165 170 175

Cys Ile Asn Tyr Ser Ser Val Cys Gln Gly Glu Lys Ser Trp Val Glu
180 185 190

Glu Pro Cys Glu Ser Ile Asn Glu Pro Gln Cys Pro Ala Gly Phe Glu
195 200 205

Thr Pro Pro Thr Leu Leu Phe Ser Leu Asp Gly Phe Arg Ala Glu Tyr
210 215 220

Leu His Thr Trp Gly Gly Leu Leu Pro Val Ile Ser Lys Leu Lys Lys
225 230 235 240

Cys Gly Thr Tyr Thr Lys Asn Met Arg Pro Val Tyr Pro Thr Lys Thr
245 250 255

Phe Pro Asn His Tyr Ser Ile Val Thr Gly Leu Tyr Pro Glu Ser His
260 265 270

Gly Ile Ile Asp Asn Lys Met Tyr Asp Pro Lys Met Asn Ala Ser Phe
275 280 285

Ser Leu Lys Ser Lys Glu Lys Phe Asn Pro Glu Trp Tyr Lys Gly Glu
290 295 300

Pro Ile Trp Val Thr Ala Lys Tyr Gln Gly Leu Lys Ser Gly Thr Phe
305 310 315 320

Phe Trp Pro Gly Ser Asp Val Glu Ile Asn Gly Ile Phe Pro Asp Ile
325 330 335

Tyr Lys Met Tyr Asn Gly Ser Val Pro Phe Glu Glu Arg Ile Leu Ala
340 345 350

Val Leu Gln Trp Leu Gln Leu Pro Lys Asp Glu Arg Pro His Phe Tyr
355 360 365

Thr Leu Tyr Leu Glu Glu Pro Asp Ser Ser Gly His Ser Tyr Gly Pro
370 375 380

Val Ser Ser Glu Val Ile Lys Ala Leu Gln Arg Val Asp Gly Met Val

385		390		395		400
Gly Met Leu Met Asp Gly Leu Lys Glu Leu Asn Leu His Arg Cys Leu						
		405		410		415
Asn Leu Ile Leu Ile Ser Asp His Gly Met Glu Gln Gly Ser Cys Lys						
		420		425		430
Lys Tyr Ile Tyr Leu Asn Lys Tyr Leu Gly Asp Val Lys Asn Ile Lys						
		435		440		445
Val Ile Tyr Gly Pro Ala Ala Arg Leu Arg Pro Ser Asp Val Pro Asp						
		450		455		460
Lys Tyr Tyr Ser Phe Asn Tyr Glu Gly Ile Ala Arg Asn Leu Ser Cys						
465		470		475		480
Arg Glu Pro Asn Gln His Phe Lys Pro Tyr Leu Lys His Phe Leu Pro						
		485		490		495
Lys Arg Leu His Phe Ala Lys Ser Asp Arg Ile Glu Pro Leu Thr Phe						
		500		505		510
Tyr Leu Asp Pro Gln Trp Gln Leu Ala Leu Asn Pro Ser Glu Arg Lys						
		515		520		525
Tyr Cys Gly Ser Gly Phe His Gly Ser Asp Asn Val Phe Ser Asn Met						
		530		535		540
Gln Ala Leu Phe Val Gly Tyr Gly Pro Gly Phe Lys His Gly Ile Glu						
545		550		555		560
Ala Asp Thr Phe Glu Asn Ile Glu Val Tyr Asn Leu Met Cys Asp Leu						
		565		570		575
Leu Asn Leu Thr Pro Ala Pro Asn Asn Gly Thr His Gly Ser Leu Asn						
		580		585		590
His Leu Leu Lys Asn Pro Val Tyr Thr Pro Lys His Pro Lys Glu Val						
		595		600		605

