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(54) **REGULATION OF APG8 PHOSPHORYLATION AND USES THEREOF**

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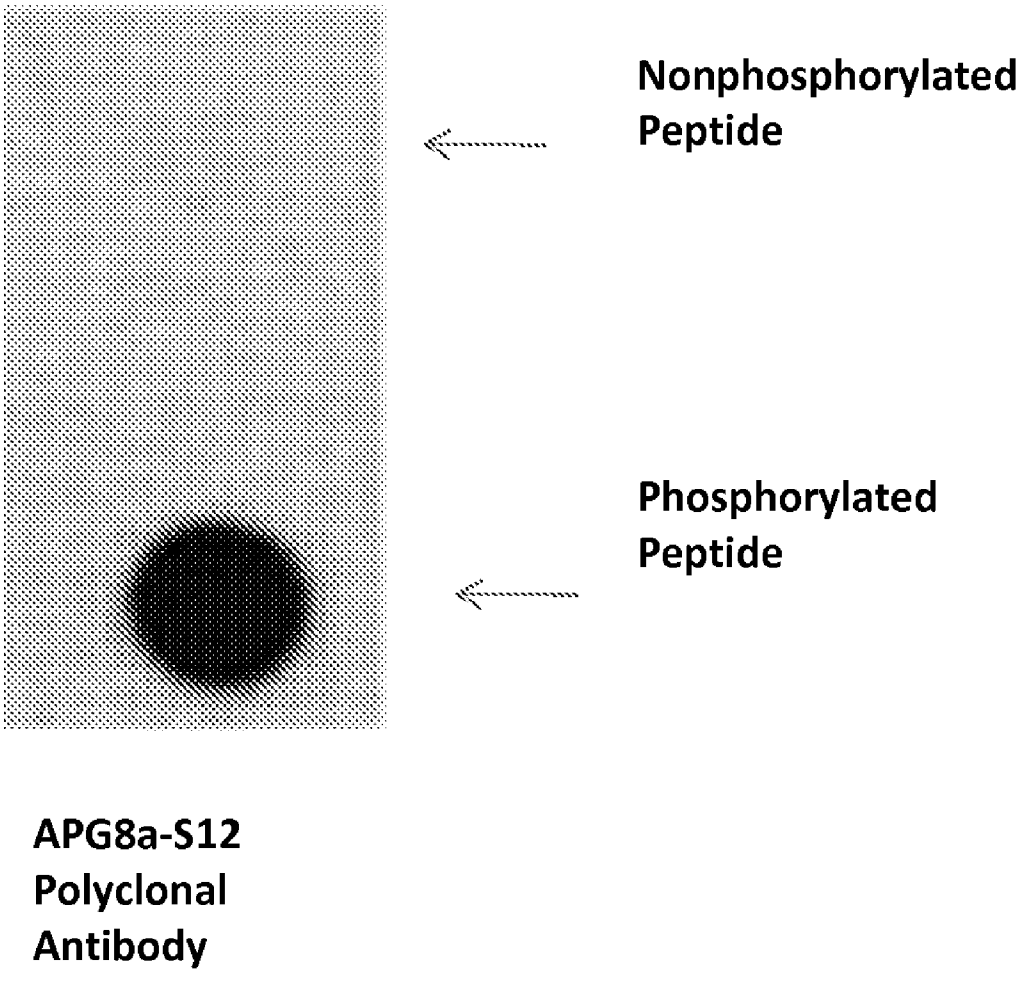
(57) **ABSTRACT**

The invention relates to proteins and peptides of the alpha isoform of light chain 3 (APG8) and antibodies to the APG8 protein, particularly antibodies that specifically bind to the alpha isoform of APG8 when either phosphorylated or not phosphorylated at serine-12 and antibodies that bind to the gamma isoform of APG8 when either phosphorylated or not phosphorylated at serine-9. The invention also relates to methods of producing these antibodies and use of these antibodies in the treatment of diseases related to autophagocytosis.



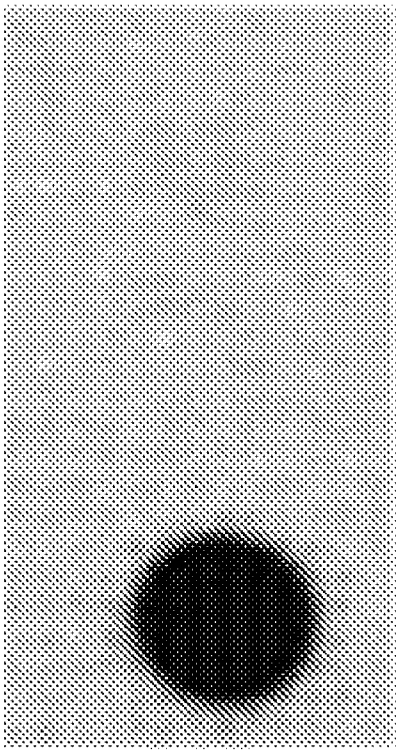
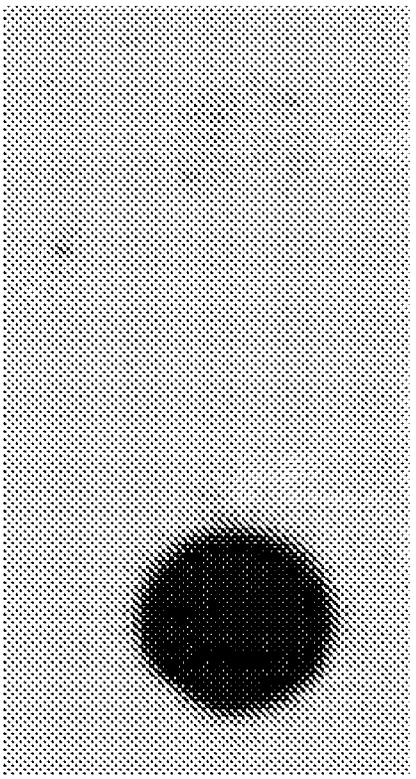

Nonphosphorylated
Peptide
Phosphorylated
Peptide
APG8a-S12
Polyclonal
Antibody

FIG. 1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Peptide
Phosphorylated
Peptide
APG8c-S9
Polyclonal
Antibody

FIG. 2

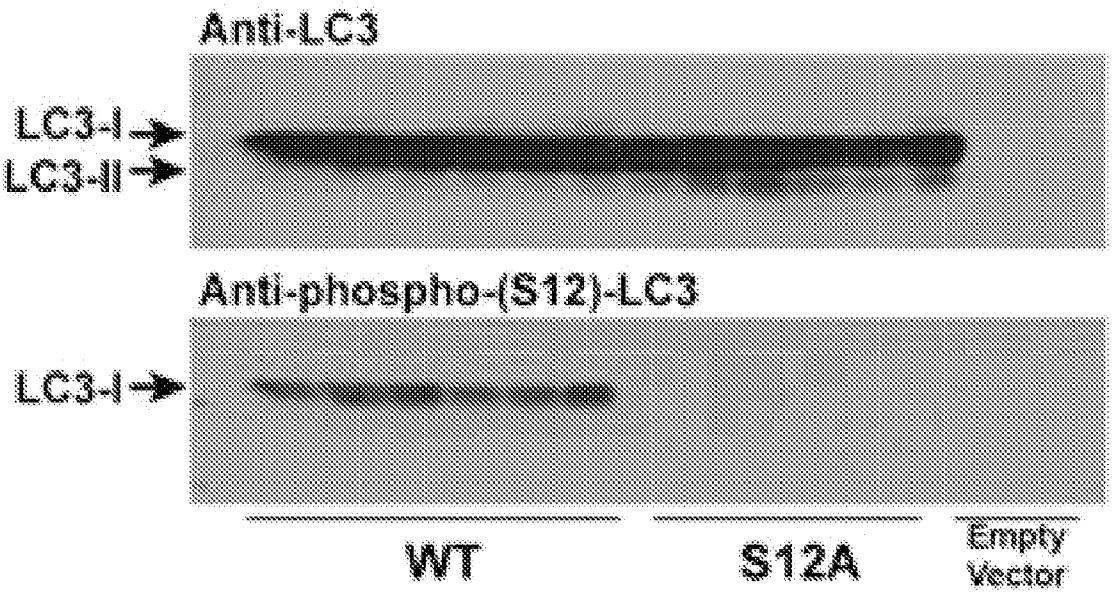
Anti-LC3
LC3-I
LC3-II
Anti-phospho-(S12)-LC3
LC3-I
WT
S12A
Empty Vector

FIG. 3

REGULATION OF APG8 PHOSPHORYLATION AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. §119(e) to U.S. Provisional Application Ser. No. 61/082,174 filed Jul. 18, 2008 and U.S. Provisional Application Ser. No. 61/082,179 filed Jul. 18, 2008, the entire contents of which are herein incorporated by reference.

REFERENCE TO SEQUENCE LISTING SUBMITTED VIA EFS-WEB

[0002] The entire content of the following electronic submission of the sequence listing via the USPTO EFS-WEB server, as authorized and set forth in MPEP §1730 II.B.2(a)(C), is incorporated herein by reference in its entirety for all purposes. The sequence listing is identified on the electronically filed text file as follows:

File Name	Date of Creation	Size (bytes)
549132000500Seqlist.txt	Nov. 6, 2009	54,365 bytes

TECHNICAL FIELD

[0003] The claimed compositions, methods, and kits are directed to an antibody to detect the alpha and gamma isoforms of APG8 in either phosphorylated or nonphosphorylated form at an N-terminal serine residue.

BACKGROUND ART

[0004] Autophagy is a process whereby cells convert proteins and organelles into amino acids as a source of food. Many cells in the human body rely on autophagy to maintain homeostasis, especially when insulin levels are low. Autophagocytosis may play a role in human disease and aging. In eukayrotic cells autophagy occur constitutively at low levels in all cells to perform housekeeping functions such as destruction of dysfunctional organelles. Dramatic upregulation occurs (e.g., cytoplasmic and organelle turnover) in the presence of external stressors (starvation, hormonal imbalance, oxidation, extreme temperature, and infection), and internal needs (generation of source materials for architectural remodeling, removal of protein aggregates). Autophagy is highly regulated through the coordinated action of various kinases, phosphatases, and guanosine triphosphatases (GTPases).

[0005] At least three different autophagy mechanisms are known, all of which result in targeting of cytosolic proteins and organelles to the lysosome in order to provide amino acids and energy in the form of catabolites. These types are macroautophagy, microautophagy, and chaperone-mediated autophagy.

[0006] Macroautophagy is a major inducible pathway for the general turnover of cytoplasmic constituents in eukaryotic cells and also plays a significant role in the degradation of active cytoplasmic enzymes and organelles during nutrient starvation. Macroautophagy involves the formation of double-membrane bound autophagosomes which enclose the cytoplasmic constituent targeted for degradation in a membrane bound structure, which then fuse with the lysosome (or vacuole) releasing a single-membrane bound autophagic bodies which are then degraded within the lysosome (or vacuole). MAP1A and MAP1B are microtubule-associated proteins which mediate the physical interactions between microtubules and components of the cytoskeleton. These proteins are involved in formation of autophagosomal vacuoles (autophagosomes). MAP1A and MAP1B each consist of a heavy chain subunit and multiple light chain subunits. Apg8a is one of the light chain subunits and can associate with either MAP1A or MAP1B. The precursor molecule is cleaved by APG4B/ATG4B to form the cytosolic form, Apg8a-I. This is activated by APG7L/ATG7, transferred to ATG3 and conjugated to phospholipid to form the membrane-bound form, Apg8a-II.

[0007] Microautophagy circumvents the autophagosomic step of macrophagy, and begins with the direct uptake of cytosolic material via invaginations and pinching off of the lysosomal membrane. The internalized cytosolic components are digested by lysosomal enzymes released when the vacuolar membrane disintegrates, as in macroautophagy.

[0008] In chaperone-mediated autophagy, specific chaperone proteins bind to target proteins containing a KFERQ (SEQ ID NO:10) sequence and channel these proteins to the surface of the lysosome. These proteins bind to Lamp2a and are then transported across the lysosomal membrane with the assistance of lysosomal chaperones, after which they are degraded by vacuolar proteases.

[0009] Mizushima, et al. describe autophagy as promoting both cell survival and cell death. By maintaining homeostasis during times of cellular stress, autophagy generally promotes survival when it is controlled. See Mizushima, N. et al. "Autophagy fights disease through cellular self-digestion" Nature (2008) 451:1069-1075.

[0010] However, dramatic upregulation of autophagy via Beclin 1 overexpression brings about cell death. Mizushima et al. describe how the autophagy and apoptosis pathways share many common regulatory factors, with the likelihood of significant cross-talk between these pathways in the cell. Since apoptosis is known to be implicated in human disease, autophagy also is likely an important phenomenon to target in order to treat disease.

[0011] Proteins that regulate autophagy in cancer cells make attractive therapeutic and diagnostic targets. Tumor cells have been observed to exhibit lower levels of autophagic activity. A number of well-known oncogenes and tumor suppressor genes recalibrate autophagic pathways, and thereby alter prospects for cell survival and proliferation. The PTEN tumor suppressor gene, class I PI 3-kinase and Akt oncogenes, Ras and Myc oncogenes are among the proteins that appear to act in this way.

[0012] Cancer cells rely on autophagy in order to evade anti-cancer treatments designed to reduce nutrient supply and enhance the stress on rapidly dividing cells. A compound that downregulates autophagy may be a useful additional drug in cancer treatment. Mizushima et al. state that since autophagy may help prevent cancer, there is a potential need to target autophagy in a context-specific manner. Therefore, the targeting of specific autophagy regulatory proteins rather than a targeting of autophagy in general may be critical in developing a treatment of cancer as well as new modes of diagnosing cancer.

[0013] Microtubule-associated protein 1 light chain 3, also known as APG8, ATG8, and LC3, is present on the autopha-

gosome membrane when conjugated to phosphatidylethanolamine. See Kuma, A. et al. "APG8A, an Autophagosome Marker, can be Incorporated into Protein Aggregates Independent of Autophagy—Caution in the Interpretation of APG8A Localization" Autophagy (2007) 3:323-328. There are at least three isoforms of APG8: APG8 alpha ("APGA8"), APG8 beta ("APG8B") and APG8 gamma ("APG8C") (exemplary sequence found in NCBI Accession # NP_001004343). A commonly used technique to assay for autophagocytosis is to use an APG8A:GFP fusion protein and monitor its localization to the cytosol, which indicates negligible autophagocytosis or APG8A:GFP may form a punctuate pattern in the cell suggestive of autophagocytosis. See page 324 of Kuma et al. However since APG8A:GFP may aggregate independently of autophagocytosis, this is a potentially unreliable marker. Therefore, there exists a need to develop an assay to monitor APG8A status that does not rely exclusively on protein localization.

[0014] Alterations in the autophagy degradation pathway have been described in normal brain aging and in age-related neurodegenerative diseases including Alzheimer's and Parkinson's diseases. See Nixon, R. "Autophagy in neurodegenerative disease: friend, foe, or turncoat?" Trends in Neurosciences (2006) 29(9):528-535. An improper clearance of proteins in these diseases may result either from a compromise in the autophagy degradation pathway or induce alterations in this pathway, and may result in neuron dysfunction and neuron loss. The targeting of specific autophagy regulatory proteins rather than a targeting of autophagy in general may be critical in developing a treatment of neurodegenerative diseases as well as new modes of diagnosing neurodegenerative diseases. Therefore, there exists a need to develop an assay to monitor the activity of autophagy proteins that does not rely exclusively on protein localization.

DISCLOSURE OF THE INVENTION

[0015] Several of the following aspects provide peptides comprising amino acids that are novel phosphorylation sites on APG8A protein, APG8C protein, and APG8 peptides. Several of the following aspects also provide antibodies that react specifically to the phosphorylated forms of these peptides, and antibodies that react specifically to the non-phosphorylated forms of these peptides.

[0016] In one aspect, the present disclosure provides an isolated APG8 peptide that comprises an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine or phosphoserine, and with the proviso that the peptide is not a full-length APG8A protein comprising an amino acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or SEQ ID NO:7 or a full-length APG8C protein comprising an amino acid sequence set forth in SEQ ID NO:8 or SEQ ID NO:9. The peptides of this embodiment are referred to as "APG8 peptides". These peptides are also "APG8 polypeptides", which include APG8 peptides. The APG8 peptides of this aspect comprised of sequence QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), or XFAD (SEQ ID NO:14) are also referred to as "APG8A peptides". The APG8 peptides of this aspect comprised of sequence KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18) are also referred to as "APG8C peptides".

[0017] In some embodiments, an isolated peptide of the present disclosure comprises an amino sequence of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRC (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), or MPSDRPFKQRRXFADR (SEQ ID NO:61). The peptides of this embodiment are a subset of possible APG8A peptides.

[0018] In some embodiments, an isolated peptide of the present disclosure comprises an amino sequence of QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVR-

PFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152). The peptides of this embodiment are a subset of possible APG8C peptides.

[0019] In another embodiment, an isolated peptide of the present disclosure comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). In some embodiments, X may be serine. In some embodiments, X may be phosphoserine.

[0020] In another embodiment, an isolated peptide of the present disclosure comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). In some embodiments, X may be serine. In some embodiments, X may be phosphoserine.

[0021] In another aspect, the disclosure provides for an immunogen, which comprises an APG8 peptide and immune response potentiator.

[0022] In another aspect, the disclosure provides for a multiple antigenic peptide (MAP), which comprises a branched oligolysine core conjugated with a plurality of isolated APG8 peptides.

[0023] In another aspect, the disclosure provides for a method for producing an antibody to an APG8 polypeptide. The method comprises introducing an isolated APG8 peptide of comprising the sequence QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), or XVRP (SEQ ID NO:18) to a mammal in an amount sufficient to produce an antibody to the APG8 peptide; and recovering the antibody from the mammal.

[0024] In another aspect, the disclosure provides for a kit for producing an antibody to an APG8 polypeptide. The kit comprises an isolated APG8 peptide, a means for introducing the isolated APG8 peptide to a mammal in an amount sufficient to produce an antibody to the APG8 peptide, and a means for recovering the antibody from the mammal.

[0025] In another aspect, the disclosure provides for a method for producing an antibody to an APG8 polypeptide. The method comprises a first step of introducing an APG8 polypeptide to a mammal in an amount sufficient to produce an antibody to the APG8 protein. The APG8 polypeptide may be a full-length APG8A or a full-length APG8C protein. The next steps of the method are recovering the antibody from the mammal, and affinity purifying an APG8 antibody that specifically binds to one of the following epitopes: KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPSDRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPX-

VRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152). This method is referred to below as the "method for producing an affinity-purified APG8A antibody" In one embodiment, the disclosure provides for an antibody to an APG8A polypeptide produced by this method.

[0026] In another aspect, the disclosure provides for a kit for producing an antibody to an APG8A polypeptide. The kit comprises an APG8A protein, a means for introducing the APG8A protein to a mammal in an amount sufficient to produce an antibody to the APG8A polypeptide, a means for recovering the antibody from the mammal, and an isolated APG8A peptide comprising the sequence QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), or XFAD (SEQ ID NO:14).

[0027] In another aspect, the disclosure provides for a kit for producing an antibody to an APG8C polypeptide. The kit comprises an APG8C protein, a means for introducing the APG8C protein to a mammal in an amount sufficient to produce an antibody to the APG8C polypeptide, a means for recovering the antibody from the mammal, and an isolated APG8C peptide comprising the sequence KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), or XVRP (SEQ ID NO:18).

[0028] In another aspect, the disclosure provides for an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine. In one embodiment, the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and an amino acid residue of APG8A protein that is outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). In another embodiment, the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and amino acid residues of APG8C protein that are outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0029] In another aspect, the disclosure provides for an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine. In one embodiment, the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and an amino acid residue of APG8C protein that is outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). In another embodiment, the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and amino acid residues of APG8A protein that are outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0030] In another aspect, the disclosure provides for a method for detecting an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample. The method comprises contacting a sample containing or suspected of containing an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine; and assessing a complex formed between the APG8A protein or fragment, if present in the sample, and the antibody, to determine the presence, absence and/or amount of the APG8A protein or fragment in the sample.

[0031] In another aspect, the disclosure provides for a method for detecting an APG8C protein or fragment comprising amino acid sequence M wherein X is serine or phosphoserine in a sample. The method comprises contacting a sample containing or suspected of containing an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine; and assessing a complex formed between the APG8C protein or fragment, if present in the sample, and the antibody, to determine the presence, absence and/or amount of the APG8C protein or fragment in the sample.

[0032] In another aspect, the disclosure provides for a kit for detecting an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample, which kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0033] In another aspect, the disclosure provides for a kit for detecting an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample, which kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid

residue X in the amino acid sequence MPSDRPFKQRRX-FADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0034] In another aspect, the disclosure provides for a kit for detecting an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample, which kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPP-PQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0035] In another aspect, the disclosure provides for a method for treating a disease or disorder associated with abnormal phosphorylation status of an APG8A protein or fragment comprising amino acid sequence MPS-DRPFKQRRSFADR (SEQ ID NO:154) wherein X is serine or phosphoserine in a sample, which method comprises administering to a subject, when such a treatment is needed or desired, a sufficient amount of an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRX-FADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0036] In another aspect, the disclosure provides for a method for treating a disease or disorder associated with abnormal phosphorylation status of an APG8C protein or fragment comprising amino acid sequence MPPPQKIPX-VRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample, which method comprises administering to a subject, when such a treatment is needed or desired, a sufficient amount of an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVR-PFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0037] Another aspect is a method for identifying a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of (1): providing APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide; and (3) assessing the phosphorylation status of the APG8A polypeptide to determine whether the test protein is a kinase for the APG8A protein on the serine residue 12.

[0038] Another aspect is a method for identifying a kinase that phosphorylates an APG8C protein on the serine residue 9. The method comprises the steps of (1): providing APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine; (2) contacting the APG8C polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8C polypeptide; and (3) assessing the phosphorylation status of the APG8C polypeptide to determine whether the test protein is a kinase for the APG8C protein on the serine residue 9.

[0039] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of: (1) providing APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a kinase that phosphorylates an APG8A protein on the serine residue 12 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide in the presence or absence of a test substance; and assessing and comparing phosphorylation status of the APG8A polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0040] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of: (1) providing APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a kinase that phosphorylates an APG8A protein on the serine residue 12 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide in the presence or absence of a test substance; and assessing and comparing phosphorylation status of the APG8A polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0041] Another aspect is a method for identifying a phosphatase that dephosphorylates an APG8C protein on the serine residue 9. The method comprises the steps of: (1) providing APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine; (2) contacting the APG8C polypeptide with a test protein and H_2O under conditions suitable for the dephosphorylation of the phosphoserine residue of the APG8C polypeptide; and (3) assessing phosphorylation status of the APG8C polypeptide to determine whether the test protein is a phosphatase for the APG8C protein on the phosphoserine residue 9.

[0042] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of: (1) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a kinase that phosphorylates an APG8A protein on the serine residue 12 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide in the presence or absence of a test substance; and (3) assessing and comparing phosphorylation status of the APG8A polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0043] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8C protein on the serine residue 9. The method comprises the steps of: (1) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine; (2) contacting the APG8C polypeptide with a kinase that phospho-

rylates an APG8C protein on the serine residue 9 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8C polypeptide in the presence or absence of a test substance; and (3) assessing and comparing phosphorylation status of the APG8C polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0044] Another aspect is an isolated nucleic acid fragment which is comprised of a sequence of nucleotides encoding an APG8A peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine. The APG8A peptide is not a full-length APG8A protein comprising an amino acid sequence set forth in SEQ ID NOs:1-7. The nucleic acid may be DNA. The nucleic acid may also be RNA.

[0045] Another aspect is an isolated nucleic acid fragment which is comprised of a sequence of nucleotides encoding an APG8C peptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine. The APG8C peptide is not a full-length APG8C protein comprising an amino acid sequence set forth in SEQ ID NOs:8-9. The nucleic acid may be DNA. The nucleic acid may also be RNA.

[0046] Other objects, features, and technical advantages of the present invention will become more apparent from a consideration of the detailed description herein and from the accompanying drawings.

[0047] All publications, patents, patent applications, GenBank sequences and ATCC deposits, cited herein are hereby expressly incorporated by reference for all purposes.

BRIEF DESCRIPTION OF THE DRAWINGS

[0048] FIG. **1** shows a dot blot of an antibody that specifically binds to APG8a that is phosphorylated at serine-12.

[0049] FIG. **2** shows a dot blot of an antibody that specifically binds to APG8c that is phosphorylated at serine-9.

[0050] FIG. **3** shows a Western blot of an antibody that specifically binds to APG8a in the top panel and a Western blot of an antibody that specifically binds to APG8a phosphorylated at serine-12 in the bottom panel.

MODES OF CARRYING OUT THE INVENTION

[0051] For clarity of disclosure, and not by way of limitation, the detailed description of the invention is divided into the subsections that follow.

Definitions

[0052] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this invention belongs. All patents, patent applications (published or unpublished), and other publications referred to herein are incorporated by reference in their entirety. If a definition set forth in this section is contrary to or otherwise inconsistent with a definition set forth in the patents, applications, published applications and other publications that are herein incorporated by reference, the definition set forth in this section prevails over the definition that is incorporated herein by reference.

[0053] As used herein, "a" or "an" means "at least one" or "one or more."

[0054] As used herein, "antibody" is used in the broadest sense. Therefore, an "antibody" can be naturally occurring or man-made such as monoclonal antibodies produced by conventional hybridoma technology and/or a functional fragment thereof. Antibodies may be monoclonal and polyclonal antibodies as well as fragments containing the antigen-binding domain and/or one or more complementarity determining regions of these antibodies. Antibodies can be of any isotype including IgM, IgG, IgD, IgA and IgE, and any sub-isotype, including IgG1, IgG2a, IgG2b, IgG3 and IgG4, IgE1, IgE2 etc. The light chains of the antibodies can either be kappa light chains or lambda light chains.

[0055] As used herein, "monoclonal antibody" refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the antibodies comprising the population are identical except for possible naturally occurring mutations that are present in minor amounts. As used herein, a "monoclonal antibody" further refers to functional fragments of monoclonal antibodies.

[0056] As used herein, the phrase "oligoclonal antibodies" refers to a predetermined mixture of distinct monoclonal antibodies. See, e.g., PCT publication WO 95/20401; U.S. Pat. Nos. 5,789,208 and 6,335,163.

[0057] As used herein, "peptide" includes all "mimetic" and "peptidomimetic" forms. The terms "mimetic" and "peptidomimetic" refer to a synthetic chemical compound which has substantially the same structural and/or functional characteristics of the polypeptides of the invention. The mimetic can be either entirely composed of synthetic, non-natural analogues of amino acids, or, is a chimeric molecule of partly natural peptide amino acids and partly non-natural analogs of amino acids. The mimetic can also incorporate any amount of natural amino acid conservative substitutions as long as such substitutions also do not substantially alter the mimetic's structure and/or activity. Routine experimentation will determine whether a mimetic is within the scope of the invention, i.e., that its structure and/or function is not substantially altered.

[0058] As used herein, "polypeptide" includes a molecular chain of amino acids linked through peptide bonds. "Polypeptide" does not refer to a specific length of the product. Thus, "peptides," "oligopeptides," and "proteins" are included within the definition of polypeptide.

[0059] As used herein, an "antigen", includes any portion of a protein (peptide, protein fragment, full-length protein), wherein the protein is naturally occurring or synthetically derived, a cellular composition (whole cell, cell lysate or disrupted cells), an organism (whole organism, lysate or disrupted cells), a carbohydrate, a lipid, or other molecule, or a portion thereof, wherein the antigen elicits an antigen-specific immune response (humoral and/or cellular immune response).

[0060] As used herein, "mammal" refers to any of the mammalian class of species. Frequently, the term "mammal," as used herein, refers to humans, human subjects or human patients.

[0061] As used herein, "treatment" means any manner in which the symptoms of a condition, disorder or disease are ameliorated or otherwise beneficially altered. Treatment also encompasses any pharmaceutical use of the compositions herein.

[0062] As used herein, "disease or disorder" refers to a pathological condition in an organism resulting from, e.g., infection or genetic defect, and characterized by identifiable symptoms.

[0063] As used herein, the term "subject" is not limited to a specific species or sample type. For example, the term "subject" may refer to a patient, and frequently a human patient. However, this term is not limited to humans and thus encompasses a variety of mammalian species.

[0064] As used herein, "afflicted" as it relates to a disease or disorder refers to a subject having or directly affected by the designated disease or disorder.

[0065] As used herein the term "sample" refers to anything which may contain an analyte for which an analyte assay is desired. The sample may be a biological sample, such as a biological fluid or a biological tissue. Examples of biological fluids include urine, blood, plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, mucus, amniotic fluid or the like. Biological tissues are aggregate of cells, usually of a particular kind together with their intercellular substance that form one of the structural materials of a human, animal, plant, bacterial, fungal or viral structure, including connective, epithelium, muscle and nerve tissues. Examples of biological tissues also include organs, tumors, lymph nodes, arteries and individual cell(s).

[0066] As used herein, the term "specifically binds" refers to the binding specificity of a specific binding pair. Recognition by an antibody of a particular target in the presence of other potential targets is one characteristic of such binding. "Binding component member" refers to a member of a specific binding pair, i.e., two different molecules wherein one of the molecules specifically binds with the second molecule through chemical or physical means. The two molecules are related in the sense that their binding with each other is such that they are capable of distinguishing their binding partner from other assay constituents having similar characteristics. The members of the binding component pair are referred to as ligand and receptor (antiligand), specific binding pair (sbp) member and sbp partner, and the like. A molecule may also be a sbp member for an aggregation of molecules; for example an antibody raised against an immune complex of a second antibody and its corresponding antigen may be considered to be an sbp member for the immune complex.

[0067] As used herein the term "does not specifically bind" refers to the specificity of particular antibodies or antibody fragments. Antibodies or antibody fragments that do not specifically bind a particular moiety generally contain a specificity such that a large percentage of the particular moiety would not be bound by such antibodies or antibody fragments. This percentage generally lies within the acceptable cross reactivity percentage with interfering moieties of assays utilizing antibodies directed to detecting a specific target. Frequently, antibodies or antibody fragments of the present disclosure do not specifically bind greater than about 90% of an interfering moiety, although higher percentages are clearly contemplated and preferred. For example, antibodies or antibody fragments of the present disclosure do not specifically bind about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, and about 99% or more of an interfering moiety. Less occasionally, antibodies or antibody fragments of the present disclosure do not specifically bind greater than about 70%, or greater than about 75%, or greater than about 80%, or greater than about 85% of an interfering moiety.

[0068] As used herein the term "isolated" refers to material removed from its original environment, and is altered from its natural state. For example, an isolated polypeptide could be coupled to a carrier, and still be "isolated" because that polypeptide is not in its original environment.

[0069] As used herein, the term "serine-12" may refer to the twelfth residue of APG8A (SEQ ID NO:1), which is a serine that may or may not be phosphorylated. Serine-12 may also refer to a residue in a peptide or protein corresponding to the serine at position 12 in the full length human APG8A protein having a sequence consisting of SEQ ID NO:1.

[0070] As used herein, the term "phosphoserine-12" residue refers to a serine-12 residue that is phosphorylated.

[0071] As used herein, the term "serine-9" may refer to the ninth residue of APG8C (SEQ ID NO:8), which is a serine that may or may not be phosphorylated. Serine-9 may also refer to a residue in a peptide or protein corresponding to the serine at position 9 in the full length human APG8C protein having a sequence consisting of SEQ ID NO:8.

[0072] As used herein, the term "APG8A polypeptide" refers to a polypeptide comprising the entire APG8A protein or a fragment of the entire APG8A protein. An APG8A polypeptide also refers to an APG8A peptide.

[0073] As used herein, the term "APG8A peptide" refers to a peptide comprising at least four consecutive amino acid residues of the sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) from the N-terminus of APG8A. The "X" residue may be serine or phosphoserine and corresponds to serine-12.

[0074] As used herein, the term "phosphorylated APG8A peptide" refers to an APG8A peptide comprising phosphoserine at a position corresponding to serine-12 of SEQ ID NO:1.

[0075] As used herein, the term "nonphosphorylated APG8A peptide" refers to an APG8A peptide comprising serine at a position corresponding to serine-12 of SEQ ID NO:1.

[0076] As used herein, the term "APG8C polypeptide" refers to a polypeptide comprising the entire APG8C protein or a fragment of the entire APG8C protein. An APG8C polypeptide also refers to an APG8C peptide.

[0077] As used herein, the term "APG8C peptide" refers to a peptide comprising at least four consecutive amino acid residues of the sequence MPPPQKIPSVRPFKQRKSLAIR (SEQ ID NO:155) from the N-terminus of APG8C. The "X" residue may be serine or phosphoserine and corresponds to serine-9.

[0078] As used herein, the term "phosphorylated APG8C peptide" refers to an APG8C peptide comprising phosphoserine at a position corresponding to serine-9 of SEQ ID NO:8.

[0079] As used herein, the term "nonphosphorylated APG8C peptide" refers to an APG8C peptide comprising serine at a position corresponding to serine-9 of SEQ ID NO:8.

[0080] The titles of each section and the examples of the following specification are not intended to be limiting.

APG8A and APG8C

[0081] There are at least three isoforms, A, B, and C, of microtubule associated protein 1 light chain 3. These isoforms share significant sequence identity, with isoform B differing from isoforms A and C primarily at the N-terminus. The N-terminus of APG8A, also known as the alpha isoform, is comprised of the sequence MPSDRPFKQRRSFADR

(SEQ ID NO:154). The N-terminus of APG8C is comprised of the sequence of MPPPQKIPSVRPFKQRKSLAIR (SEQ ID NO:155). Serine-12 of APG8A and serine-9 of APG8C are phosphorylation sites and may be key sites for regulation of these proteins' activity in autophagy.

APG8A Peptide

[0082] APG8A is phosphorylated at serine-12 of APG8A (SEQ ID NO:1). This sequence is found at the N-terminus of the human alpha isoform of APG8A. Additionally, this sequence is found at the N-terminus of bovine APG8A (SEQ ID NO:2) and zebrafish APG8A (SEQ ID NO:3). The phosphorylation of serine at this sequence may regulate the localization and function of APG8A in autophagy. Detection of the phosphorylated and nonphosphorylated forms of APG8A using antibodies that recognize these specific forms of APG8A may serve as a useful diagnostic marker for autophagy. Additionally, antibodies to the phosphorylated or nonphosphorylated forms of APG8A may affect the degree of autophagy.

[0083] There are multiple embodiments of APG8A peptides contemplated. Broadly, the APG8A peptide may include sequences that form epitopes comprising sequence having a minimum length of four amino acids of the sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), that are useful to produce antibodies that recognize serine or phosphoserine at position 12 of APG8A (SEQ ID NO:1), provided that the APG8A peptide does not comprise the full-length sequence of APG8A (SEQ ID NOs: 1, 2, 3, 4, 5, 6, and 7).

[0084] The APG8A peptide may have the following sequences that correspond to epitopes adjacent to and including serine-12: QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine or phosphoserine. The APG8A peptide may have the following sequences having lengths from 5 to 18 residues that correspond to these longer epitopes adjacent to and including serine-12: KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), or MPSDRPFKQRRXFADR (SEQ ID NO:61). For any of the above APG8A peptides, X may be serine or phosphoserine.

APG8C Peptide

[0085] APG8C is phosphorylated at serine-9 (SEQ ID NO:8) at the N-terminus. The phosphorylation of serine at this sequence may regulate the localization and function of APG8C in autophagy. Detection of the phosphorylated and nonphosphorylated forms of APG8C using antibodies that recognize these specific forms of APG8C may serve as a useful diagnostic marker for autophagy. Additionally, antibodies to the phosphorylated or nonphosphorylated forms of APG8C may affect the degree of autophagy.

[0086] There are also multiple embodiments of APG8C peptides contemplated. Broadly, the APG8C peptide may include sequences that form epitopes comprising sequence having a minimum length of four amino acids of the sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), that are useful to produce antibodies that recognize serine or phosphoserine at position 9 of APG8C (SEQ ID NO:8), provided that the APG8C peptide does not comprise the full-length sequence of APG8C (SEQ ID NO:8).

[0087] The APG8C peptide may have the following sequences that correspond to epitopes adjacent to and including serine-9: KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine or phosphoserine. The APG8C peptide may have the following sequences having lengths from 5 to 18 residues that correspond to these longer epitopes adjacent to and including serine-9: QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF

(SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152). For any of the above APG8C peptides, X may be serine or phosphoserine.