His Pro Leu Val Gln Cys Pro Phe Thr Arg Asn Pro Arg Asp Asn Leu
610 615 620

Gly Cys Ser Cys Asn Pro Ser Ile Leu Pro Ile Glu Asp Phe Gln Thr
625 630 635 640

Gln Phe Asn Leu Thr Val Ala Glu Glu Lys Ile Ile Lys His Glu Thr
645 650 655

Leu Pro Tyr Gly Arg Pro Arg Val Leu Gln Lys Glu Asn Thr Ile Cys
660 665 670

Leu Leu Ser Gln His Gln Phe Met Ser Gly Tyr Ser Gln Asp Ile Leu
675 680 685

Met Pro Leu Trp Thr Ser Tyr Thr Val Asp Arg Asn Asp Ser Phe Ser
690 695 700

Thr Glu Asp Phe Ser Asn Cys Leu Tyr Gln Asp Phe Arg Ile Pro Leu
705 710 715 720

Ser Pro Val His Lys Cys Ser Phe Tyr Lys Asn Asn Thr Lys Val Ser
725 730 735

Tyr Gly Phe Leu Ser Pro Pro Gln Leu Asn Lys Asn Ser Ser Gly Ile
740 745 750

Tyr Ser Glu Ala Leu Leu Thr Thr Asn Ile Val Pro Met Tyr Gln Ser
755 760 765

Phe Gln Val Ile Trp Arg Tyr Phe His Asp Thr Leu Leu Arg Lys Tyr
770 775 780

Ala Glu Glu Arg Asn Gly Val Asn Val Val Ser Gly Pro Val Phe Asp
785 790 795 800

Phe Asp Tyr Asp Gly Arg Cys Asp Ser Leu Glu Asn Leu Arg Gln Lys
805 810 815

Arg Arg Val Ile Arg Asn Gln Glu Ile Leu Ile Pro Thr His Phe Phe

820

825

830

Ile Val Leu Thr Ser Cys Lys Asp Thr Ser Gln Thr Pro Leu His Cys
 835 840 845

Glu Asn Leu Asp Thr Leu Ala Phe Ile Leu Pro His Arg Thr Asp Asn
 850 855 860

Ser Glu Ser Cys Val His Gly Lys His Asp Ser Ser Trp Val Glu Glu
 865 870 875 880

Leu Leu Met Leu His Arg Ala Arg Ile Thr Asp Val Glu His Ile Thr
 885 890 895

Gly Leu Ser Phe Tyr Gln Gln Arg Lys Glu Pro Val Ser Asp Ile Leu
 900 905 910

Lys Leu Lys Thr His Leu Pro Thr Phe Ser Gln Glu Asp Arg Ser Gly
 915 920 925

Ser Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val
 930 935 940

Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys
 945 950 955 960

Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys
 965 970 975

Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr
 980 985 990

Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr
 995 1000 1005

Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His
 1010 1015 1020

Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu
 1025 1030 1035

Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu
1040 1045 1050

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
1055 1060 1065

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe
1070 1075 1080

Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val
1085 1090 1095

Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr
1100 1105 1110

Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala
1115 1120 1125

Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu
1130 1135 1140

Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser
1145 1150 1155

Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
1160 1165 1170

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr
1175 1180 1185

Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His
1190 1195 1200

Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys
1205 1210 1215

Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr
1220 1225 1230

Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu

1235	1240	1245
Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala 1250 1255 1260		
Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala 1265 1270 1275		
Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg 1280 1285 1290		
His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys 1295 1300 1305		
Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro 1310 1315 1320		
Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu 1325 1330 1335		
Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys 1340 1345 1350		
Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr 1355 1360 1365		
Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala 1370 1375 1380		
Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu 1385 1390 1395		
Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu 1400 1405 1410		
Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His 1415 1420 1425		
Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys 1430 1435 1440		

Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
1445 1450 1455

Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro
1460 1465 1470

Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu
1475 1480 1485

Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val
1490 1495 1500

Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala
1505 1510 1515

Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr
1520 1525 1530

Arg Cys Lys Asp Ala Leu Ala Arg Ser Trp Ser His Pro Gln Phe
1535 1540 1545

Glu Lys
1550

<210> 30
<211> 1147
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP121-NPP3-Fc sequence

<220>
<221> SIGNAL
<222> (95)..(96)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (921)..(1147)