[0088] The APG8A peptide may be comprised of a sequence near serine-12, MPSDRPFKQRRXFADR (SEQ ID NO:61), in which X may be serine or phosphoserine. The APG8C peptide may be comprised of a sequence near serine-9, MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), in which X may be serine or phosphoserine. These sequences, as well as the above shorter sequences of these sequences, may be particularly strong antigens for the production of antibodies.

[0089] In all aspects and embodiments, the APG8A peptide may not be the full length APG8A protein in any organism that is comprised of the sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). Exemplary full-length APG8A proteins are the human APG8A protein of SEQ ID NO:1 (NCBI Accession # 115903), the bovine APG8A protein of SEQ ID NO:2, the zebrafish APG8A protein of SEQ ID NO:3, the *Xenopus laevis* APG8A sequence of SEQ ID NO:4, the mouse APG8A sequence of SEQ ID NO:5, the chimpanzee APG8A sequence of SEQ ID NO:6, and the rat APG8A sequence of SEQ ID NO:7. Further, in all embodiments, the APG8C peptide may not be the full length APG8C protein in any organism that is comprised of the sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). Exemplary full-length APG8C proteins have the sequence set forth in SEQ ID NO:8 and SEQ ID NO:9.

[0090] In another embodiment, an isolated peptide of the present disclosure comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). In another embodiment, the peptide comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). In some embodiments, X may be serine. In some embodiments, X may be phosphoserine.

Pharmaceutical Compositions

[0091] In some embodiments, the disclosure provides for a pharmaceutical composition comprising a pharmaceutically acceptable carrier, an excipient, and an isolated APG8 peptide. The pharmaceutical compositions can be used to promote or otherwise enhance the rate of autophagy in vertebrate animals including mammals. Alternatively, the pharmaceutical compositions can be used to inhibit or reduce the rate of autophagy in vertebrate animals, including mammals. Accordingly, the compositions are considered useful for treating or preventing a variety of conditions including ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0092] The peptide compounds may be formulated into the compositions as neutral or salt forms. Pharmaceutically acceptable non-toxic salts include the acid addition salts (formed with the free amino groups) and which are formed by reaction with inorganic acids such as, for example, hydrochloric, sulfuric or phosphoric acids, or organic acids such as, for example, acetic, oxalic, tartaric, mandelic, citric, malic, and the like. Salts formed with the free carboxyl groups may be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases such as amines, i.e., isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

[0093] An APG8 peptide is suitably administered to a subject, e.g., a human or a non-human mammal, such as a domestic animal. The amount administered may vary depending on various factors including, but not limited to, the agent chosen, the disease, and whether prevention or treatment is to be achieved. The peptides may be administered locally or systemically. Administration of the therapeutic agents may be continuous or intermittent, depending, for example, upon the recipient's physiological condition, whether the purpose of the administration is therapeutic or prophylactic, and other factors known to skilled practitioners. The administration of the agents of the invention may be essentially continuous over a preselected period of time or may be in a series of spaced doses.

[0094] One or more suitable unit dosage forms comprising an APG8 peptide can be administered by a variety of routes including oral, or parenteral, including by rectal, buccal, vaginal and sublingual, transdermal, subcutaneous, intravenous, intramuscular, intraperitoneal, intrathoracic, intracoronary, intrapulmonary and intranasal routes. The dosage form may optionally be formulated for sustained release. The formulations may, where appropriate, be conveniently presented in discrete unit dosage forms and may be prepared by any of the methods well known to pharmacy. Such methods may include the step of bringing into association the therapeutic agent with liquid carriers, solid matrices, semi-solid carriers, finely divided solid carriers or combinations thereof, and then, if necessary, introducing or shaping the product into the desired delivery system.

[0095] When the APG8 peptide is prepared for oral administration, it is preferably combined with a pharmaceutically

acceptable carrier, diluent or excipient to form a pharmaceutical formulation, or unit dosage form. The total active ingredients in such formulations comprise from 0.1 to 99.9% by weight of the formulation. By "pharmaceutically acceptable" it is meant the carrier, diluent, excipient, and/or salt must be compatible with the other ingredients of the formulation, and not deleterious to the recipient thereof. The active ingredient for oral administration may be present as a powder or as granules; as a solution, a suspension or an emulsion; or in achievable base such as a synthetic resin for ingestion of the active ingredients from a chewing gum. The active ingredient may also be presented as a bolus, electuary or paste. A useful reference describing pharmaceutically acceptable carriers, diluents and excipients is Remington's Pharmaceutical Sciences (Mack Publishing Co. N.J. USA, 1991) which is incorporated herein by reference. Supplementary active compounds can also be incorporated into the compositions.

[0096] Pharmaceutical formulations containing an APG8 protein can be prepared by procedures known in the art using well known and readily available ingredients. For example, the natriuretic peptide can be formulated with common excipients, diluents, or carriers, and formed into tablets, capsules, suspensions, powders, and the like. Examples of excipients, diluents, and carriers that are suitable for such formulations include the following fillers and extenders such as starch, sugars, mannitol, and silicic derivatives; binding agents such as carboxymethyl cellulose, HPMC and other cellulose derivatives, alginates, gelatin, and polyvinyl-pyrrolidone; moisturizing agents such as glycerol; disintegrating agents such as calcium carbonate and sodium bicarbonate; agents for retarding dissolution such as paraffin; resorption accelerators such as quaternary ammonium compounds; surface active agents such as cetyl alcohol, glycerol monostearate; adsorptive carriers such as kaolin and bentonite; and lubricants such as talc, calcium and magnesium stearate, and solid polyethyl glycols.

[0097] For example, tablets or caplets containing the nucleic acid molecule or peptide of the invention can include buffering agents such as calcium carbonate, magnesium oxide and magnesium carbonate. Caplets and tablets can also include inactive ingredients such as cellulose, pregelatinized starch, silicon dioxide, hydroxy propyl methyl cellulose, magnesium stearate, microcrystalline cellulose, starch, talc, titanium dioxide, benzoic acid, citric acid, corn starch, mineral oil, polypropylene glycol, sodium phosphate, and zinc stearate, and the like. Hard or soft gelatin capsules containing the nucleic acid molecule or peptide of the invention can contain inactive ingredients such as gelatin, microcrystalline cellulose, sodium lauryl sulfate, starch, talc, and titanium dioxide, and the like, as well as liquid vehicles such as polyethylene glycols (PEGs) and vegetable oil. Moreover, enteric coated caplets or tablets of the nucleic acid molecule or peptide of the invention are designed to resist disintegration in the stomach and dissolve in the more neutral to alkaline environment of the duodenum.

[0098] The APG8 peptide may be prepared in an injectable formulation. Injectable preparations, for example sterile injectable aqueous or oleaginous suspensions, are formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation can also be a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed including synthetic mono- or di-glycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

APG8 Immunogens

[0099] The APG8 peptide may be used as an immunogen, with an exemplary use being to generate antibodies. The APG8 peptide may consist of phosphoserine or serine. In some embodiments, the isolated APG8 peptide of the above embodiments may be conjugated to a carrier to enhance the peptide's immunogenicity. Use of carriers while immunizing the animal is preferred when producing antibodies against an APG8 peptide. It is generally appreciated in the art that antigens must be at least 10 kDa in order to elicit a satisfactory immune response. The size of an antigen can be effectively increased by association of the antigen with a carrier.

[0100] The carrier may be a carrier protein. Alternatively, the APG8 peptide and the carrier protein may be part of a fusion protein. Exemplary carriers include, but are not limited to, Keyhole limpet cyanin, BSA, cationized BSA, ovalbumin, blue carrier immunogenic protein, avidin, BTG, bovine G globulin, bovine Immunoglobulin G (BlgG), bovine thyroglobulin, conalbumin, colloidal gold, edestin, exoprotein A (recombinant) from *P. aeruginosa*, hemocyanin from crab *P. camtschatica, Helix promatia* Hemocyanin (HPH), HSA, KTI (Kuntz trypsin inhibitor from soybeans), LPH (Heamocyanin from *Limulus polyphemus*), Pam3Cys-Th, polylysine, porcine thyroglobulin (PTG), purified protein derivative (PPD), rabbit serum albumin (RSA), soybean trypsin inhibitor (STI), sunflower globulin (SFG), and Tetanus toxoid. The carrier protein may be coupled to the peptide as described in Lateef, S. et al J. Biomol. Tech. (2007) 8:173-176.

[0101] In another aspect, the immunogen may comprise an APG8 peptide and an immune response potentiator. In some embodiments, the immune response potentiator may be Bacille Calmette-Guerin (BCG), *Corynebacterium Parvum, Brucella abortus* extract, glucan, levamisole, tilorone, an enzyme or a non-virulent virus.

Multiple Antigenic Peptide

[0102] In another aspect, a multiple antigenic peptide (MAP) is provided, which MAP comprises a branched oligolysine core conjugated with a plurality of an APG8 peptide as described herein. On occasion, the branched oligolysine core comprises 3, 7 or 15 lysine residues, also on occasion, the MAP comprises 4, 8 or 16 copies of the APG8 peptide. The plurality of the APG8 peptide comprises the same or different APG8 peptides. In some embodiments, the plurality of the APG8 peptide is conjugated to the branched oligolysine core via a spacer. Frequently, the spacer may be one or more amino acid residues. Multiple antigenic peptides comprise generally known technology. See, e.g., Adermann, K., et al., Innovations and Perspectives in Solid Phase Synthesis 429-32 (R. Epton, ed., Mayflower Worldwide 1994). Furthermore, in some embodiments, the plurality of APG8 peptides is comprised of the same peptide or different peptides.

Method of Producing an APG8 Antibody

[0103] In another aspect is a method for producing an antibody to an APG8 polypeptide.

[0104] The method comprises introducing an isolated an APG8 peptide into a mammal in an amount sufficient to produce an antibody to the APG8 peptide and recovering the antibody from the mammal. This method and variations thereof in order to enhance antibody specificity can be appreciated by one of skill in the art.

[0105] In one embodiment of this aspect, the X in the isolated APG8 peptide is serine and the method is used to produce an antibody to an APG8A polypeptide that is not phosphorylated at the corresponding serine. In practicing this and subsequent embodiments of this aspect, one of skill in the art may test the specificity of the produced antibody against an APG8 peptide or protein with serine phosphorylated or not phosphorylated in order to determine specificity.

[0106] In another embodiment of this aspect, X in the isolated APG8 peptide sequence is phosphoserine and the method is used to produce an antibody to a phosphorylated APG8 polypeptide. This embodiment may further comprise a step of removing an antibody that binds to an isolated APG8A peptide having a sequence in which X is serine.

[0107] In some embodiments of the method for producing an APG8 antibody, the isolated APG8 peptide is conjugated to a carrier to enhance the peptide's immunogenicity. Alternatively, in some embodiments, the isolated APG8 peptide is comprised in an immunogen comprised of an isolated APG8 peptide and an immune response potentiator. The carrier, immunogen, and immune response potentiator may be in any of the forms described above.

[0108] In another embodiment of the method for producing an APG8 antibody, the isolated APG8 peptide is comprised in a multiple antigenic peptide (MAP), in which the MAP comprises a branched oligolysine core conjugated with a plurality of an isolated APG8 peptides. The MAP may be in any of the forms as described above.

Method of Producing an APG8A Antibody with Subsequent Affinity Purification

[0109] Another aspect is a method for producing an antibody to an APG8 polypeptide. The method comprises introducing an APG8 protein to a mammal in an amount sufficient to produce an antibody to the APG8 protein, recovering the antibody from the mammal, and affinity purifying an APG8 antibody that specifically binds to an epitope comprising the sequence QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18) using the APG8 peptide. The APG8 protein may be a full-length APG8 proteins of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, or 9. The APG8A protein may be a truncated form of the full-length proteins of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, or 9 that at least comprises the sequence of the APG8 peptide used in affinity purification. It will be appreciated by one of skill in the art that affinity purification of the antibody leads to an enrichment of antibodies that specifically bind to the APG8 peptide used in affinity purification, as well as a high possibility of enriching for antibodies that bind to epitopes containing phosphorylated serine-12 (APG8A) and serine-9 (APG8C).

[0110] In some embodiments of this method, the APG8 protein is nonphosphorylated and the method is used to produce a nonphosphorylated APG8 polypeptide. As an example, the APG8A protein used to immunize the animal is not phosphorylated at serine-12 and affinity purification is performed using a nonphosphorylated APG8A peptide. As another example, the APG8C protein used to immunize the animal is not phosphorylated at serine-9 and affinity purification is performed using a nonphosphorylated APG8C peptide.

[0111] In some embodiments of this method, the X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) of the APG8A protein is phosphoserine and the method is used to produce an antibody to a phosphorylated APG8A polypeptide. In some embodiments of the method, the X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) of the APG8C protein is phosphoserine and the method is used to produce an antibody to a phosphorylated APG8C polypeptide. As an example, the APG8A protein used to immunize the animal is phosphorylated at serine-12 and affinity purification is performed using a phosphorylated APG8A peptide. Optionally, this method further comprises a step of removing an antibody that binds to an isolated nonphosphorylated APG8 peptide, wherein X is serine. As an example, the antibody sample can be passed through a column containing bound nonphosphorylated APG8A peptide such that antibodies specific to nonphosphorylated APG8A peptide are removed by remaining bound to the column.

Kit for Preparing Antibody to an APG8A Polypeptide

[0112] A kit may be used to prepare an antibody to an APG8A or an APG8C polypeptide. One embodiment of the kit comprises an APG8A protein and a means for introducing the APG8A protein to a mammal in an amount sufficient to produce an antibody to an APG8A polypeptide. Another embodiment of the kit comprises an APG8C protein and a means for introducing the APG8C protein to a mammal in an amount sufficient to produce an antibody to an APG8C polypeptide.

[0113] The kit also comprises a means for recovering the antibody from the mammal and an isolated APG8 peptide comprised of one of the following sequences: QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

[0114] One exemplary kit contains a full length APG8A protein and reagents containing appropriate immunogens, adjuvants, and buffers such that the APG8A protein can be prepared for introduction into a mammal. The exemplary kit further contains an APG8A peptide as well as affinity purification columns that can be used to enrich for antibodies that specifically bind to the APG8A peptide.

Isolated Antibodies

[0115] Another aspect is an isolated antibody that specifically binds to an epitope that comprises the amino acid X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine. Alternatively, the epitope may be MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine. Multiple embodiments of these aspects are discussed as follows.

[0116] In one further embodiment of this aspect, the antibody is a monoclonal or polyclonal antibody or an antibody fragment.

[0117] In some embodiments, the epitope of the above antibody comprises both the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and an amino acid residue of the APG8A protein that is

outside of the amino acid sequence MPSDRPFKQRRX-FADR (SEQ ID NO:61). Alternatively, the epitope comprises both the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and an amino acid residue of the APG8C protein that is outside of the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). Of these two embodiments, an exemplary epitope may arise from protein folding in which a residue outside of MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is brought into close proximity with the first epitope. Optionally, a kit may be prepared that is comprised of an antibody of this embodiment, a pharmaceutically acceptable carrier and an excipient.

[0118] In some embodiments, the epitope comprises the amino acid X in the amino acid sequence MPSDRPFKQR-RXFADR (SEQ ID NO:61) and amino acid residues of APG8A protein that are outside of the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). Alternatively, in some embodiments, the epitope comprises the amino acid X in the amino acid sequence MPPPQKIPXVRPFKQRK-SLAIR (SEQ ID NO:153) and amino acid residues of APG8C protein that are outside of the amino acid sequence MPP-PQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0119] In some embodiments, the epitope is comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) or of the amino acid sequence MPPPQKIPXVR-PFKQRKSLAIR (SEQ ID NO:153).

[0120] In another further embodiment, the epitope is comprised of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRX-FADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRX-FADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPS-DRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPX-VRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPX-VRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPX-VRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVR-PFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVR-PFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVR-PFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPX-VRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVR-PFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), or PXVRPFKQRKSLAIR (SEQ ID NO:152). X is serine or phosphoserine.

[0121] In another further embodiment, the epitope is comprised of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), or XVRP (SEQ ID NO:18), wherein X is serine or phosphoserine.

[0122] In some embodiments, the antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine. Alternatively, in some embodiments, the antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid

sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0123] In some embodiments, the antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. Alternatively, in some embodiments, the antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0124] In some embodiments, the antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. Alternatively, in some embodiments, the antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0125] In another further embodiment, the antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0126] In some embodiments, the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in an APG8A protein or fragment. In one variation of this embodiment, the antibody specifically binds to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). In another variation of this embodiment, the antibody specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). In a third variation of this embodiment, the antibody specifically binds to the full length APG8A protein at its natural conformation.

[0127] In some embodiments, the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in an APG8C protein or fragment. In one variation of this embodiment, the antibody specifically binds to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). In another variation of this embodiment, the antibody specifically binds to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). In a third variation of this embodiment, the antibody specifically binds to the full length APG8C protein at its natural conformation.

[0128] It will be appreciated by one of skill in the art, that there are many approaches to produce antibodies of this aspect. The following are some exemplary techniques of preparing antibodies.

[0129] Antibodies may be prepared using recombinant techniques to generate a Fab fragment that binds to an antigen. The Fab fragment may be generated by sequencing the amino acid residues of a desired monoclonal antibody and determining the sequence of the light chain and the variable and constant regions of the heavy chain that are associated with that particular light chain. Then, two peptides may be designed with these sequences. The peptides may be produced recombinantly in any system, preferably *E. coli* and *B. subtilis*, by designing a vector that contains sequence encoding these two peptides.

[0130] Animals are generally required for at least one stage of antibody production. The following exemplary animals may be used: rabbits, chickens, goats, guinea pigs, hamsters, horses, mice, rats, and sheep. Factors governing which animal to choose include: 1) the amount of antibody needed, 2) phylogenetic relationship between the donor of the antigen and the antibody producing animal and 3) the specific desired characteristics of the antibodies. If large amounts of antibody is the overriding concern, then horses, goats, and sheep may be preferred. If a distant phylogenetic relationship is important, then chickens are preferred. Mice and rats are preferred for monoclonal antibody production since only small amounts of antigen are needed to generate antibody producing cells needed for subsequent cloning. Rabbits are a preferred choice for laboratory scale polyclonal antibody production.

[0131] Various embodiments of this and other aspects use the following methods to enhance antibody production in an animal: use of carriers (i.e. keyhole limpet cyanin) and immune response potentiators (i.e. multiple antigen peptide such as branched oligolysine).

[0132] The amount of antigen used to immunize the animal may vary. Larger amounts of antigen are correlated with higher titer antibody production. For high titer antibody production, the following exemplary amounts of antigen may be used: 250-1000 micrograms for a rabbit, 50-200 micrograms for a mouse, 150 to 500 micrograms for a guinea pig, 750 to 5000 micrograms for a goat. Additionally, antibody production may be enhanced by administering small priming doses to an animal before a larger dose as above. The following exemplary amounts of antigen may be used for priming: 50-200 micrograms for a rabbit, 10-50 micrograms for a mouse, 50-500 micrograms for a guinea pig, 250 to 750 micrograms for a goat. Additional amounts of antigen may be administered in the form of a booster, which may be in an amount roughly equal to the priming doses.

[0133] Adjuvants may be combined with the antigen in order to stimulate the immune response. Exemplary adjuvants include Freund's complete, Freund's incomplete, Titermax, and Ribi.

[0134] Monoclonal antibodies may be produced using phage display techniques. An APG8 peptide may be attached to a support medium, such as a column. Phage that express a plurality of antibodies or fragments of antibodies, such as a phage display library, may be exposed to the APG8-bound support medium. An exemplary phage display library used for this purpose is described in Schofield, D. et al. Genome Biology (2007) 8(11):R254. Phage that bind to the support may then be further analyzed to determine if they express a

molecule that may be an antibody to an APG8 polypeptide. Optionally, a phage display library may be used to isolate an antibody fragment that binds to an APG8A polypeptide. See Teunissen, S. et al. RNA (1998) 4(9): 1124-1133, for an example of using phage display to isolate an antibody fragment.

[0135] An antibody may also be produced by using a clonal expansion of B cells to isolate an original light chain-heavy chain pairing. An example of this method is described in de Wildt R. et al J. Immunol. Methods (1997) 207(1): 61-67.

Variant Antibodies In some embodiments, the antibody can be an intact, four immunoglobulin chain antibody comprising two heavy chains and two light chains. The heavy chain of the antibody can be of any isotype including IgM, IgG, IgE, IgG, IgA or IgD or sub-isotype including IgG1, IgG2, IgG3, IgG4, IgE1, IgE2, etc. The light chain can be a kappa light chain or a lambda light chain.

[0136] In some embodiments, an antibody may have fewer than 4 chains. Such exemplary antibodies include, but are not limited to, single chain antibodies, Camelid antibodies and the like and components of the antibody, including a heavy chain or a light chain. Such exemplary antibodies include small modular immunopharmaceuticals or SMIPs™, Fab and $F(ab')_2$ fragments, etc. These antibodies may be produced by papain or pepsin digestion of antibodies. Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, whose name reflects its ability to crystallize readily. Pepsin treatment of an antibody yields an $F(ab')_2$ fragment that has two antigen-combining sites and is still capable of cross-linking antigen. The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab' fragments differ from Fab fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments that have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[0137] In some embodiments, the antibody may comprise an "Fv" domain. "Fv" usually refers to the minimum antibody fragment that contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the CDRs confer antigen-binding specificity to the antibody.

[0138] In some embodiments, the antibody may have a single variable domain (or half of an Fv comprising three CDRs specific for an antigen), since the single variable domain may have the ability to recognize and bind antigen, although likely at a lower affinity than the entire binding site.

[0139] In some embodiments, the antibody comprises a single-chain Fv antibody fragment. "Single-chain Fv" or "scFv" antibody fragments comprise the V_H and V_L domains of an antibody, wherein these domains are present in a single polypeptide chain. In certain embodiments, the Fv polypeptide further comprises a polypeptide linker between the VH and V_L domains that enables the scFv to form the desired structure for antigen binding. For a review of scFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore, eds. (Springer-Verlag: New York, 1994), pp. 269-315.

[0140] In some embodiments, the antibody may comprise a SMTP. SMIPs are a class of single-chain peptides engineered to include a target binding region and effector domain (CH2 and CH3 domains). See, e.g., U.S. Patent Application Publication No. 20050238646. The target binding region may be derived from the variable region or CDRs of an antibody, e.g., a phosphorylation site-specific antibody of the application. Alternatively, the target binding region is derived from a protein that binds a phosphorylation site.

[0141] In some embodiments, a therapeutic agent may be placed on one arm of the antibody. The therapeutic agent can be a drug, toxin, enzyme, DNA, radionuclide, etc.

[0142] In some embodiments, the antigen-binding fragment can be a diabody. The term "diabody" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) in the same polypeptide chain (V_H-V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90: 6444-6448 (1993).

[0143] In some embodiments, antibodies may comprise camelid antibodies. Camelid antibodies refer to a unique type of antibodies that are devoid of light chain, initially discovered from animals of the camelid family. The heavy chains of camelid antibodies bind their antigen by one single domain, the variable domain of the heavy immunoglobulin chain, referred to as VHH. VHHs show homology with the variable domain of heavy chains of the human VHIII family. The VHHs obtained from an immunized camel, dromedary, or llama have a number of advantages, such as effective production in microorganisms such as *Saccharomyces cerevisiae.*

[0144] In some embodiments, the antibodies can be humanized, chimerized, deimmunized, or fully human. Numerous publications set forth the many types of antibodies and the methods of engineering such antibodies. For example, see U.S. Pat. Nos. 6,355,245; 6,180,370; 5,693,762; 6,407,213; 6,548,640; 5,565,332; 5,225,539; 6,103,889; and 5,260,203. The chimeric antibody is an antibody having portions derived from different antibodies. For example, a chimeric antibody may have a variable region and a constant region derived from two different antibodies. The donor antibodies may be from different species. In certain embodiments, the variable region of a chimeric antibody is non-human, e.g., murine, and the constant region is human.

[0145] The genetically altered antibodies used in the invention include CDR grafted humanized antibodies. In one embodiment, the humanized antibody comprises heavy and/or light chain CDRs of a non-human donor immunoglobulin and heavy chain and light chain frameworks and constant regions of a human acceptor immunoglobulin. The method of making humanized antibody is disclosed in U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,761; 5,693,762; and 6,180,370 each of which is incorporated herein by reference in its entirety.

[0146] In some embodiments, the antibody may be an "antigen-binding fragment of an antibody", which is any portion of an antibody that retains specific binding of the

intact antibody. An exemplary antigen-binding fragment of an antibody is the heavy chain and/or light chain CDR, or the heavy and/or light chain variable region. Antigen-binding fragments of the antibodies of the invention, which retain the binding specificity of the intact antibody, are also included in the invention. Examples of these antigen-binding fragments include, but are not limited to, partial or full heavy chains or light chains, variable regions, or CDR regions of any phosphorylation site-specific antibodies described herein.

[0147] In some embodiments, the antibody may be an immunoglobulin chain comprised in order from 5' to 3', of a variable region and a constant region. The variable region may comprise three complementarity determining regions (CDRs), with interspersed framework (FR) regions for a structure FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. In these embodiments, the antibody may further comprise heavy or light chain variable regions, framework regions and CDRs.

[0148] In some embodiments, the antibody may comprise a heavy chain constant region that comprises some or all of a CH1 region, hinge, CH2 and CH3 region.

[0149] In some embodiments, the antibody may have an binding affinity (K_D) of 1×10^{7} M or less. In other embodiments, the antibody binds with a K_D of 1×10^{8} M, 1×10^{9} M, 1×10^{10} M, 1×10^{11} M, 1×10^{12} M or less. In certain embodiments, the K_D is 1 μM to 500 μM, between 500 μM to 1 μM, or between 1 μM to 100 nM.

[0150] In some embodiments, the antibodies may be genetically-altered, wherein the amino acid sequence of the native antibody has been varied. Because of the relevance of recombinant DNA techniques to this application, one need not be confined to the sequences of amino acids found in natural antibodies; antibodies can be redesigned to obtain desired characteristics. The possible variations are many and range from the changing of just one or a few amino acids to the complete redesign of, for example, the variable or constant region. Changes in the constant region may be made in order to improve or alter characteristics, such as complement fixation, interaction with membranes and other effector functions. Changes in the variable region may be made in order to improve the antigen binding characteristics. Modified antibodies may provide improved stability or/and therapeutic efficacy. Examples of modified antibodies include those with conservative substitutions of amino acid residues, and one or more deletions or additions of amino acids that do not significantly deleteriously alter the antigen binding utility. Substitutions can range from changing or modifying one or more amino acid residues to complete redesign of a region as long as the therapeutic utility is maintained. Antibodies can be modified post-translationally (e.g., acetylation, and/or phosphorylation) or can be modified synthetically (e.g., the attachment of a labeling group).

[0151] In preferred embodiments, genetically altered antibodies are functionally equivalent to the above-mentioned natural antibodies.

[0152] Oligoclonal antibodies may be used in various embodiments. In some embodiments, oligoclonal antibodies consisting of a predetermined mixture of antibodies against one or more epitopes are generated in a single cell. In other embodiments, oligoclonal antibodies comprise a plurality of heavy chains capable of pairing with a common light chain to generate antibodies with multiple specificities (e.g., PCT publication WO 04/009618). It is appreciated by one of skill in the art that oligoclonal antibodies are particularly useful when it is desired to target multiple epitopes on a single target molecule. In view of the assays and epitopes disclosed herein, those skilled in the art can generate or select antibodies or mixtures of antibodies that are applicable for an intended purpose and desired need.

[0153] Recombinant antibodies against the novel phosphorylation sites identified in the disclosure may be used in various embodiments. These recombinant antibodies have the same amino acid sequence as the natural antibodies or have altered amino acid sequences of the natural antibodies in the present application. They can be made in any expression systems including both prokaryotic and eukaryotic expression systems or using phage display methods (see, e.g., Dower et al., WO91/17271 and McCafferty et al., WO92/01047; U.S. Pat. No. 5,969,108, which are herein incorporated by reference in their entirety).

[0154] In some embodiments, antibodies have variant constant or Fc regions. Such antibodies can be useful in modulating effector functions, i.e. antigen-dependent cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Such antibodies may be useful in instances where a parent singling protein is expressed in normal tissue; variant antibodies without effector function in these instances may elicit the desired therapeutic response while not damaging normal tissue.

[0155] In some embodiments, the antibody fragments are truncated chains (truncated at the carboxyl end). These truncated chains may possess one or more immunoglobulin activities (e.g., complement fixation activity). Examples of truncated chains include, but are not limited to, Fab fragments (consisting of the VL, VH, CL and CH1 domains); Fd fragments (consisting of the VH and CH1 domains); Fv fragments (consisting of VL and VH domains of a single chain of an antibody); dAb fragments (consisting of a VH domain); isolated CDR regions; $(FaW)_2$ fragments, bivalent fragments (comprising two Fab fragments linked by a disulphide bridge at the hinge region). The truncated chains can be produced by conventional biochemical techniques, such as enzyme cleavage, or recombinant DNA techniques, each of which is known in the art. These polypeptide fragments may be produced by proteolytic cleavage of intact antibodies by methods well known in the art, or by inserting stop codons at the desired locations in the vectors using site-directed mutagenesis, such as after CH1 to produce Fab fragments or after the hinge region to produce $(Fab')_2$ fragments. Single chain antibodies may be produced by joining VL- and VH-coding regions with a DNA that encodes a peptide linker connecting the VL and VH protein fragments.

[0156] In some embodiments, single chain antibodies, and chimeric, humanized or primatized (CDR-grafted) antibodies, as well as chimeric or CDR-grafted single chain antibodies, comprising portions derived from different species, are also encompassed by the present disclosure as antigen-binding fragments of an antibody. The various portions of these antibodies can be joined together chemically by conventional techniques, or can be prepared as a contiguous protein using genetic engineering techniques. For example, nucleic acids encoding a chimeric or humanized chain can be expressed to produce a contiguous protein. See, e.g., U.S. Pat. Nos. 4,816,567 and 6,331,415; U.S. Pat. No. 4,816,397; European Patent No. 0,120,694; WO 86/01533; European Patent No. 0,194,276 B1; U.S. Pat. No. 5,225,539; and European Patent No. 0,239,400 B1. See also, Newman et al., BioTechnology, 10: 1455-1460 (1992), regarding primatized antibody. See, e.g.,

Ladner et ah, U.S. Pat. No. 4,946,778; and Bird et al., Science, 242: 423-426 (1988)), regarding single chain antibodies.

[0157] In addition, functional fragments of antibodies, including fragments of chimeric, humanized, primatized or single chain antibodies, can also be produced. Functional fragments of the subject antibodies retain at least one binding function and/or modulation function of the full-length antibody from which they are derived.

[0158] Since the immunoglobulin-related genes contain separate functional regions, each having one or more distinct biological activities, the genes of the antibody fragments may be fused to functional regions from other genes (e.g., enzymes, U.S. Pat. No. 5,004,692, which is incorporated by reference in its entirety) to produce fusion proteins or conjugates having novel properties.

[0159] In some embodiments, non-immunoglobulin binding polypeptides are also contemplated. For example, CDRs from an antibody disclosed herein may be inserted into a suitable non-immunoglobulin scaffold to create a non-immunoglobulin binding polypeptide. Suitable candidate scaffold structures may be derived from, for example, members of fibronectin type III and cadherin superfamilies.

[0160] Some embodiments may comprise other equivalent non-antibody molecules, such as protein binding domains or aptamers. which bind, in a phospho-specific manner, to an amino acid sequence comprising a novel phosphorylation site of the invention. See, e.g., Neuberger et al, Nature 312: 604 (1984). Aptamers are oligonucleic acid or peptide molecules that bind a specific target molecule. DNA or RNA aptamers are typically short oligonucleotides, engineered through repeated rounds of selection to bind to a molecular target. Peptide aptamers typically consist of a variable peptide loop attached at both ends to a protein scaffold. This double structural constraint generally increases the binding affinity of the peptide aptamer to levels comparable to an antibody (nanomolar range).

[0161] In some embodiments, phosphorylation site-specific antibodies may be conjugated with immunotoxins. Conjugates that are immunotoxins including antibodies have been widely described in the art. The toxins may be coupled to the antibodies by conventional coupling techniques or immunotoxins containing protein toxin portions can be produced as fusion proteins. In certain embodiments, antibody conjugates may comprise stable linkers and may release cytotoxic agents inside cells (see U.S. Pat. Nos. 6,867,007 and 6,884,869). The conjugates of the present application can be used in a corresponding way to obtain such immunotoxins. Illustrative of such immunotoxins are those described by Byers et al., Seminars Cell Biol 2:59-70 (1991) and by Fanger et al., Immunol Today 12:51-54 (1991). Exemplary immunotoxins include radiotherapeutic agents, ribosome-inactivating proteins (RIPs), chemotherapeutic agents, toxic peptides, or toxic proteins.

Antibody Pharmaceutical Compositions

[0162] Another aspect is a pharmaceutical composition that comprises an antibody of any other aspect disclosed. The pharmaceutical composition may further comprise a carrier. Suitable carriers include any material that when combined with the therapeutic composition retains the anti-tumor function of the therapeutic composition and is generally non-reactive with the patient's immune system. Examples include, but are not limited to, any of a number of standard pharmaceutical carriers such as sterile phosphate buffered saline solutions, bacteriostatic water, and the like (see, generally, Remington's Pharmaceutical Sciences 16.sup.th Edition, A. Osal., Ed., 1980). PEG may be used as a pharmaceutical carrier. PEG may be covalently attached to the antibody in the pharmaceutical composition.

Method for Detecting APG8A Protein

[0163] Another aspect is a method for detecting an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample. The method comprises contacting a sample containing or suspected of containing an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine; and assessing a complex formed between the APG8A protein or fragment, if present in the sample, and the antibody, to determine the presence, absence and/or amount of the APG8A protein or fragment in the sample.

[0164] In an embodiment of this method, the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and an amino acid residue of APG8A protein that is outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0165] In another embodiment of this method, the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and amino acid residues of APG8A protein that are outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0166] In another embodiment, the epitope is comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0167] In another embodiment, the epitope is comprised in an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID

NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), and MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0168] In another embodiment, the epitope is comprised in an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14).

[0169] In another embodiment, the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0170] In another embodiment, the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0171] In another embodiment, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine. The antibody does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0172] In another embodiment, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. The antibody does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0173] In another embodiment, the isolated antibody specifically binds to the full length APG8A protein at its natural conformation.

[0174] In another embodiment, the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0175] In another embodiment, the complex is assessed by a format selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), immunoblotting, immunoprecipitation, radioimmunoassay (RIA), immunostaining, latex agglutination, indirect hemagglutination assay (IHA), complement fixation, indirect immunofluorescent assay (IFA), nephelometry, flow cytometry assay, plasmon resonance assay, chemiluminescence assay, lateral flow immunoassay, u-capture assay, inhibition assay and avidity assay.

[0176] In another embodiment, the complex is assessed in a homogeneous or a heterogeneous assay format.

Method for Detecting APG8C Protein

[0177] Another aspect is a method for detecting an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample. The method comprises contacting a sample containing or suspected of containing an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine; and assessing a complex formed between the APG8C protein or fragment, if present in the sample, and the antibody, to determine the presence, absence and/or amount of the APG8C protein or fragment in the sample.

[0178] In an embodiment of this method, the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and an amino acid residue of APG8C protein that is outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0179] In another embodiment of this method, the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and amino acid residues of APG8C protein that are outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0180] In another embodiment, the epitope is comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0181] In another embodiment, the epitope is comprised in an amino acid sequence selected from the group consisting of QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVR-

PFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

[0182] In another embodiment, the epitope is comprised in an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

[0183] In another embodiment, the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0184] In another embodiment, the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0185] In another embodiment, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine. The antibody does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0186] In another embodiment, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine. The antibody does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0187] In another embodiment, the isolated antibody specifically binds to the full length APG8C protein at its natural conformation.

[0188] In another embodiment, the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0189] In another embodiment, the complex is assessed by a format selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), immunoblotting, immunoprecipitation, radioimmunoassay (RIA), immunostaining, latex agglutination, indirect hemagglutination assay (IHA), complement fixation, indirect immunofluorescent assay (IFA), nephelometry, flow cytometry assay, plasmon resonance assay, chemiluminescence assay, lateral flow immunoassay, u-capture assay, inhibition assay and avidity assay.

[0190] In another embodiment, the complex is assessed in a homogeneous or a heterogeneous assay format.

Immunoassay

[0191] Although a variety of assay types are contemplated, the present methods frequently assess the complex formed between the whole APG8 protein and the antibody via a sandwich or competitive assay format. On occasion, the complex is assessed in a homogeneous or a heterogeneous assay format. Also frequently, the complex is assessed by a format selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), immunoblotting, immunoprecipitation, radioimmunoassay (RIA), immunostaining, latex agglutination, indirect hemagglutination assay (IHA), complement fixation, indirect immunofluorescent assay (IFA), nephelometry, flow cytometry assay, plasmon resonance assay, chemiluminescence assay, lateral flow immunoassay, u-capture assay, inhibition assay and avidity assay.