<400> 30

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly

1		5		10		15											
Gly	Arg	Ala	Pro	Arg	Glu	Gly	Pro	Ala	Gly	Asn	Gly	Arg	Asp	Arg	Gly		
			20					25					30				
Arg	Ser	His	Ala	Ala	Glu	Ala	Pro	Gly	Asp	Pro	Gln	Ala	Ala	Ala	Ser		
		35					40					45					
Leu	Leu	Ala	Pro	Met	Asp	Val	Gly	Glu	Glu	Pro	Leu	Glu	Lys	Ala	Ala		
	50					55					60						
Arg	Ala	Arg	Thr	Ala	Lys	Asp	Pro	Asn	Thr	Tyr	Lys	Ile	Ile	Ser	Leu		
65					70					75					80		
Phe	Thr	Phe	Ala	Val	Gly	Val	Asn	Ile	Cys	Leu	Gly	Phe	Thr	Ala	Lys		
				85					90					95			
Gln	Gly	Ser	Cys	Arg	Lys	Lys	Cys	Phe	Asp	Ala	Ser	Phe	Arg	Gly	Leu		
			100					105					110				
Glu	Asn	Cys	Arg	Cys	Asp	Val	Ala	Cys	Lys	Asp	Arg	Gly	Asp	Cys	Cys		
		115					120					125					
Trp	Asp	Phe	Glu	Asp	Thr	Cys	Val	Glu	Ser	Thr	Arg	Ile	Trp	Met	Cys		
	130					135					140						
Asn	Lys	Phe	Arg	Cys	Gly	Glu	Arg	Leu	Glu	Ala	Ser	Leu	Cys	Ser	Cys		
145					150					155					160		
Ser	Asp	Asp	Cys	Leu	Gln	Arg	Lys	Asp	Cys	Cys	Ala	Asp	Tyr	Lys	Ser		
				165					170					175			
Val	Cys	Gln	Gly	Glu	Thr	Ser	Trp	Leu	Glu	Glu	Asn	Cys	Asp	Thr	Ala		
			180					185					190				
Gln	Gln	Ser	Gln	Cys	Pro	Glu	Gly	Phe	Asp	Leu	Pro	Pro	Val	Ile	Leu		
		195					200					205					
Phe	Ser	Met	Asp	Gly	Phe	Arg	Ala	Glu	Tyr	Leu	Tyr	Thr	Trp	Asp	Thr		
	210					215					220						

Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys Gly Ile His Ser Lys
225 230 235 240

Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Thr
245 250 255

Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Asn
260 265 270

Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser Leu Ser Ser Lys Glu
275 280 285

Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro Met Trp Leu Thr Ala
290 295 300

Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe Trp Pro Gly Ser Glu
305 310 315 320

Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr Met Pro Tyr Asn Gly
325 330 335

Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu Leu Lys Trp Leu Asp
340 345 350

Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr Met Tyr Phe Glu Glu
355 360 365

Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val Ser Ala Arg Val Ile
370 375 380

Lys Ala Leu Gln Val Val Asp His Ala Phe Gly Met Leu Met Glu Gly
385 390 395 400

Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn Ile Ile Leu Leu Ala
405 410 415

Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys Met Glu Tyr Met Thr
420 425 430

Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met Tyr Glu Gly Pro Ala

435

440

445

Pro Arg Ile Arg Ala His Asn Ile Pro His Asp Phe Phe Ser Phe Asn
 450 455 460

Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg Lys Pro Asp Gln His
 465 470 475 480

Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro Lys Arg Leu His Tyr Ala
 485 490 495

Lys Asn Val Arg Ile Asp Lys Val His Leu Phe Val Asp Gln Gln Trp
 500 505 510

Leu Ala Val Arg Ser Lys Ser Asn Thr Asn Cys Gly Gly Gly Asn His
 515 520 525

Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala Ile Phe Leu Ala His
 530 535 540

Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu Pro Phe Glu Asn Ile
 545 550 555 560

Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg Ile Gln Pro Ala Pro
 565 570 575

Asn Asn Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Val Pro Phe
 580 585 590

Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys Phe Ser Val Cys Gly
 595 600 605

Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp Cys Phe Cys Pro His
 610 615 620

Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn Gln Met Leu Asn Leu
 625 630 635 640

Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val Asn Leu Pro Phe Gly
 645 650 655

Arg Pro Arg Val Leu Gln Lys Asn Val Asp His Cys Leu Leu Tyr His
660 665 670

Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met Arg Met Pro Met Trp
675 680 685

Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr Ser Pro Leu Pro Pro
690 695 700

Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg Val Pro Pro Ser Glu
705 710 715 720

Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys Asn Ile Thr His Gly
725 730 735

Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser Asp Ser Gln Tyr Asp
740 745 750

Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr Glu Glu Phe Arg Lys
755 760 765

Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile Lys His Ala Thr Glu
770 775 780

Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile Phe Asp Tyr Asn Tyr
785 790 795 800

Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His Leu Ala Asn
805 810 815

Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu Thr Ser Cys
820 825 830

Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp Leu Asp Val
835 840 845

Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu Ser Cys Pro
850 855 860

Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe Thr Ala His

865		870		875		880									
Ile	Ala	Arg	Val	Arg	Asp	Val	Glu	Leu	Leu	Thr	Gly	Leu	Asp	Phe	Tyr
				885					890					895	
Gln	Asp	Lys	Val	Gln	Pro	Val	Ser	Glu	Ile	Leu	Gln	Leu	Lys	Thr	Tyr
			900					905					910		
Leu	Pro	Thr	Phe	Glu	Thr	Thr	Ile	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro
		915					920					925			
Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro
	930					935					940				
Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr
945					950					955					960
Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn
				965					970					975	
Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg
			980					985					990		
Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val
		995					1000					1005			
Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	
	1010					1015					1020				
Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	
	1025					1030					1035				
Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	
	1040					1045					1050				
Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	
	1055					1060					1065				
Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	
	1070					1075					1080				

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
1085 1090 1095

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
1100 1105 1110

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
1115 1120 1125

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
1130 1135 1140

Ser Pro Gly Lys
1145

<210> 31
<211> 1542
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP121-NPP3-Albumin sequence

<220>
<221> SIGNAL
<222> (95)..(96)
<223> Cleavage point of the signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (935)..(1542)
<223> Indicate Albumin sequence

<400> 31

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala Lys
85 90 95

Gln Gly Ser Cys Arg Lys Lys Cys Phe Asp Ala Ser Phe Arg Gly Leu
100 105 110

Glu Asn Cys Arg Cys Asp Val Ala Cys Lys Asp Arg Gly Asp Cys Cys
115 120 125

Trp Asp Phe Glu Asp Thr Cys Val Glu Ser Thr Arg Ile Trp Met Cys
130 135 140

Asn Lys Phe Arg Cys Gly Glu Arg Leu Glu Ala Ser Leu Cys Ser Cys
145 150 155 160

Ser Asp Asp Cys Leu Gln Arg Lys Asp Cys Cys Ala Asp Tyr Lys Ser
165 170 175

Val Cys Gln Gly Glu Thr Ser Trp Leu Glu Glu Asn Cys Asp Thr Ala
180 185 190

Gln Gln Ser Gln Cys Pro Glu Gly Phe Asp Leu Pro Pro Val Ile Leu
195 200 205

Phe Ser Met Asp Gly Phe Arg Ala Glu Tyr Leu Tyr Thr Trp Asp Thr
210 215 220

Leu Met Pro Asn Ile Asn Lys Leu Lys Thr Cys Gly Ile His Ser Lys
225 230 235 240

Tyr Met Arg Ala Met Tyr Pro Thr Lys Thr Phe Pro Asn His Tyr Thr
245 250 255

Ile Val Thr Gly Leu Tyr Pro Glu Ser His Gly Ile Ile Asp Asn Asn
260 265 270

Met Tyr Asp Val Asn Leu Asn Lys Asn Phe Ser Leu Ser Ser Lys Glu
275 280 285

Gln Asn Asn Pro Ala Trp Trp His Gly Gln Pro Met Trp Leu Thr Ala
290 295 300

Met Tyr Gln Gly Leu Lys Ala Ala Thr Tyr Phe Trp Pro Gly Ser Glu
305 310 315 320

Val Ala Ile Asn Gly Ser Phe Pro Ser Ile Tyr Met Pro Tyr Asn Gly
325 330 335

Ser Val Pro Phe Glu Glu Arg Ile Ser Thr Leu Leu Lys Trp Leu Asp
340 345 350

Leu Pro Lys Ala Glu Arg Pro Arg Phe Tyr Thr Met Tyr Phe Glu Glu
355 360 365

Pro Asp Ser Ser Gly His Ala Gly Gly Pro Val Ser Ala Arg Val Ile
370 375 380

Lys Ala Leu Gln Val Val Asp His Ala Phe Gly Met Leu Met Glu Gly
385 390 395 400

Leu Lys Gln Arg Asn Leu His Asn Cys Val Asn Ile Ile Leu Leu Ala
405 410 415

Asp His Gly Met Asp Gln Thr Tyr Cys Asn Lys Met Glu Tyr Met Thr
420 425 430

Asp Tyr Phe Pro Arg Ile Asn Phe Phe Tyr Met Tyr Glu Gly Pro Ala
435 440 445

Pro Arg Ile Arg Ala His Asn Ile Pro His Asp Phe Phe Ser Phe Asn
450 455 460

Ser Glu Glu Ile Val Arg Asn Leu Ser Cys Arg Lys Pro Asp Gln His
465 470 475 480

Phe Lys Pro Tyr Leu Thr Pro Asp Leu Pro Lys Arg Leu His Tyr Ala
485 490 495

Lys Asn Val Arg Ile Asp Lys Val His Leu Phe Val Asp Gln Gln Trp
500 505 510

Leu Ala Val Arg Ser Lys Ser Asn Thr Asn Cys Gly Gly Gly Asn His
515 520 525

Gly Tyr Asn Asn Glu Phe Arg Ser Met Glu Ala Ile Phe Leu Ala His
530 535 540

Gly Pro Ser Phe Lys Glu Lys Thr Glu Val Glu Pro Phe Glu Asn Ile
545 550 555 560

Glu Val Tyr Asn Leu Met Cys Asp Leu Leu Arg Ile Gln Pro Ala Pro
565 570 575

Asn Asn Gly Thr His Gly Ser Leu Asn His Leu Leu Lys Val Pro Phe
580 585 590

Tyr Glu Pro Ser His Ala Glu Glu Val Ser Lys Phe Ser Val Cys Gly
595 600 605

Phe Ala Asn Pro Leu Pro Thr Glu Ser Leu Asp Cys Phe Cys Pro His
610 615 620

Leu Gln Asn Ser Thr Gln Leu Glu Gln Val Asn Gln Met Leu Asn Leu
625 630 635 640

Thr Gln Glu Glu Ile Thr Ala Thr Val Lys Val Asn Leu Pro Phe Gly
645 650 655

Arg Pro Arg Val Leu Gln Lys Asn Val Asp His Cys Leu Leu Tyr His
660 665 670

Arg Glu Tyr Val Ser Gly Phe Gly Lys Ala Met Arg Met Pro Met Trp
675 680 685

Ser Ser Tyr Thr Val Pro Gln Leu Gly Asp Thr Ser Pro Leu Pro Pro
690 695 700

Thr Val Pro Asp Cys Leu Arg Ala Asp Val Arg Val Pro Pro Ser Glu
705 710 715 720

Ser Gln Lys Cys Ser Phe Tyr Leu Ala Asp Lys Asn Ile Thr His Gly
725 730 735

Phe Leu Tyr Pro Pro Ala Ser Asn Arg Thr Ser Asp Ser Gln Tyr Asp
740 745 750