[0192] In a sandwich assay format, the antibody that that specifically binds to an epitope that comprises the amino acid residue X in either the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is used as a first antibody. The antibody that is capable of binding to a portion of whole APG8A other than the sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), which binds to the first antibody, is used as a second antibody. Alternatively, in a sandwich assay, the antibody that that specifically binds to an epitope that comprises the amino acid residue X in either the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is used as a first antibody. The antibody that is capable of binding to a portion of whole APG8C other than the sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), which binds to the first antibody, is used as a second antibody.

[0193] Either the first antibody or the second antibody is frequently attached to a surface and functions as a capture antibody. The attachment can be direct or indirect. In a preferred embodiment, the attachment is provided via a biotin-avidin (or streptavidin) linking pair.

Determination of Phosphorylation Status

[0194] In this aspect is a method to determine the phosphorylation status of an APG8 protein or fragment by detecting a polypeptide comprising either the amino acid sequence MPSDRPFKQRRSFADR (SEQ ID NO:154) (APG8A) or MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) (APG8C). The method comprises contacting a sample containing or suspected of containing this protein with an isolated antibody that specifically binds to an epitope that comprises serine-12 in MPSDRPFKQRRSFADR (SEQ ID NO:154) or an antibody that specifically binds to an epitope that comprises serine-9 in MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). The antibody may recognize either the phosphorylated or nonphosphorylated form of this epitope, i.e. serine or phosphoserine. The method further comprises a step of assessing a complex formed between the APG8 protein or fragment, if present in the sample, to determine the phosphorylation status of the APG8 protein.

[0195] An example of this embodiment involves using two antibodies, one that specifically recognizes serine and one that specifically recognizes phosphoserine. It can be appreciated that one of skill in the art can measure the phosphorylation status by determining the relative degree of staining of the two antibodies in various standards containing known amounts of phosphorylated and nonphosphorylated APG8 peptides to determine the phosphorylation status of an APG8 protein.

[0196] A further embodiment of this aspect is to determine the phosphorylation status of a full length APG8 protein. Optionally, this embodiment is used to determine the phosphorylation status of a full length APG8 protein in a biological sample. The biological sample may be a clinical sample. The determination of the phosphorylation status of an APG8 protein, or optionally a full length APG8 protein, in a biological sample may be conducted for the prognosis, diagnosis and/or treatment monitoring of a disease or disorder associ-

ated with abnormal phosphorylation status of an APG8 protein or fragment comprising either the amino acid sequence MPSDRPFKQRRSFADR (SEQ ID NO:154) (APG8A) or MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) (APG8C). Exemplary disease types associated with abnormal phosphorylation status of an APG8 protein or fragment may include ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

Method for Identifying a Phosphatase

[0197] Another aspect is a method for identifying a phosphatase that dephosphorylates an APG8A protein on the serine residue 12. The method comprises the following steps: (1) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is phosphoserine, (2) contacting the APG8A polypeptide with a test protein and H_2O under conditions suitable for the dephosphorylation of the phosphoserine residue of the APG8A polypeptide; and (3) assessing the phosphorylation status of the APG8A polypeptide to determine whether the test protein is a phosphatase for the APG8A protein on the phosphoserine residue 12.

[0198] In a further embodiment, the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is phosphoserine. Optionally, the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. An example of this embodiment is the detection of nonphosphorylated APG8A protein by detecting binding of an antibody that specifically binds to the nonphosphorylated epitope and does not bind to the phosphorylated epitope.

[0199] Another aspect is a method for identifying a phosphatase that dephosphorylates an APG8C protein on the serine residue 9. The method comprises the following steps: (1) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine, (2) contacting the APG8C polypeptide with a test protein and H_2O under conditions suitable for the dephosphorylation of the phosphoserine residue of the APG8C polypeptide; and (3) assessing the phosphorylation status of the APG8C polypeptide to determine whether the test protein is a phosphatase for the APG8C protein on the phosphoserine residue 9.

[0200] In a further embodiment, the APG8C protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is phosphoserine. Optionally, the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. An example of this embodiment is the detection of nonphosphorylated APG8C protein by detecting binding of an antibody that specifically binds to the nonphosphorylated epitope and does not bind to the phosphorylated epitope.

Method for Identifying a Phosphatase Modulator

[0201] Another aspect is a method for identifying a modulator of a phosphatase that dephosphorylates an APG8A protein on the serine residue 12. The method comprises the following steps: (1) providing APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is phosphoserine; (2) contacting the APG8A polypeptide with a phosphatase that dephosphorylates an APG8A protein on the serine residue 12 and H_2O under conditions suitable for the dephosphorylation of the phosphoserine residue of the APG8A polypeptide in the presence or absence of a test substance; and (3) assessing and comparing dephosphorylation status of the APG8A polypeptide by the phosphatase to determine whether the test substance modulates the phosphatase.

[0202] In a further embodiment of this aspect, the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is phosphoserine. Optionally, the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0203] Another aspect is a method for identifying a modulator of a phosphatase that dephosphorylates an APG8C protein on the serine residue 9. The method comprises the following steps: (1) providing APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine; (2) contacting the APG8C polypeptide with a phosphatase that dephosphorylates an APG8C protein on the serine residue 9 and H_2O under conditions suitable for the dephosphorylation of the phosphoserine residue of the APG8C polypeptide in the presence or absence of a test substance; and (3) assessing and comparing dephosphorylation status of the APG8C polypeptide by the phosphatase to determine whether the test substance modulates the phosphatase.

[0204] In a further embodiment of this aspect, the APG8C protein or fragment comprises an amino acid sequence MPP-

PQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is phosphoserine. Optionally, the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPP-PQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

Kit for Protein Detection

[0205] In another aspect is a kit for detecting an APG8A protein or fragment comprising amino acid sequence MPS-DRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample. The kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0206] An exemplary use of the kit is to specifically detect native APG8A protein that is phosphorylated at serine-12. Another exemplary use of the kit is to specifically detect native APG8A protein that is not phosphorylated at serine-12.

[0207] In another aspect is a kit for detecting an APG8C protein or fragment comprising amino acid sequence MPP-PQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample. The kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0208] An exemplary use of the kit is to specifically detect native APG8C protein that is phosphorylated at serine-9. Another exemplary use of the kit is to specifically detect native APG8A protein that is not phosphorylated at serine-9.

Method of Treating Disease

[0209] The following aspect relates to a method of treating a disease or disorder associated with abnormal phosphorylation status of an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine.

[0210] The method comprises administering, to a subject when such a treatment is needed or desired, a sufficient amount of an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine. The subject may be a mammal. The subject may be a human.

[0211] In some embodiments, the isolated antibody specifically binds to the full length APG8A protein at its natural conformation.

[0212] In some embodiments, the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0213] Some embodiments further comprise the step of administering a pharmaceutically acceptable carrier and excipient.

[0214] In one embodiment of the above aspect the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPS-DRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine. Optionally, the disease or disorder is associated with an abnormal phosphorylation level of an APG8A protein or fragment, and the binding of the antibody to the APG8A protein or fragment prevents or reduces the phosphorylation level of the APG8A protein or fragment. As a further option, the diseases or disorders associated with an abnormal phosphorylation level of an APG8A protein or fragment include ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0215] In another embodiment of the above aspect, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0216] Optionally, the disease or disorder is associated with an abnormal phosphorylation level of an APG8A protein or fragment, and the binding of the antibody to the APG8A protein or fragment prevents or reduces dephosphorylation of the APG8A protein or fragment. As a further option, the disease or disorder associated with an abnormal phosphorylation level of an APG8A protein or fragment is cancer (especially in the context of tumor formation), neurodegenerative diseases involving amyloid proteins, myopathies, diseases involving elevated muscle wasting, liver diseases, heart disease where autophagy is harmful in reperfusion, and diseases involving microbes that exploit autophagy.

[0217] In another embodiment of the above aspect, the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in a full length APG8A protein and the isolated antibody specifically binds to the full length APG8A protein. As a first option, the isolated antibody specifically binds to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61). As a second option, the isolated antibody specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0218] The following aspect relates to a method of treating a disease or disorder associated with abnormal phosphorylation status of an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine. The method comprises administering, to a subject when such a treatment is needed or desired, a sufficient amount of an

isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine. The subject may be a mammal. The subject may be a human.

[0219] In some embodiments, the isolated antibody specifically binds to the full length APG8A protein at its natural conformation.

[0220] In some embodiments, the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0221] Some embodiments further comprise the step of administering a pharmaceutically acceptable carrier and excipient. In one embodiment of the above aspect the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine. Optionally, the disease or disorder is associated with an abnormal phosphorylation level of an APG8C protein or fragment, and the binding of the antibody to the APG8C protein or fragment prevents or reduces phosphorylation level of the APG8C protein or fragment. As a further option, the diseases or disorders associated with an abnormal phosphorylation level of an APG8C protein or fragment include ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0222] In another embodiment of the above aspect, the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine. Optionally, the disease or disorder is associated with an abnormal phosphorylation level of an APG8C protein or fragment, and the binding of the antibody to the APG8C protein or fragment prevents or reduces dephosphorylation of the APG8C protein or fragment. As a further option, the disease or disorder associated with abnormally low phosphorylation level of an APG8C protein or fragment include ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0223] In another embodiment of the above aspect, the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in a full length APG8C protein and the isolated antibody specifically binds to the full length APG8C protein. As a first option, the isolated antibody specifically binds to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153). As a second option, the isolated antibody specifically binds to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

Identification of a Kinase

[0224] Another aspect is a method for identifying a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of (1) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide; and (3) assessing the phosphorylation status of the APG8A polypeptide to determine whether the test protein is a kinase for the APG8A protein on the serine residue 12.

[0225] In another embodiment of this aspect, the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine.

[0226] In another embodiment, the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0227] Another aspect is a method for identifying a kinase that phosphorylates an APG8C protein on the serine residue 9. The method comprises the steps of (1) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine; (2) contacting the APG8C polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8C polypeptide; and (3) assessing the phosphorylation status of the APG8C polypeptide to determine whether the test protein is a kinase for the APG8C protein on the serine residue 9.

[0228] In another embodiment of this aspect, the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine.

[0229] In another embodiment, the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

Identification of a Kinase Modulator

[0230] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8A protein on the serine residue 12. The method comprises the steps of: (1) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), and XFAD (SEQ ID NO:14), wherein X is serine; (2) contacting the APG8A polypeptide with a kinase that phosphorylates an APG8A protein on the serine residue 12 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8A polypeptide in the presence or absence of a test substance; and (3) assessing and comparing phosphorylation status of the APG8A polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0231] In one embodiment of this aspect, the APG8A protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine.

[0232] In another embodiment of this aspect, the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0233] Another aspect is a method for identifying a modulator of a kinase that phosphorylates an APG8C protein on the serine residue 12. The method comprises the steps of: (1) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine; (2) contacting the APG8C polypeptide with a kinase that phosphorylates an APG8C protein on the serine residue 12 and ATP under conditions suitable for the phosphorylation of the serine residue of the APG8C polypeptide in the presence or absence of a test substance; and (3) assessing and comparing phosphorylation status of the APG8C polypeptide by the kinase to determine whether the test substance modulates the kinase.

[0234] In one embodiment of this aspect, the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine.

[0235] In another embodiment of this aspect, the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

Isolated Nucleic Acid Fragment

[0236] Another aspect is an isolated nucleic acid fragment which is comprised of a sequence of nucleotides encoding an APG8 peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine. The APG8 peptide is not a full-length APG8 protein comprising an amino acid sequence set forth in SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, or 9. The nucleic acid may be DNA. The nucleic acid may also be RNA.

[0237] In another embodiment, the APG8 peptide comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) (APG8A).

[0238] In another embodiment, the APG8 peptide comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) (APG8C).

[0239] In another embodiment there is a plasmid which comprises the nucleic acid fragments of this aspect.

[0240] In another embodiment there is a vector which comprises the nucleic acid fragments of this aspect.

[0241] In another embodiment, there may be a cell which comprises the plasmids or vectors of this aspect. The cell may be a bacterial cell, a yeast cell, a fungal cell, a plant cell, an insect cell, an animal cell or a human cell. The cell may be used in a method for producing an APG8 peptide, comprising growing the cell under conditions whereby the APG8 peptide is expressed by the cell, and recovering the expressed APG8 peptide. Optionally, the method further comprises a step of phosphorylating the APG8 peptide at the serine residue.

Screening for Compounds

[0242] In another aspect is a method for identifying a compound that binds to specifically to a phosphorylated APG8 polypeptide. The method comprises the following steps: 1) providing a phosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine; 2) contacting said phosphorylated APG8 polypeptide with a test compound and H_2O under conditions suitable for binding of the test protein with APG8 polypeptide; 3) assessing binding of the phosphorylated APG8 polypeptide with the test compound; 4) providing a nonphosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine; 5) contacting said nonphosphorylated APG8 polypeptide with a test compound and H_2O under conditions suitable for binding of the test protein with APG8 polypeptide; and 6) assessing binding of the nonphosphorylated APG8 polypeptide with the test compound. In the method, the compound that binds specifically to a phosphorylated APG8 polypeptide is a test compound which binds to phosphorylated APG8 polypeptide according to step 3 but does not bind

to nonphosphorylated APG8 polypeptide according to step 5. In some embodiments, the test compound may be a polypeptide. In some embodiments, the test compound may be a peptide. In some embodiments the test compound may be a nucleic acid. In some embodiments, the compound may be a small molecule.

[0243] In another aspect is a method for identifying a compound that binds to specifically to a nonphosphorylated APG8 polypeptide. The method comprises the following steps: 1) providing a nonphosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine; 2) contacting said nonphosphorylated APG8 polypeptide with a test compound and H_2O under conditions suitable for binding of the test protein with APG8 polypeptide; 3) assessing binding of the nonphosphorylated APG8 polypeptide with the test compound; 4) providing a phosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine; 5) contacting said phosphorylated APG8 polypeptide with a test compound and H_2O under conditions suitable for binding of the test protein with APG8 polypeptide; and 6) assessing binding of the phosphorylated APG8 polypeptide with the test compound. In the method, the compound that binds specifically to a nonphosphorylated APG8 polypeptide is a test compound which binds to nonphosphorylated APG8 polypeptide according to step 3 but does not bind to phosphorylated APG8 polypeptide according to step 5. In some embodiments, the test compound may be a polypeptide. In some embodiments, the test compound may be a peptide. In some embodiments the test compound may be a nucleic acid. In some embodiments, the compound may be a small molecule.

Method of Treating Disease by Modulating Phosphorylation of APG8

[0244] Diseases may be treated by modulating the phosphorylation of APG8. These diseases may arise from abnormal phosphorylation of APG8. Alternatively, the phosphorylation status of APG8 may be normal, but the disease may be treated by modulating the phosphorylation of APG8 to enhance or reduce autophagy. Such exemplary diseases include ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0245] By increasing the rate of autophagy, there can be enhanced cleaning and turnover of damaged organelles, protein aggregates, and other unwanted cellular features that can be removed by autophagy. By decreasing the rate of autophagy, a diseased cell, such as a cancer cell, may be more susceptible to treatment by chemotherapeutic and other agents.

[0246] APG8 phosphorylation may be increased in order to increase autophagy.

[0247] Alternatively, APG8 phosphorylation may be decreased in order to decrease autophagy.

[0248] APG8 phosphorylation may be decreased in order to increase autophagy.

[0249] Alternatively, APG8 phosphorylation may be increased in order to decrease autophagy.

Antibody Microarrays

[0250] In another aspect is a microarray comprising an antibody disclosed above. Microarrays are useful for screening potential binding partners for binding to proteins on an array, in a high-throughput manner. Microarrays are typically comprised of a large number of a library of target or capture reagents robotically arrayed or spotted in high density onto a solid support. Potential binding partners for screening are labeled, usually with fluorescence, and contacted with to a target or capture reagent immobilized on the array under conditions to allow for binding. Following a wash step, binding to the individual targets may be measured and quantified. Each collection of binding partners may be tested individually, with results from individual arrays compared.

[0251] An antibody microarray using antibodies of the disclosure has substantial utility. The microarray may be used as a diagnostic tool to monitor the phosphorylation of autophagy proteins in a variety of tissue samples from a patient in order to determine whether the patient has a disease that is correlated with an abnormal degree of autophagy. Additionally, the microarray may be used to screen for drugs and other compounds that affect the phosphorylation status of autophagy proteins.

Example 1

Production of an APG8a Phosphospecific Polyclonal Antibody

[0252] A 16 amino acid phospho-peptide antigen, MPSDRPFKQRRS*FADRC (SEQ ID NO:156) (where S*=phosphoserine), corresponding to residues 1-16 of human APG8a (SEQ ID NO:1) plus cysteine on the C-terminal for coupling, was constructed according to standard synthesis techniques using a Rainin/Protein Technologies, Inc., Symphony peptide synthesizer. See, e.g., ANTIBODIES: A LABORATORY MANUAL, Chapter 5, pages 75 76, Harlow & Lane Eds., Cold Spring Harbor Laboratory (1988); Czernik, Methods In Enzymology, 201: 264 283 (1991); Merrifield, J. Am. Chem. Soc. 85: 21-49 (1962)).

[0253] This peptide was coupled to KLH, and rabbits were injected intradermally (ID) on the back with antigen in complete Freunds adjuvant (200 μg antigen per rabbit). The rabbits were boosted with same antigen in incomplete Freund adjuvant (100 μg antigen per rabbit) weekly for eight. Coincident with the dates of the third through eighth boosts, 15-20 mL bleed per rabbit was collected. One week after the eight boost, a terminating bleed of 40-60 mL per rabbit was collected. The sera were purified by Protein A-affinity chroma-

tography as previously described (see ANTIBODIES: A LABORATORY MANUAL, Cold Spring Harbor, supra.). The eluted immunoglobulins were further loaded onto MPSDRPFKQRRSFADRC (SEQ ID NO:157)-resin Knotes column. The flow through fraction was collected and applied onto MPSDRPFKQRRS*FADRC (SEQ ID NO:156)-resin column. After washing the column extensively, the phospho-APG8a antibodies were eluted and kept in antibody storage buffer.

[0254] The antibody was confirmed for phosphospecificity against the peptide antigen using Dot blot assay. 50 ng of phosphopeptide and 50 ng of the nonphosphorylated version of the peptide were spotted separately onto a nitrocellulose membrane. The membrane was allowed to dry. Non-specific sites were blocked by soaking in 5% BSA in TBS-T (0.5-1 hr, RT). A 10 cm petri dish was used for the reaction chamber. The membrane was incubated with the purified APG8a phosphospecific polyclonal antibody at a concentration of 0.5 μg/mL dissolved in BSA/TBS-T for 30 min at room temperature. The membrane was washed three times with TBS-T (3×5 min). The membrane was incubated with secondary antibody conjugated to HRP using manufacturer's recommended dilution for 30 min at room temperature. The membrane was then washed three times with TBS-T (15 min×1, 5 min×2), then once with TBS (5 min). The membrane was then incubated with ECL reagent for 1 min, covered with Saranwrap after removing excess solution from the surface, and then exposed to X-ray film in a dark room at several different lengths of exposure. The results of the dot blot are shown in FIG. **1**. As shown in this Figure, the antibody, as expected, only recognized the phosphorylated peptide. It did not recognize the non-phosphorylated peptide.

Example 2

Western Blot Assay Using APG8a Antibody

[0255] The antibody described in Example 1 is tested for phosphospecificity in detection of cellular protein using Western blot assay. Jurkat and 293 cells are collected, washed with PBS and directly lysed in cell lysis buffer. The loading buffer is added into the respective cell lysate and the mixture is boiled at 100° C. for 5 minutes. 10-20 μg of lysate is added onto 7.5% SDS-PAGE gel. A standard Western blot is performed according to the Immunoblotting Protocol set out in the Abgent 2006-2008 Catalog and Technical Reference, p. 262. APG8a phosphospecific polyclonal antibody dilutions are optimized between 1:60 and 1:1000 from a stock concentration of 0.25 mg/mL. For each lysate, sample is incubated as follows: Lane 1, negative sera; Lane 2, phosphospecific APG8a antibody; Lane 3, phosphospecific APG8a antibody that is pre-incubated with phosphorylated peptide MPSDRPFKQRRS*FADRC (SEQ ID NO:156) (optimized in the range of 1:4 to 1:50 stoichiometric ratio); Lane 4, phosphospecific APG8a antibody that is pre-incubated with nonphosphorylated peptide MPSDRPFKQRRSFADRC (SEQ ID NO:157)(at the same stoichiometric ratio as Lane 3). The phosphorylated peptide competes for the antibody with phosphorylated native protein, but the nonphosphorylated peptide does not; therefore a band corresponding to the phosphorylated protein is observed in Lanes 2 and 4, but not Lane 3. demonstrating phosphospecificity of the APG8a phospho-specific polyclonal antibody.

Example 3

Production of an APG8c Phosphospecific Polyclonal Antibody

[0256] A 16 amino acid phospho-peptide antigen, QKIPS*VRPFKQRC (SEQ ID NO:158) (where S*=phosphoserine), corresponding to residues 5-16 of human APG8c (SEQ ID NO:8) plus cysteine on the C-terminal for coupling, was constructed according to standard synthesis techniques using a Rainin/Protein Technologies, Inc., Symphony peptide synthesizer. See, e.g., ANTIBODIES: A LABORATORY MANUAL, Chapter 5, p. 75 76, Harlow & Lane Eds., Cold Spring Harbor Laboratory (1988); Czernik, Methods In Enzymology, 201: 264 283 (1991); Merrifield, J. Am. Chem. Soc. 85: 21 49 (1962)).

[0257] This peptide was coupled to KLH, and rabbits were injected intradermally (ID) on the back with antigen in complete Freunds adjuvant (200 μg antigen per rabbit). The rabbits were boosted with same antigen in incomplete Freund adjuvant (100 μg antigen per rabbit) weekly for eight. Coincident with the dates of the third through eighth boosts, 15-20 mL bleed per rabbit was collected. One week after the eight boost, a terminating bleed of 40-60 mL per rabbit was collected. The sera were purified by Protein A-affinity chromatography as previously described (see ANTIBODIES: A LABORATORY MANUAL, Cold Spring Harbor, supra.). The eluted immunoglobulins were further loaded onto QKIPSVRPFKQRC (SEQ ID NO:159)-resin Knotes column. The flow through fraction was collected and applied onto QKIPS*VRPFKQRC (SEQ ID NO:158)-resin column. After washing the column extensively, the phospho-APG8c antibodies were eluted and kept in antibody storage buffer.

[0258] The antibody was confirmed for phosphospecificity against the peptide antigen using Dot blot assay. 50 ng of phospho-peptide and 50 ng of the nonphosphorylated version of the peptide were spotted separately onto a nitrocellulose membrane. The membrane was allowed to dry. Non-specific sites were blocked by soaking in 5% BSA in TBS-T (0.5-1 hr, RT). A 10 cm petri dish was used for the reaction chamber. The membrane was incubated with the purified APG8c phosphospecific polyclonal antibody at a concentration of 0.5 μg/mL dissolved in BSA/TBS-T for 30 min at room temperature. The membrane was washed three times with TBS-T (3×5 min). The membrane was incubated with secondary antibody conjugated to HRP using manufacturer's recommended dilution for 30 min at room temperature. The membrane was then washed three times with TBS-T (15 min×1, 5 min×2), then once with TBS (5 min). The membrane was then incubated with ECL reagent for 1 min, covered with Saranwrap after removing excess solution from the surface, and then exposed to X-ray film in a dark room at several different lengths of exposure. The results of the dot blot are shown in FIG. **2**. As shown in this Figure, the antibody, as expected, only recognized the phosphorylated peptide. It did not recognize the non-phosphorylated peptide.

Example 4

Western Blot Assay for APG8c Antibody

[0259] The antibody described in Example 3 is tested for phosphospecificity in detection of cellular protein using Western blot assay. Jurkat and 293 cells are collected, washed with PBS and directly lysed in cell lysis buffer. The loading buffer was added into the respective cell lysate and the mixture is boiled at 100° C. for 5 minutes. 10-20 μg of lysate is added onto 7.5% SDS-PAGE gel. A standard Western blot was performed according to the Immunoblotting Protocol set out in the Abgent 2006-2008 Catalog and Technical Reference, p. 262. APG8c phosphospecific polyclonal antibody dilutions are optimized between 1:60 and 1:1000 from a stock

concentration of 0.25 mg/mL. For each lysate, sample is incubated as follows: Lane 1, negative sera; Lane 2, phospho-specific APG8c antibody; Lane 3, phosphospecific APG8c antibody that is pre-incubated with phosphorylated peptide QKIPS*VRPFKQRC (SEQ ID NO:158) (optimized in the range of 1:4 to 1:50 stoichiometric ratio); Lane 4, phospho-specific APG8a antibody that is pre-incubated with nonphosphorylated peptide QKIPSVRPFKQRC (SEQ ID NO:159) (at the same stoichiometric ratio as Lane 3). The phosphorylated peptide competes for the antibody with phosphorylated native protein, but the nonphosphorylated peptide does not; therefore a band corresponding to the phosphorylated protein is observed in Lanes 2 and 4, but not Lane 3, demonstrating phosphospecificity of the APG8c phosphospecific polyclonal antibody.

Example 5

Western Blot Determination of Antibody Specific to APG8a Phosphorylated at Serine-12

[0260] Immunoblots of phosphorylated APG8a (also known as phospho-LC3) were performed on lysates of three CHO cell cultures. APG8a vector was transfected into one set of CHO cells. This vector encodes wild-type APG8a, which can be phosphorylated at serine-12. In a first control set of CHO cells, an APG8a 512A mutant vector was transfected that cannot undergo such phosphorylation. Empty vector was transfected into a second control set of CHO cells.

[0261] The cell lysates were separated with SDS-PAGE and two Western blots were then conducted. In both blots, lysates from CHO cells transfected wild-type APG8a were loaded in the first six lanes of the SDS-PAGE gel (indicated as WT in FIG. **3**). In the next six lanes of both blots, the APG8a 512A mutant was loaded (indicated as 512A in FIG. **3**). Lysates from the CHO cells transfected with empty vector were loaded into the last three lanes of both blots. Results of the first blot that was performed using a primary antibody against Apg8a and is shown in the top panel of FIG. **3** (indicated as Anti-LC3 in FIG. **3**). Bands with sizes matching those of APG8a-I at 16 kDa and Apg8a-II at 14 kDa were observed. No bands were observed in the cell lysates of the empty vector CHO cells.

[0262] Results of the second blot performed using a primary antibody against Apg8a phsophorylated at serine-12 (anti-phospho-Apg8a S12 antibody) are shown in the bottom panel of FIG. **3** (indicated as Anti-phospho-(S12)-LC3 in FIG. **3**). As can be seen, the anti-phospho-Apg8a S12 antibody specifically reacts with the wildtype, but not the Apg8 S12A mutant. This is because bands are only observed in the first six lanes of the lower panel of FIG. **3**. Furthermore, only the Apg8a-I band was observed in this Western blot using the anti-phospho-Apg8a S12 antibody. No bands were observed in the cell lysates of the empty vector CHO cells. The results indicate that the form of Apg8a phosphorylated at serine-12 is Apg8a-I and that the Anti-phospho-(S12)-Apg8a can specifically detect Apg8a-I phosphorylated at serine-12.

Example 6

Production of an APG8a Phosphospecific Monoclonal Antibody

[0263] An APG8a phosphospecific monoclonal antibody will be produced from spleen cells of an immunized BALB/c mouse, following standard procedures (Harlow and Lane, 1988). The mouse spleen cells are fused to SP2/0 mouse myeloma fusion partner cells according to the protocol of Kohler and Milstein (1975). Colonies originating from the fusion are screened by ELISA for reactivity to the phospho-peptide and non-phospho-peptide. Colonies found to be positive by ELISA to the phospho-peptide while negative to the non-phospho-peptide are further characterized by Western blot analysis as described in Example 1. Colonies found to be positive by Western blot analysis are subcloned by limited dilution. 500 mL cultures of selected subclones are produced and purified by Protein G affinity purification. The purified clones are expected to give similar results on Western blot analysis as observed previously with the cell culture supernatant, indicating phospho-specificity of APG8a phospho-specific monoclonal antibody.

Example 7

Production of an APG8c Phosphospecific Monoclonal Antibody

[0264] An APG8c phosphospecific monoclonal antibody is produced from spleen cells of an immunized BALB/c mouse, following standard procedures (Harlow and Lane, 1988). The mouse is fused to SP2/0 mouse myeloma fusion partner cells according to the protocol of Kohler and Milstein (1975). Colonies originating from the fusion are screened by ELISA for reactivity to the phospho-peptide and non-phospho-peptide. Colonies found to be positive by ELISA to the phospho-peptide while negative to the non-phospho-peptide are further characterized by Western blot analysis as described in Example 2. Colonies found to be positive by Western blot analysis are subcloned by limited dilution. 500 mL cultures of selected subclones are produced and purified by Protein G affinity purification. The purified clones are expected to give similar results on Western blot analysis as observed previously with the cell culture supernatant, indicating phospho-specificity of APG8c phospho specific monoclonal antibody.

[0265] The following are further exemplary embodiments:

[0266] 1. An isolated APG8 peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18) wherein X is serine or phosphoserine, and with the proviso that the peptide is not a full-length APG8 protein.

[0267] 2. An isolated APG8 peptide of embodiment 1 wherein the peptide does not comprise a sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, or SEQ ID NO:9.

[0268] 3. The isolated APG8 peptide of embodiment 1, which comprises an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRX-FADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34),

RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPSDRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

[0269] 4. The isolated APG8 peptide of embodiment 1, which comprises an amino acid sequence selected from the group consisting of MPSDRPFKQRRXFADR (SEQ ID NO:61) and MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0270] 5. The isolated APG8 peptide of embodiment 1, wherein X is serine.

[0271] 6. The isolated APG8 peptide of embodiment 1, wherein X is phosphoserine.

[0272] 7. A pharmaceutical composition, which comprises an isolated APG8 peptide of embodiment 1 and a pharmaceutically acceptable carrier and excipient.

[0273] 8. The isolated APG8 peptide of embodiment 1, which is conjugated to a carrier to enhance the peptide's immunogenicity.

[0274] 9. The isolated APG8 peptide of embodiment 8, wherein the carrier is a carrier protein.

[0275] 10. The isolated APG8 peptide of embodiment 9, wherein the APG8 peptide and the carrier protein are parts of a fusion protein.

[0276] 11. An immunogen, which immunogen comprises:

[0277] (a) an isolated APG8 peptide of embodiment 1; and

[0278] (b) an immune response potentiator.

[0279] 12. The immunogen of embodiment 11, wherein the immune response potentiator is selected from the group consisting of Bacille Calmette-Guerin (BCG), *Corynebacterium Parvum, Brucella abortus* extract, glucan, levamisole, tilorone, an enzyme and a non-virulent virus.

[0280] 13. A multiple antigenic peptide (MAP), which MAP comprises a branched oligolysine core conjugated with a plurality of an isolated APG8 peptide of embodiment 1.

[0281] 14. The MAP of embodiment 13, wherein the branched oligolysine core comprises 3, 7 or 15 lysine residues.

[0282] 15. The MAP of embodiment 13, wherein the plurality of the APG8 peptide is conjugated to the branched oligolysine core via a spacer.

[0283] 16. The MAP of embodiment 13, wherein the spacer is one or more amino acid residues.

[0284] 17. The MAP of embodiment 13, which comprises 4, 8 or 16 copies of the APG8 peptide.

[0285] 18. The MAP of embodiment 13, wherein the plurality of the APG8 peptide comprises same or different peptides.

[0286] 19. A method for producing an antibody to an APG8 polypeptide, which method comprises:

[0287] (a) introducing an isolated APG8 peptide of embodiment 1 to a mammal in an amount sufficient to produce an antibody to said APG8 peptide; and

[0288] (b) recovering said antibody from said mammal.

[0289] 20. The method of embodiment 19, wherein the X in the isolated APG8 peptide is serine and the method is used to produce an antibody to a nonphosphorylated APG8 polypeptide.

[0290] 21. The method of embodiment 19, wherein the X in the isolated APG8 peptide is phosphoserine and the method is used to produce an antibody to a phosphorylated APG8 polypeptide.

[0291] 22. The method of embodiment 21, which further comprises a step of removing an antibody that binds to an isolated APG8 peptide of embodiment 1 wherein X is serine.

[0292] 23. The method of embodiment 19, wherein the isolated APG8 peptide is conjugated to a carrier to enhance the peptide's immunogenicity.

[0293] 24. The method of embodiment 19, wherein the isolated APG8 peptide is comprised in an immunogen of embodiment 10 or a MAP of embodiment 12.

[0294] 25. An antibody to an APG8 polypeptide produced by the method of embodiment 19.

[0295] 26. A kit for producing an antibody to an APG8 polypeptide, which kit comprises:

[0296] (a) an isolated APG8 peptide of embodiment 1;

[0297] (b) means for introducing said isolated APG8 peptide to a mammal in an amount sufficient to produce an antibody to said APG8 peptide; and

[0298] (c) means for recovering said antibody from said mammal.

[0299] 27. A method for producing an antibody to an APG8 polypeptide, which method comprises:

[0300] (a) introducing an APG8 polypeptide to a mammal in an amount sufficient to produce an antibody to said APG8 polypeptide;

[0301] (b) recovering said antibody from said mammal; and

[0302] (c) affinity purifying an APG8 antibody that specifically binds to an epitope comprised in an APG8 peptide of embodiment 1 using said APG8 peptide.

[0303] 28. The method of embodiment 27, wherein the APG8 polypeptide comprises a full-length APG8 protein.

[0304] 29. The method of embodiments 27 and 28, wherein the APG8 polypeptide is nonphosphorylated and the method is used to produce an antibody to a nonphosphorylated APG8 polypeptide.

[0305] 30. The method of embodiments 27 and 28, wherein the APG8 polypeptide is an APG8A polypeptide, the X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) of the APG8A polypeptide is phosphoserine, and the method is used to produce an antibody to a phosphorylated APG8A polypeptide.

[0306] 31. The method of embodiments 27 and 28, wherein the APG8 polypeptide is an APG8C polypeptide, the X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) of the APG8C polypeptide is phosphoserine, and the method is used to produce an antibody to a phosphorylated APG8C polypeptide.

[0307] 32. The method of embodiments 30 and 31, which further comprises a step of removing an antibody that binds to an isolated APG8 peptide of embodiment 1 wherein X is serine.

[0308] 33. An antibody to an APG8 polypeptide produced by the method of embodiment 26.

[0309] 34. A kit for producing an antibody to an APG8 polypeptide, which kit comprises:

[0310] (a) an APG8 protein;

[0311] (b) means for introducing said an APG8 protein to a mammal in an amount sufficient to produce an antibody to said APG8 polypeptide;

[0312] (c) means for recovering said antibody from said mammal; and

[0313] (d) an isolated APG8 peptide of embodiment 1.

[0314] 35. An isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0315] 36. The isolated antibody of embodiment 35, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and an amino acid residue of APG8A protein that is outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0316] 37. The isolated antibody of embodiment 35, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and amino acid residues of APG8A protein that are outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0317] 38. The isolated antibody of embodiment 35, wherein the epitope is comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0318] 39. The isolated antibody of embodiment 35, wherein the epitope is comprised of an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPSDRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID

NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

[0319] 40. The isolated antibody of embodiment 35, wherein the epitope is comprised of an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

[0320] 41. The isolated antibody of embodiment 35, which specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0321] 42. The isolated antibody of embodiment 35, which specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0322] 43. The isolated antibody of embodiment 35, which specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0323] 44. The isolated antibody of embodiment 35, which specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0324] 45. The isolated antibody of embodiment 35, wherein the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in an APG8A protein or fragment.

[0325] 46. The isolated antibody of embodiment 45, wherein the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in a full length APG8A protein and the isolated antibody specifically binds to the full length APG8 protein.

[0326] 47. The isolated antibody of embodiment 46, which specifically binds to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0327] 48. The isolated antibody of embodiment 46, which specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0328] 49. The isolated antibody of embodiment 46, which specifically binds to the full length APG8 protein at its natural conformation.

[0329] 50. The isolated antibody of embodiment 35, which is a monoclonal or polyclonal antibody or an antibody fragment.