Ala Leu Ile Thr Ser Asn Leu Val Pro Met Tyr Glu Glu Phe Arg Lys
755 760 765

Met Trp Asp Tyr Phe His Ser Val Leu Leu Ile Lys His Ala Thr Glu
770 775 780

Arg Asn Gly Val Asn Val Val Ser Gly Pro Ile Phe Asp Tyr Asn Tyr
785 790 795 800

Asp Gly His Phe Asp Ala Pro Asp Glu Ile Thr Lys His Leu Ala Asn
805 810 815

Thr Asp Val Pro Ile Pro Thr His Tyr Phe Val Val Leu Thr Ser Cys
820 825 830

Lys Asn Lys Ser His Thr Pro Glu Asn Cys Pro Gly Trp Leu Asp Val
835 840 845

Leu Pro Phe Ile Ile Pro His Arg Pro Thr Asn Val Glu Ser Cys Pro
850 855 860

Glu Gly Lys Pro Glu Ala Leu Trp Val Glu Glu Arg Phe Thr Ala His
865 870 875 880

Ile Ala Arg Val Arg Asp Val Glu Leu Leu Thr Gly Leu Asp Phe Tyr
885 890 895

Gln Asp Lys Val Gln Pro Val Ser Glu Ile Leu Gln Leu Lys Thr Tyr
900 905 910

Leu Pro Thr Phe Glu Thr Thr Ile Gly Gly Gly Ser Gly Gly Gly Gly
915 920 925

Ser Gly Gly Gly Gly Ser Met Lys Trp Val Thr Phe Leu Leu Leu Leu
930 935 940

Phe Val Ser Gly Ser Ala Phe Ser Arg Gly Val Phe Arg Arg Glu Ala
945 950 955 960

His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His
965 970 975

Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys
980 985 990

Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala
995 1000 1005

Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser
1010 1015 1020

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
1025 1030 1035

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu
1040 1045 1050

Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
1055 1060 1065

Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr
1070 1075 1080

Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His
1085 1090 1095

Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
1100 1105 1110

Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
1115 1120 1125

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val
1130 1135 1140

Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys
1145 1150 1155

Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
1160 1165 1170

Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu
1175 1180 1185

Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys
1190 1195 1200

Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu
1205 1210 1215

Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu
1220 1225 1230

Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu
1235 1240 1245

Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile
1250 1255 1260

Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala
1265 1270 1275

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser
1280 1285 1290

Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala
1295 1300 1305

Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn
1310 1315 1320

Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu
1325 1330 1335

Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr
1340 1345 1350

Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg
1355 1360 1365

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu
1370 1375 1380

Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu
1385 1390 1395

Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala
1400 1405 1410

Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser
1415 1420 1425

Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg
1430 1435 1440

Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys
1445 1450 1455

Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr
1460 1465 1470

Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala
1475 1480 1485

Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys
1490 1495 1500

Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys
1505 1510 1515

Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu
1520 1525 1530

Val Thr Arg Cys Lys Asp Ala Leu Ala
1535 1540

<210> 32
<211> 98
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP121GLK Protein Export Signal Sequence

<400> 32

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala Gly
85 90 95

Leu Lys

<210> 33
<211> 623
<212> PRT
<213> Artificial Sequence

<220>
<223> Albumin Sequence

<400> 33

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met
1 5 10 15

Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala Phe
20 25 30

Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala His
35 40 45

Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile
50 55 60

Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys
65 70 75 80

Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu
85 90 95

Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
100 105 110

Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp
115 120 125

Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
130 135 140

Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu
145 150 155 160

Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His
165 170 175

Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
180 185 190

Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys
195 200 205

Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val
210 215 220

Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser
225 230 235 240

Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
245 250 255

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys
260 265 270

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp
275 280 285

Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys
290 295 300

Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys
305 310 315 320

Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr
325 330 335

Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln
340 345 350

Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr
355 360 365

Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu
370 375 380

Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys
385 390 395 400

Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe
405 410 415

Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp
420 425 430

Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val
435 440 445

Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu
450 455 460

Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro
465 470 475 480

Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu
485 490 495

Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
500 505 510

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser
515 520 525

Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu
530 535 540

Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys
545 550 555 560

Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro
565 570 575

Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln
580 585 590

Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
595 600 605

Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
610 615 620

<210> 34

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Human IgG Fc domain, Fc

<400> 34

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 35
<211> 618
<212> PRT
<213> Artificial Sequence

<220>
<223> Albumin Sequence

<400> 35

Met Lys Trp Val Thr Phe Leu Leu Leu Leu Phe Val Ser Gly Ser Ala
1 5 10 15

Phe Ser Arg Gly Val Phe Arg Arg Glu Ala His Lys Ser Glu Ile Ala
20 25 30

His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu
35 40 45

Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala
50 55 60

Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala
100 105 110

Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala
130 135 140

Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly
145 150 155 160

His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys
180 185 190

Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly
195 200 205

Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys
210 215 220

Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
225 230 235 240

Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr
245 250 255

Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
260 265 270

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met
275 280 285

Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp
290 295 300

Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp
305 310 315 320

Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp
325 330 335

Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
340 345 350

Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser
355 360 365

Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys
370 375 380

Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu
385 390 395 400

Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys
405 410 415

Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu
420 425 430

Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val
435 440 445

Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu
450 455 460

Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile
465 470 475 480

Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His
485 490 495

Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
500 505 510

Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala
515 520 525

Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu
530 535 540

Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys
545 550 555 560

Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala
565 570 575

Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe
580 585 590

Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
595 600 605

Arg Ser Trp Ser His Pro Gln Phe Glu Lys
610 615

<210> 36
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> ENPP2 Signal Peptide

<400> 36

Leu Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala
1 5 10 15

<210> 37
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal Sequence ENPP7

<400> 37

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala
20

<210> 38
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal sequence ENPP7

<400> 38

Met Arg Gly Pro Ala Val Leu Leu Thr Val Ala Leu Ala Thr Leu Leu
1 5 10 15

Ala Pro Gly Ala Gly Ala
20

<210> 39

<211> 95

<212> PRT

<213> Artificial Sequence

<220>

<223> Signal Sequence ENPP1-2-1

<400> 39

Met Glu Arg Asp Gly Cys Ala Gly Gly Gly Ser Arg Gly Gly Glu Gly
1 5 10 15

Gly Arg Ala Pro Arg Glu Gly Pro Ala Gly Asn Gly Arg Asp Arg Gly
20 25 30

Arg Ser His Ala Ala Glu Ala Pro Gly Asp Pro Gln Ala Ala Ala Ser
35 40 45

Leu Leu Ala Pro Met Asp Val Gly Glu Glu Pro Leu Glu Lys Ala Ala
50 55 60

Arg Ala Arg Thr Ala Lys Asp Pro Asn Thr Tyr Lys Ile Ile Ser Leu
65 70 75 80

Phe Thr Phe Ala Val Gly Val Asn Ile Cys Leu Gly Phe Thr Ala
85 90 95

<210> 40

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> exENPP3

<400> 40

Leu Leu Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg
1 5 10 15

Lys

<210> 41
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal Sequence ENPP5

<400> 41

Met Thr Ser Lys Phe Leu Leu Val Ser Phe Ile Leu Ala Ala Leu Ser
1 5 10 15

Leu Ser Thr Thr Phe Ser
20

<210> 42
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal Sequence - Azurocidin