[0330] 51. A method for detecting an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample, which method comprises:

[0331] (a) contacting a sample containing or suspected of containing an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine; and

[0332] (b) assessing a complex formed between said APG8A protein or fragment, if present in said sample, and said antibody, to determine the presence, absence and/or amount of said APG8A protein or fragment in said sample.

[0333] 52. The method of embodiment 51, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and an amino acid residue of APG8A protein that is outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0334] 53. The method of embodiment 51, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) and amino acid residues of APG8A protein that are outside the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0335] 54. The method of embodiment 51, wherein the epitope is comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0336] 55. An isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0337] 56. The isolated antibody of embodiment 55, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and an amino acid residue of APG8C protein that is outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0338] 57. The isolated antibody of embodiment 55, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and amino acid residues of APG8C protein that are outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0339] 58. The isolated antibody of embodiment 55, wherein the epitope is comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0340] 59. The isolated antibody of embodiment 55, which specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0341] 60. The isolated antibody of embodiment 55, which specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0342] 61. The isolated antibody of embodiment 55, which specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0343] 62. The isolated antibody of embodiment 55, which specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0344] 63. The isolated antibody of embodiment 55, wherein the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in an APG8C protein or fragment.

[0345] 64. The isolated antibody of embodiment 63, wherein the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in a full length APG8C protein and the isolated antibody specifically binds to the full length APG8 protein.

[0346] 65. The isolated antibody of embodiment 64, which specifically binds to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0347] 66. The isolated antibody of embodiment 64, which specifically binds to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0348] 67. A method for detecting an APG8C polypeptide or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample, which method comprises:

[0349] (a) contacting a sample containing or suspected of containing an APG8C polypeptide or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine with an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine; and

[0350] (b) assessing a complex formed between said APG8C polypeptide or fragment, if present in said sample, and said antibody, to determine the presence, absence and/or amount of said APG8A protein or fragment in said sample.

[0351] 68. The method of embodiment 67, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and an amino acid residue of APG8C protein that is outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0352] 69. The method of embodiment 67, wherein the epitope comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) and amino acid residues of APG8A protein that are outside the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0353] 70. The method of embodiment 67, wherein the epitope is comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0354] 71. The method of embodiments 51 and 67, wherein the epitope is comprised in an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID

NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPSDRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

[0355] 72. The method of embodiments 51 and 67, wherein the epitope is comprised in an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

[0356] 73. The method of embodiment 51, wherein the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0357] 74. The method of embodiment 51, wherein the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0358] 75. The method of embodiment 51, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0359] 76. The method of embodiment 51, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0360] 77. The method of embodiment 51, wherein the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in a full length APG8A protein and the isolated antibody specifically binds to the full length APG8A protein.

[0361] 78. The method of embodiment 77, wherein the isolated antibody specifically binds to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) to determine the presence, absence and/or amount of nonphosphorylated full length APG8A protein in the sample.

[0362] 79. The method of embodiment 77, wherein the isolated antibody specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) to determine the presence, absence and/or amount of phosphorylated full length APG8A protein in the sample.

[0363] 80. The method of embodiment 67, wherein the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0364] 81. The method of embodiment 67, wherein the isolated antibody specifically binds to the epitope that com-

prises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0365] 82. The method of embodiment 67, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0366] 83. The method of embodiment 67, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0367] 84. The method of embodiment 67, wherein the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in a full length APG8C protein and the isolated antibody specifically binds to the full length APG8C protein.

[0368] 85. The method of embodiment 84, wherein the isolated antibody specifically binds to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) to determine the presence, absence and/or amount of nonphosphorylated full length APG8C protein in the sample.

[0369] 86. The method of embodiment 84, wherein the isolated antibody specifically binds to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) to determine the presence, absence and/or amount of phosphorylated full length APG8C protein in the sample.

[0370] 87. The method of embodiment 51, wherein the isolated antibody specifically binds to the full length APG8A protein at its natural conformation.

[0371] 88. The method of embodiment 51, wherein the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0372] 89. The method of embodiment 51, wherein the complex is assessed by a sandwich or competitive assay format.

[0373] 90. The method of embodiment 89, wherein the antibody that that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is used as a first antibody and an antibody that is capable of binding to a portion of APG8A protein or fragment other than the portion that binds to the first antibody is used as a second antibody in a sandwich assay format.

[0374] 91. The method of embodiment 89 wherein the antibody that that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is used as a first antibody and an antibody that is capable of binding to a portion of APG8C protein or fragment other than the portion that binds to the first antibody is used as a second antibody in a sandwich assay format.

[0375] 92. The method of embodiments 90 and 91, wherein either the first antibody or the second antibody is attached to a surface and functions as a capture antibody.

[0376] 93. The method of embodiment 92, wherein the capture antibody is attached to the surface directly or indirectly.

[0377] 94. The method of embodiment 92, wherein the capture antibody is attached to the surface via a biotin-avidin (or streptavidin) linking pair.

[0378] 95. The method of embodiments 51 and 67, wherein the complex is assessed by a format selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), immunoblotting, immunoprecipitation, radioimmunoassay (RIA), immuno staining, latex agglutination, indirect hemagglutination assay (IHA), complement fixation, indirect immunofluorescent assay (IFA), nephelometry, flow cytometry assay, plasmon resonance assay, chemiluminescence assay, lateral flow immunoassay, u-capture assay, inhibition assay and avidity assay.

[0379] 96. The method of embodiments 51 and 67, wherein the complex is assessed in a homogeneous or a heterogeneous assay format.

[0380] 97. The method of embodiment 51, which is used to determine the phosphorylation status of an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRSFADR (SEQ ID NO:154).

[0381] 98. The method of embodiment 67, which is used to determine the phosphorylation status of an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0382] 99. The method of embodiment 97, which is used to determine the phosphorylation status of a full length APG8A protein.

[0383] 100. The method of embodiment 99, which is used to determine the phosphorylation status of a full length APG8A protein in a biological sample.

[0384] 101. The method of embodiment 100, wherein the biological sample is a clinical sample.

[0385] 102. The method of embodiment 100, which is used for the prognosis, diagnosis and/or treatment monitoring of a disease or disorder associated with abnormal phosphorylation status of an APG8 protein or fragment comprising amino acid sequence selected from the group of MPSDRPFKQRRSFADR (SEQ ID NO:154) and MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0386] 103. The method of embodiment 102, wherein the APG8A protein is a full length APG8A protein.

[0387] 104. The method of embodiment 102, wherein the disease or disorder associated with abnormal phosphorylation status of an APG8A protein or fragment is selected from the group consisting of ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency

(MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0388] 105. A kit for detecting an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine in a sample, which kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0389] 106. A method for treating a disease or disorder associated with abnormal phosphorylation status of an APG8A protein or fragment comprising amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine or phosphoserine, which method comprises administering, to a subject when such a treatment is needed or desired, a sufficient amount of an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

[0390] 107. The method of embodiment 106, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0391] 108. The method of embodiment 107, wherein the disease or disorder is associated with abnormally high phosphorylation level of an APG8A protein or fragment, and the binding of the antibody to the APG8A protein or fragment prevents or reduces phosphorylation level of the APG8A protein or fragment.

[0392] 109. The method of embodiment 107, wherein the disease or disorder is associated with abnormally high phosphorylation level of an APG8A protein or fragment, and the binding of the antibody to the APG8A protein or fragment inhibits phosphorylation level of the APG8A protein or fragment.

[0393] 110. The method of embodiment 106, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0394] 111. The method of embodiment 110, wherein the disease or disorder is associated with abnormally low phosphorylation level of an APG8A protein or fragment, and the binding of the antibody to the APG8A protein or fragment prevents or reduces dephosphorylation of the APG8A protein or fragment.

[0395] 112. The method of embodiments 108, 110, and 111, wherein the disease or disorder associated with abnormally low phosphorylation level of an APG8A protein or fragment is selected from the group consisting of ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0396] 113. The method of embodiment 106, wherein the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) is comprised in a full length APG8A protein and the isolated antibody specifically binds to the full length APG8A protein.

[0397] 114. The method of embodiment 113, wherein the isolated antibody specifically binds to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0398] 115. The method of embodiment 113, wherein the isolated antibody specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0399] 116. A kit for detecting an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine in a sample, which kit comprises, in a container, an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0400] 117. A method for treating a disease or disorder associated with abnormal phosphorylation status of an APG8C protein or fragment comprising amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine or phosphoserine, which method comprises administering, to a subject when such a treatment is needed or desired, a sufficient amount of an isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

[0401] 118. The method of embodiment 117, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0402] 119. The method of embodiment 118, wherein the disease or disorder is associated with abnormally high phosphorylation level of an APG8C protein or fragment, and the binding of the antibody to the APG8C protein or fragment prevents or reduces phosphorylation level of the APG8C protein or fragment.

[0403] 120. The method of embodiment 118, wherein the disease or disorder is associated with abnormally high phosphorylation level of an APG8C protein or fragment, and the

binding of the antibody to the APG8C protein or fragment inhibits phosphorylation level of the APG8C protein or fragment.

[0404] 121. The method of embodiment 117, wherein the isolated antibody specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0405] 122. The method of embodiment 121, wherein the disease or disorder is associated with abnormally low phosphorylation level of an APG8C protein or fragment, and the binding of the antibody to the APG8C protein or fragment prevents or reduces dephosphorylation of the APG8C protein or fragment.

[0406] 123. The method of embodiments 119, 121, and 122, wherein the disease or disorder associated with abnormally low phosphorylation level of an APG8C protein or fragment is selected from the group consisting of ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0407] 124. The method of embodiment 117, wherein the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) is comprised in a full length APG8C protein and the isolated antibody specifically binds to the full length APG8C protein.

[0408] 125. The method of embodiment 124, wherein the isolated antibody specifically binds to the full length APG8C protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8C protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0409] 126. The method of embodiment 124, wherein the isolated antibody specifically binds to the full length APG8A protein when X is phosphoserine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) but does not specifically bind to the full length APG8A protein when X is serine in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0410] 127. The method of embodiment 106, wherein the isolated antibody specifically binds to the full length APG8A protein at its natural conformation.

[0411] 128. The method of embodiment 106, wherein the isolated antibody is a monoclonal or polyclonal antibody or antibody fragment.

[0412] 129. The method of embodiment 106, which further comprises administering a pharmaceutically acceptable carrier and excipient.

[0413] 130. The method of embodiment 106, wherein the subject is a mammal.

[0414] 131. The method of embodiment 130, wherein the mammal is a human.

[0415] 132. A pharmaceutical composition, which comprises an isolated antibody of embodiment 106 and a pharmaceutically acceptable carrier and excipient.

[0416] 133. A method for identifying a kinase that phosphorylates an APG8A protein on the serine-12 residue, which method comprises:

[0417] (a) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine;

[0418] (b) contacting said APG8A polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of said serine residue of said APG8A polypeptide; and

[0419] (c) assessing phosphorylation status of said APG8A polypeptide to determine whether said test protein is a kinase for said APG8A protein on the serine-12 residue.

[0420] 134. The method of embodiment 133, wherein the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine.

[0421] 135. The method of embodiment 133, wherein the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0422] 136. A method for identifying a modulator of a kinase that phosphorylates an APG8A protein on the serine-12 residue, which method comprises:

[0423] (a) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine;

[0424] (b) contacting said APG8A polypeptide with a kinase that phosphorylates an APG8A protein on the serine-12 residue and ATP under conditions suitable for the phosphorylation of said serine residue of said APG8A polypeptide in the presence or absence of a test substance; and

[0425] (c) assessing and comparing phosphorylation status of said APG8A polypeptide by said kinase to determine whether said test substance modulates said kinase.

[0426] 137. The method of embodiment 136, wherein the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is serine.

[0427] 138. The method of embodiment 136, wherein the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine.

[0428] 139. A method for identifying a kinase that phosphorylates an APG8C polypeptide on the serine-12 residue, which method comprises:

[0429] (a) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine;

[0430] (b) contacting said APG8C polypeptide with a test protein and ATP under conditions suitable for the phosphorylation of said serine residue of said APG8A polypeptide; and

[0431] (c) assessing phosphorylation status of said APG8C polypeptide to determine whether said test protein is a kinase for said APG8C protein on the serine-12 residue.

[0432] 140. The method of embodiment 139, wherein the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine.

[0433] 141. The method of embodiment 139, wherein the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0434] 142. A method for identifying a modulator of a kinase that phosphorylates an APG8C protein on the serine-9 residue, which method comprises:

[0435] (a) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine;

[0436] (b) contacting said APG8C polypeptide with a kinase that phosphorylates an APG8C protein on the serine-9 residue and ATP under conditions suitable for the phosphorylation of said serine residue of said APG8C polypeptide in the presence or absence of a test substance; and

[0437] (c) assessing and comparing phosphorylation status of said APG8C polypeptide by said kinase to determine whether said test substance modulates said kinase.

[0438] 143. The method of embodiment 142, wherein the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is serine.

[0439] 144. The method of embodiment 142, wherein the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

[0440] 145. A method for identifying a phosphatase that dephosphorylates an APG8A protein on the serine-12 residue, which method comprises:

[0441] (a) providing an APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0442] (b) contacting said APG8A polypeptide with a test protein and H_2O under conditions suitable for the dephosphorylation of said phosphoserine residue of said APG8A polypeptide; and

[0443] (c) assessing phosphorylation status of said APG8A polypeptide to determine whether said test protein is a phosphatase for said APG8A protein on the phosphoserine-12 residue.

[0444] 146. The method of embodiment 145, wherein the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is phosphoserine.

[0445] 147. The method of embodiment 146, wherein the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0446] 148. A method for identifying a phosphatase that dephosphorylates an APG8C protein on the serine-9 residue, which method comprises:

[0447] (a) providing an APG8C polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0448] (b) contacting said APG8C polypeptide with a test protein and H_2O under conditions suitable for the dephosphorylation of said phosphoserine residue of said APG8A polypeptide; and

[0449] (c) assessing phosphorylation status of said APG8C polypeptide to determine whether said test protein is a phosphatase for said APG8C protein on the phosphoserine-12 residue.

[0450] 149. The method of embodiment 148, wherein the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is phosphoserine.

[0451] 150. The method of embodiment 149, wherein the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0452] 151. A method for identifying a modulator of a phosphatase that dephosphorylates an APG8A protein on the serine-12 residue, which method comprises:

[0453] (a) providing APG8A polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0454] (b) contacting said APG8A polypeptide with a phosphatase that dephosphorylates an APG8A protein on the serine-12 residue and H_2O under conditions suitable for the

dephosphorylation of said phosphoserine residue of said APG8A polypeptide in the presence or absence of a test substance; and

[0455] (c) assessing and comparing dephosphorylation status of said APG8A polypeptide by said phosphatase to determine whether said test substance modulates said phosphatase.

[0456] 152. The method of embodiment 151, wherein the APG8A protein or fragment comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61) wherein X is phosphoserine.

[0457] 153. The method of embodiment 152, wherein the phosphorylation status of the APG8A polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is phosphoserine.

[0458] 154. An isolated nucleic acid fragment, which isolated nucleic acid fragment comprises a sequence of nucleotides encoding an APG8A peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine, and with the proviso that the peptide is not a full-length APG8A protein comprising an amino acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or SEQ ID NO:7.

[0459] 155. The isolated nucleic acid fragment of embodiment 154, wherein the APG8A peptide comprises an amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61).

[0460] 156. A method for identifying a modulator of a phosphatase that dephosphorylates an APG8C protein on the serine-9 residue, which method comprises:

[0461] (a) providing APG8C polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0462] (b) contacting said APG8C polypeptide with a phosphatase that dephosphorylates an APG8C protein on the serine-9 residue and H_2O under conditions suitable for the dephosphorylation of said phosphoserine residue of said APG8C polypeptide in the presence or absence of a test substance; and

[0463] (c) assessing and comparing dephosphorylation status of said APG8C polypeptide by said phosphatase to determine whether said test substance modulates said phosphatase.

[0464] 157. The method of embodiment 156, wherein the APG8C protein or fragment comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153) wherein X is phosphoserine.

[0465] 158. The method of embodiment 157, wherein the phosphorylation status of the APG8C polypeptide is assessed by an isolated antibody that specifically binds to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine, but does not specifically bind to an epitope comprised in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

[0466] 159. An isolated nucleic acid fragment, which isolated nucleic acid fragment comprises a sequence of nucleotides encoding an APG8C peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine, and with the proviso that the peptide is not a full-length APG8C protein comprising an amino acid sequence set forth in SEQ ID NO:8 or SEQ ID NO:9.

[0467] 160. The isolated nucleic acid fragment of embodiment 159, wherein the APG8C peptide comprises an amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

[0468] 161. The isolated nucleic acid fragment of embodiment 154, wherein the nucleic acid is DNA.

[0469] 162. The isolated nucleic acid fragment of embodiment 154, wherein the nucleic acid is RNA.

[0470] 163. A plasmid, which plasmid comprises the nucleic acid fragment of embodiment 154.

[0471] 164. A vector, which vector comprises the nucleic acid fragment of embodiment 154.

[0472] 165. A cell, which cell comprises the plasmid of embodiment 163 or the vector of embodiment 164.

[0473] 166. The cell of embodiment 165, which is selected from the group consisting of a bacterial cell, a yeast cell, a fungal cell, a plant cell, an insect cell, an animal cell and a human cell.

[0474] 167. A method for producing an APG8 peptide, which method comprises growing the cell of embodiment 165 under conditions whereby said APG8 peptide is expressed by the cell, and recovering said expressed APG8A peptide.

[0475] 168. The method of embodiment 167, further comprises a step of phosphorylating the APG8A peptide at the serine-12 residue.

[0476] 169. A method for identifying a compound that binds to specifically to a phosphorylated APG8 polypeptide, which method comprises:

[0477] a) providing a phosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0478] b) contacting said phosphorylated APG8 polypeptide with a test compound under conditions suitable for binding of the test protein with APG8 polypeptide;

[0479] c) assessing binding of the phosphorylated APG8 polypeptide with the test compound;

[0480] d) providing a nonphosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0481] e) contacting said nonphosphorylated APG8 polypeptide with the test compound under conditions suitable for binding of the test protein with APG8 polypeptide;

[0482] f) assessing binding of the nonphosphorylated APG8 polypeptide with the test compound

[0483] wherein the compound that binds specifically to a phosphorylated APG8 polypeptide is a test compound which binds to phosphorylated APG8 polypeptide according to step c) but does not bind to nonphosphorylated APG8 polypeptide according to step e).