<400> 42

Met Thr Arg Leu Thr Val Leu Ala Leu Leu Ala Gly Leu Leu Ala Ser
1 5 10 15

Ser Arg Ala

<210> 43
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<220>

<221> MISC_FEATURE

<223> Features section of the listing that any one or all of amino acids 1-15 can either be present or absent

<400> 43

Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Arg
1				5						10					15

<210> 44

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<400> 44

Asp	Ser	Ser	Ser	Glu	Glu	Lys	Phe	Leu	Arg	Arg	Ile	Gly	Arg	Phe	Gly
1				5					10					15	

<210> 45

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<400> 45

Glu	Glu	Glu	Glu	Glu	Glu	Glu	Pro	Arg	Gly	Asp	Thr
1				5					10		

<210> 46

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<400> 46

Ala	Pro	Trp	His	Leu	Ser	Ser	Gln	Tyr	Ser	Arg	Thr
1				5					10		

<210> 47

<211> 12

<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 47

Ser Thr Leu Pro Ile Pro His Glu Phe Ser Arg Glu
1 5 10

<210> 48
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 48

Val Thr Lys His Leu Asn Gln Ile Ser Gln Ser Tyr
1 5 10

<210> 49
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<220>
<221> MISC_FEATURE
<223> Features section of the listing that any one or all of amino
acids 2-15 can either be present or absent

<400> 49

Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu
1 5 10 15

<210> 50
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 50

Gly Gly Ser Gly Gly Ser
1 5

<210> 51

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<400> 51

Arg Ser Gly Ser Gly Gly Ser
1 5

<210> 52

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<220>

<221> MISC_FEATURE

<223> Features section of the listing that any one or all of amino acids 2-15 can either be present or absent

<400> 52

Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp
1 5 10 15

<210> 53

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<400> 53

Leu Val Ile Met Ser Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys
1 5 10 15

<210> 54
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 54

Val	Ile	Met	Ser	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Arg	Lys
1				5				10					15	

<210> 55
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 55

Ile	Met	Ser	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Arg	Lys
1				5				10					

<210> 56
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 56

Met	Ser	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Arg	Lys
1				5				10				

<210> 57
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 57

Ser	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Gly	Leu	Arg	Lys
1				5				10			

<210> 58
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 58

Leu Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys
1 5 10

<210> 59
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 59

Gly Leu Gly Leu Gly Leu Gly Leu Arg Lys
1 5 10

<210> 60
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 60

Leu Gly Leu Gly Leu Gly Leu Arg Lys
1 5

<210> 61
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 61

Gly Leu Gly Leu Gly Leu Arg Lys
1 5

<210> 62
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 62

Leu Gly Leu Gly Leu Arg Lys
1 5

<210> 63
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 63

Gly Leu Gly Leu Arg Lys
1 5

<210> 64
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 64

Leu Gly Leu Arg Lys
1 5

<210> 65
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 65

Gly Leu Arg Lys
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<210> 66

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<220>

<221> MISC_FEATURE

<223> Features section of the listing that any one or all of amino acids 1-15 can either be present or absent

<400> 66

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

<210> 67

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<220>

<221> MISC_FEATURE

<223> Features section of the listing that any one or all of amino acids 2-15 can either be present or absent

<400> 67

Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp
1 5 10 15

<210> 68

<211> 50

<212> PRT

<213> Artificial Sequence

<220>

<223> Linker

<220>
 <221> MISC_FEATURE
 <223> Amino acids 6-50 can either be present or absent in groups of 5(GGGGS) starting at position 6

<400> 68

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Gly Ser
 50

<210> 69
 <211> 2625
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> ENPP3 Nucleotide sequence

<400> 69
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 ctggggcttg gactcaggaa actggaaaag caaggcagct gcaggaagaa gtgctttgat 180
 gcatcattta gaggactgga gaactgccgg tgtgatgtgg catgtaaaga ccgaggtgat 240
 tgctgctggg attttgaaga cacctgtgtg gaatcaactc gaatatggat gtgcaataaa 300
 tttcgttgtg gagagaccag attagaggcc agcctttgct cttgttcaga tgactgtttg 360
 cagaggaaag attgctgtgc tgactataag agtgtttgcc aaggagaaac ctcatggctg 420
 gaagaaaact gtgacacagc ccagcagtct cagtgccag aagggtttga cctgccacca 480
 gttatcttgt tttctatgga tggatttaga gctgaatatt tatacacatg ggatacttta 540
 atgccaaata tcaataaact gaaaacatgt ggaattcatt caaaatacat gagagctatg 600
 tatcctacca aaaccttccc aaatcattac accattgtca cgggcttgta tccagagtca 660

catggcatca ttgacaataa tatgtatgat gtaaattctca acaagaattht ttcacttttct	720
tcaaaggaac aaaataatcc agcctgggtgg catgggcaac caatgtggct gacagcaatg	780
tatcaaggtht taaaagccgc tacctacttht tggcccggat cagaagtggc tataaatggc	840
tcctttcctt ccatatacat gccttacaac ggaagtgtcc catttgaaga gaggatttct	900
acactgttaa aatggctgga cctgccccaa gctgaaagac ccaggthtta taccatgtat	960
tttgaagaac ctgattcctc tggacatgca ggtggaccag tcagtgccag agtaattaaa	1020
gccttacagg tagtagatca tgctthtggg atgttgatgg aaggcctgaa gcagcggaat	1080
ttgcacaact gtgtcaatat catccttctg gctgaccatg gaatggacca gacttattgt	1140
aacaagatgg aatacatgac tgattatttht cccagaataa acttcttcta catgtacgaa	1200
gggcctgccc cccgcatccg agctcataat atacctcatg actthtthtag thttaattct	1260
gaggaaattg ttagaaacct cagttgccga aaacctgatc agcatttcaa gccctatttg	1320
actcctgatt tgccaaagcg actgcactat gccaagaacg tcagaatcga caaagthcat	1380
ctctthtgg atcaacagtg gctggctgtt aggagtaaat caaatacaaa ttgtggagga	1440
ggcaaccatg gttataacaa tgagthtagg agcatggagg ctatctthtct ggcacatgga	1500
cccagthtta aagagaagac tgaagttgaa ccatttgaaa atattgaagt ctataaccta	1560
atgtgtgatc ttctacgcat tcaaccagca ccaaacaatg gaacccatgg tagthtaaac	1620
catctthtga aggtgccttht ttatgagcca tcccatgcag aggaggtgtc aaagthttht	1680
gthtgtggct ttgctaatcc attgcccaca gagtctcttg actgthtctg ccctcaccta	1740
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acatcagata gccaatatga tgctthtaatt actagcaatt tggthacctat gtatgaagaa	2160
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aatggagtaa atgtggthtag tggaccaata thtgattata attatgatgg ccattthgat	2280

gctccagatg aaattaccaa acatttagcc aacactgatg ttcccatccc aacacactac	2340
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ctggatgtcc taccctttat catccctcac cgacctacca acgtggagag ctgtcctgaa	2460
ggtaaaccag aagctctttg ggttgaagaa agatttacag ctcacattgc ccgggtccgt	2520
gatgtagaac ttctcactgg gcttgacttc tatcaggata aagtgcagcc tgtctctgaa	2580
attttgcaac taaagacata tttaaccaaca ttgaaacca ctatt	2625

<210> 70

<211> 2775

<212> DNA

<213> Artificial Sequence

<220>

<223> ENPP1 Nucleotide sequence

<400> 70

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ggcgatcctc aggctgtgtc ttctctgtctg gccccatgg atgtgggcga ggaacctctg	180
gaaaaggccg ccagagccag aaccgccaag gacccaaca cctacaaggt gctgagcctg	240
gtgctgtccg tgtgctgtgt gaccaccatc ctgggctgca tcttcggcct gaagcccagc	300
tgcgccaaag aagtgaagtc ctgcaagggc cggtgcttcg agcggacctt cggcaactgc	360
agatgcgacg ccgccttgtt ggaactgggc aactgctgcc tggactacca ggaaacctgc	420
atcgagcccc agcacatctg gacctgcaac aagttcagat gcggcgagaa gcggctgacc	480
agatccctgt gtgcctgcag cgacgactgc aaggacaagg gcgactgctg catcaactac	540
agcagcgtgt gccagggcga gaagtcctgg gtggaagaac cctgcgagag catcaacgag	600
ccccagtgcc ctgccggctt cgagacacct cctaccctgc tgttcagcct ggacggcttt	660
cgggccgagt acctgcacac atggggaggc ctgctgcccc tgatcagcaa gctgaagaag	720
tgcggcacct acaccaagaa catgcggccc gtgtacccca ccaagacctt cccaaccac	780
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gacccaaga tgaacgccag cttcagcctg aagtccaaag agaagttcaa ccccgagtgg	900
tataagggcg agcccatctg ggtcaccgcc aagtaccagg gcctgaaaag cggcacattc	960

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gacgtgcccc	acaagtacta	cagcttcaac	tacgagggaa	tcgcccggaa	cctgagctgc	1440
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<210> 71
 <211> 3255
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Azurocidin-ENPP1-FC Nucleotide sequence

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