[0484] 170. A method for identifying a compound that binds to specifically to a nonphosphorylated APG8 polypeptide, which method comprises:

[0485] a) providing a nonphosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is serine;

[0486] b) contacting said nonphosphorylated APG8 polypeptide with a test compound under conditions suitable for binding of the test protein with APG8 polypeptide;

[0487] c) assessing binding of the nonphosphorylated APG8 polypeptide with the test compound;

[0488] d) providing a phosphorylated APG8 polypeptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18), wherein X is phosphoserine;

[0489] e) contacting said phosphorylated APG8 polypeptide with the test compound conditions suitable for binding of the test protein with APG8 polypeptide;

[0490] f) assessing binding of the phosphorylated APG8 polypeptide with the test compound

[0491] wherein the compound that binds specifically to a nonphosphorylated APG8 polypeptide is a test compound which binds to nonphosphorylated APG8 polypeptide according to step c) but does not bind to phosphorylated APG8 polypeptide according to step e).

[0492] 171. The methods of embodiments 169 and 170, wherein the test compound is a protein.

[0493] 172. The methods of embodiments 169 and 170, wherein the test compound is a peptide.

[0494] 173. The methods of embodiments 169 and 170, wherein the test compound is a nucleic acid.

[0495] 174. The methods of embodiments 169 and 170, wherein the test compound is a small molecule.

[0496] 175. A method of treating a disease comprising modulating phosphorylation status of an APG8 polypeptide by administering an APG8 antibody, an APG8 peptide, or compounds from the screening process of embodiments 133-158, wherein the disease is selected from the group consisting of ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0497] 176. The method of embodiment 175, wherein said modulation of phosphorylation status involves inducing phosphorylation of

[0498] 177. A array comprising an antibody of embodiments 25, 33, 35-50, and 55-66.

[0499] 178. A method of array detection comprising use of an antibody of embodiments 25, 33, 35-50, and 55-66.

[0500] 179. A microarray comprising a solid support and a plurality of antibodies of embodiments 25, 33, 35-50, and 55-66 immobilized on the solid support at a known predetermined position.

[0501] 180. A microarray comprising a solid support and a plurality of polypeptides of embodiments 1-11.

[0502] 181. The use of a microarray of embodiments 179 and 180 for assessing the phosphorylation status of APG8a or APG8c in the autophagy pathway.

[0503] 182. A method of monitoring the phosphorylation of APG8a or APG8c, wherein the monitoring uses a microarray of embodiments 179 and 180.

[0504] 183. A method of treating a disease comprising modulating the phosphorylation of APG8a at serine-12 or APG8c at serine-9.

[0505] 184. The method of embodiment 183, wherein the disease is selected from the group consisting of ischemic brain injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, prion diseases and polyglutamine disorders including Huntington's disease and various spinocerebellar ataxias, transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease, breast cancer, ovarian cancer, brain cancer, pancreatic cancer, esophageal cancer, colorectal cancer, liver cancer, prostate cancer, renal cancer, lung cancer, Myocardial ischemia, cardiac remodeling, cardiomyopathy, hemodynamic stress, myocardial hypertrophy, Neuronal ceroid-lipofuscinosis (adult and juvenile), Multiple Sulfatase Deficiency (MSD) and Mucopolysaccharidosis type IIIA, Batten disease, Niemann-Pick C, Danon disease, Pompe disease, and dysfunction of innate and adaptive immunity against intracellular pathogens.

[0506] 185. The method of embodiments 183 and 184, wherein phosphorylation of APG8a polypeptide is increased.

[0507] 186. The method of embodiments 183 and 184, wherein phosphorylation of the APG8a polypeptide is decreased.

[0508] 187. The method of embodiments 183, 185, and 186, wherein the phosphorylation status of the APG8a polypeptide is abnormal.

[0509] 188. The method of embodiments 183, 185, and 186, wherein the phosphorylation status of the APG8a polypeptide is normal and wherein the disease is treatable by modulating the phosphorylation status of APG8a.

[0510] 189. The method of embodiments 183 and 184, wherein phosphorylation of the APG8c polypeptide is increased.

[0511] 190. The method of embodiments 183 and 184, wherein phosphorylation of the APG8c polypeptide is decreased.

[0512] 191. The method of embodiments 183, 185, and 186, wherein the phosphorylation status of the APG8c polypeptide is abnormal.

[0513] 192. The method of embodiments 183, 185, and 186, wherein the phosphorylation status of the APG8c polypeptide is normal and wherein the disease is treatable by modulating the phosphorylation status of APG8c.

TABLE 1

Full-length sequences of APG8A and APG8C proteins.

SEQ ID NO: and Name	Sequence
1 (Human APG8A protein NP_115903)	Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Phe
2 (Bovine APG8A protein NCBI AAI13349)	Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Glu Gln His Pro Ser Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Phe
3 (Zebrafish APG8A protein NCBI AAH67189)	Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Glu Gln His Pro Asn Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ser Glu Ile Tyr Glu Gln Glu Arg Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Cys
4 (*Xenopus laevis* APG8A protein)	Met Pro Ser Glu Arg Pro Phe Lys His Arg Arg Ser Phe Ala Glu Arg Cys Ala Glu Val Arg Gln Ile Arg Glu Gln His Pro Asn Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Leu Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly His
5 (Mouse APG8A protein)	Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Phe
6 (Pan troglodytes APG8A protein)	Met Pro Ser Asp Arg Thr Phe Gln Gln Arg Arg Ser Phe Ser Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Phe

TABLE 1-continued

Full-length sequences of APG8A and APG8C proteins.

SEQ ID NO: and Name	Sequence
7 (*Rattus norvegicus* APG8A protein)	Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val Tyr Ala Ser Gln Glu Thr Phe Gly Phe
8 (Human APG8C protein)	Met Pro Pro Pro Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala Ile Arg Gln Glu Glu Val Ala Gly Ile Arg Ala Lys Phe Pro Asn Lys Ile Pro Val Val Val Glu Arg Tyr Pro Arg Glu Thr Phe Leu Pro Pro Leu Asp Lys Thr Lys Phe Leu Val Pro Gln Glu Leu Thr Met Thr Gln Phe Leu Ser Ile Ile Arg Ser Arg Met Val Leu Arg Ala Thr Glu Ala Phe Tyr Leu Leu Val Asn Asn Lys Ser Leu Val Ser Met Ser Ala Thr Met Ala Glu Ile Tyr Arg Asp Tyr Lys Asp Glu Asp Gly Phe Val Tyr Met Thr Tyr Ala Ser Gln Glu Thr Phe Gly Cys Leu Glu Ser Ala Ala Pro Arg Asp Gly Ser Ser Leu Glu Asp Arg Pro Cys Asn Pro Leu
9 (Pan troglodytes APG8C protein)	Met Pro Pro Pro Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala Ile Arg Gln Glu Glu Val Ala Gly Ile Arg Ala Lys Phe Pro Asn Lys Ile Pro Val Ile Val Glu Arg Tyr Pro Arg Glu Thr Phe Leu Pro Leu Leu Asp Lys Thr Lys Phe Leu Val Pro Gln Glu Leu Thr Met Thr Gln Phe Leu Ser Ile Ile Arg Ser Arg Met Val Leu Arg Ala Thr Glu Ala Phe Tyr Leu Leu Val Asn Asn Lys Ser Leu Val Ser Met Ser Ala Thr Met Ala Glu Ile Tyr Arg Asp Tyr Lys Asp Glu Asp Gly Phe Val Tyr Met Thr Tyr Ala Ser Gln Glu Thr Phe Gly Cys Leu Glu Ser Ala Ala Pro Arg Asp Gly Ser Ser Leu Glu Asp Arg Pro Cys Asn Pro Leu

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SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 159

<210> SEQ ID NO 1
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Human APG8A protein NP_115903

<400> SEQUENCE: 1

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1               5                   10                  15

Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro
            20                  25                  30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35                  40                  45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50                  55                  60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65                  70                  75                  80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala
                85                  90                  95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100                 105                 110

Tyr Ala Ser Gln Glu Thr Phe Gly Phe
        115                 120
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<212> TYPE: PRT
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Bovine APG8A protein NCBI AAI13349

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1 5 10 15

Cys Lys Glu Val Gln Gln Ile Arg Glu Gln His Pro Ser Lys Ile Pro
            20 25 30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35 40 45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50 55 60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65 70 75 80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala
                85 90 95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100 105 110

Tyr Ala Ser Gln Glu Thr Phe Gly Phe
        115 120

<210> SEQ ID NO 3
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Zebrafish APG8A protein NCBI AAH67189

<400> SEQUENCE: 3

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
1 5 10 15

Cys Lys Glu Val Gln Gln Ile Arg Glu Gln His Pro Asn Lys Ile Pro
            20 25 30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35 40 45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50 55 60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65 70 75 80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ser
                85 90 95

Glu Ile Tyr Glu Gln Glu Arg Asp Glu Asp Gly Phe Leu Tyr Met Val
            100 105 110

Tyr Ala Ser Gln Glu Thr Phe Gly Cys
        115 120

<210> SEQ ID NO 4
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Xenopus laevis APG8A protein

<400> SEQUENCE: 4

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1               5                   10                  15

Cys Ala Glu Val Arg Gln Ile Arg Glu Gln His Pro Asn Lys Ile Pro
            20                  25                  30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35                  40                  45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50                  55                  60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65                  70                  75                  80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Leu
                85                  90                  95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100                 105                 110

Tyr Ala Ser Gln Glu Thr Phe Gly His
        115                 120


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<223> OTHER INFORMATION: Mouse APG8A protein

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Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
1               5                   10                  15

Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro
            20                  25                  30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35                  40                  45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50                  55                  60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65                  70                  75                  80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala
                85                  90                  95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100                 105                 110

Tyr Ala Ser Gln Glu Thr Phe Gly Phe
        115                 120


<210> SEQ ID NO 6
<211> LENGTH: 121
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<223> OTHER INFORMATION: Pan troglodytes APG8A protein

<400> SEQUENCE: 6

Met Pro Ser Asp Arg Thr Phe Gln Gln Arg Arg Ser Phe Ser Asp Arg
1               5                   10                  15

Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro
            20                  25                  30
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Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35                  40                  45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50                  55                  60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65                  70                  75                  80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala
                85                  90                  95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100                 105                 110

Tyr Ala Ser Gln Glu Thr Phe Gly Phe
        115                 120


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<400> SEQUENCE: 7

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
1               5                   10                  15

Cys Lys Glu Val Gln Gln Ile Arg Asp Gln His Pro Ser Lys Ile Pro
            20                  25                  30

Val Ile Ile Glu Arg Tyr Lys Gly Glu Lys Gln Leu Pro Val Leu Asp
        35                  40                  45

Lys Thr Lys Phe Leu Val Pro Asp His Val Asn Met Ser Glu Leu Val
    50                  55                  60

Lys Ile Ile Arg Arg Arg Leu Gln Leu Asn Pro Thr Gln Ala Phe Phe
65                  70                  75                  80

Leu Leu Val Asn Gln His Ser Met Val Ser Val Ser Thr Pro Ile Ala
                85                  90                  95

Asp Ile Tyr Glu Gln Glu Lys Asp Glu Asp Gly Phe Leu Tyr Met Val
            100                 105                 110

Tyr Ala Ser Gln Glu Thr Phe Gly Phe
        115                 120


<210> SEQ ID NO 8
<211> LENGTH: 147
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Human APG8C protein

<400> SEQUENCE: 8

Met Pro Pro Pro Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg
1               5                   10                  15

Lys Ser Leu Ala Ile Arg Gln Glu Glu Val Ala Gly Ile Arg Ala Lys
            20                  25                  30

Phe Pro Asn Lys Ile Pro Val Val Val Glu Arg Tyr Pro Arg Glu Thr
        35                  40                  45

Phe Leu Pro Pro Leu Asp Lys Thr Lys Phe Leu Val Pro Gln Glu Leu
    50                  55                  60
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Thr Met Thr Gln Phe Leu Ser Ile Ile Arg Ser Arg Met Val Leu Arg
65                  70                  75                  80

Ala Thr Glu Ala Phe Tyr Leu Leu Val Asn Asn Lys Ser Leu Val Ser
                85                  90                  95

Met Ser Ala Thr Met Ala Glu Ile Tyr Arg Asp Tyr Lys Asp Glu Asp
            100                 105                 110

Gly Phe Val Tyr Met Thr Tyr Ala Ser Gln Glu Thr Phe Gly Cys Leu
        115                 120                 125

Glu Ser Ala Ala Pro Arg Asp Gly Ser Ser Leu Glu Asp Arg Pro Cys
    130                 135                 140

Asn Pro Leu
145
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<210> SEQ ID NO 9
<211> LENGTH: 147
<212> TYPE: PRT
<213> ORGANISM: Pan troglodytes
<220> FEATURE:
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<223> OTHER INFORMATION: Pan troglodytes APG8C protein

<400> SEQUENCE: 9

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Met Pro Pro Pro Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg
1               5                   10                  15

Lys Ser Leu Ala Ile Arg Gln Glu Glu Val Ala Gly Ile Arg Ala Lys
            20                  25                  30

Phe Pro Asn Lys Ile Pro Val Ile Val Glu Arg Tyr Pro Arg Glu Thr
        35                  40                  45

Phe Leu Pro Leu Leu Asp Lys Thr Lys Phe Leu Val Pro Gln Glu Leu
    50                  55                  60

Thr Met Thr Gln Phe Leu Ser Ile Ile Arg Ser Arg Met Val Leu Arg
65                  70                  75                  80

Ala Thr Glu Ala Phe Tyr Leu Leu Val Asn Asn Lys Ser Leu Val Ser
                85                  90                  95

Met Ser Ala Thr Met Ala Glu Ile Tyr Arg Asp Tyr Lys Asp Glu Asp
            100                 105                 110

Gly Phe Val Tyr Met Thr Tyr Ala Ser Gln Glu Thr Phe Gly Cys Leu
        115                 120                 125

Glu Ser Ala Ala Pro Arg Asp Gly Ser Ser Leu Glu Asp Arg Pro Cys
    130                 135                 140

Asn Pro Leu
145
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<210> SEQ ID NO 10
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<223> OTHER INFORMATION: Synthetic peptide

<400> SEQUENCE: 10

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Lys Phe Glu Arg Gln
1               5
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<213> ORGANISM: Artificial Sequence
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<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 11

Gln Arg Arg Xaa
1

<210> SEQ ID NO 12
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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 12

Arg Arg Xaa Phe
1

<210> SEQ ID NO 13
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 13

Arg Xaa Phe Ala
1

<210> SEQ ID NO 14
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
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<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 14

Xaa Phe Ala Asp
1

<210> SEQ ID NO 15
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

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<400> SEQUENCE: 15

Lys Ile Pro Xaa
1

<210> SEQ ID NO 16
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<223> OTHER INFORMATION: Synthetic peptide
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<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 16

Ile Pro Xaa Val
1

<210> SEQ ID NO 17
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<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 17

Pro Xaa Val Arg
1

<210> SEQ ID NO 18
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<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 18

Xaa Val Arg Pro
1

<210> SEQ ID NO 19
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 19

Lys Gln Arg Arg Xaa
1   5

<210> SEQ ID NO 20
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 20

Gln Arg Arg Xaa Phe
1 5

<210> SEQ ID NO 21
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 21

Arg Arg Xaa Phe Ala
1 5

<210> SEQ ID NO 22
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 22

Arg Xaa Phe Ala Asp
1 5

<210> SEQ ID NO 23
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 23

Xaa Phe Ala Asp Arg
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<210> SEQ ID NO 24
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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
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<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

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<400> SEQUENCE: 24

Phe Lys Gln Arg Arg Xaa
1 5

<210> SEQ ID NO 25
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<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 25

Lys Gln Arg Arg Xaa Phe
1 5

<210> SEQ ID NO 26
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 26

Gln Arg Arg Xaa Phe Ala
1 5

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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 27

Arg Arg Xaa Phe Ala Asp
1 5

<210> SEQ ID NO 28
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<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 28

Arg Xaa Phe Ala Asp Arg
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<210> SEQ ID NO 29

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<211> LENGTH: 7
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<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 29

Pro Phe Lys Gln Arg Arg Xaa
1 5

<210> SEQ ID NO 30
<211> LENGTH: 7
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 30

Phe Lys Gln Arg Arg Xaa Phe
1 5

<210> SEQ ID NO 31
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<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 31

Lys Gln Arg Arg Xaa Phe Ala
1 5

<210> SEQ ID NO 32
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<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 32

Gln Arg Arg Xaa Phe Ala Asp
1 5

<210> SEQ ID NO 33
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 33

Arg Arg Xaa Phe Ala Asp Arg
1 5

<210> SEQ ID NO 34
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<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 34

Arg Pro Phe Lys Gln Arg Arg Xaa
1 5

<210> SEQ ID NO 35
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 35

Pro Phe Lys Gln Arg Arg Xaa Phe
1 5

<210> SEQ ID NO 36
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<212> TYPE: PRT
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<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 36

Phe Lys Gln Arg Arg Xaa Phe Ala
1 5

<210> SEQ ID NO 37
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 37

Lys Gln Arg Arg Xaa Phe Ala Asp
1 5

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<210> SEQ ID NO 38
<211> LENGTH: 8
<212> TYPE: PRT
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<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 38

Gln Arg Arg Xaa Phe Ala Asp Arg
1 5

<210> SEQ ID NO 39
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<223> OTHER INFORMATION: Synthetic peptide
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<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 39

Arg Pro Phe Lys Gln Arg Arg Xaa Phe
1 5

<210> SEQ ID NO 40
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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 40

Pro Phe Lys Gln Arg Arg Xaa Phe Ala
1 5

<210> SEQ ID NO 41
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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 41

Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5

<210> SEQ ID NO 42
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<212> TYPE: PRT
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<220> FEATURE:
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<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 42

Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5

<210> SEQ ID NO 43
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 43

Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa
1 5 10

<210> SEQ ID NO 44
<211> LENGTH: 10
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 44

Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala
1 5 10

<210> SEQ ID NO 45
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 45

Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5 10

<210> SEQ ID NO 46
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 46

Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10

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<210> SEQ ID NO 47
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 47

Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5 10

<210> SEQ ID NO 48
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 48

Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10

<210> SEQ ID NO 49
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 49

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa
1 5 10

<210> SEQ ID NO 50
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 50

Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe
1 5 10

<210> SEQ ID NO 51
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 51

Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala
1 5 10

<210> SEQ ID NO 52
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 52

Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10

<210> SEQ ID NO 53
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 53

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe
1 5 10

<210> SEQ ID NO 54
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 54

Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala
1 5 10

<210> SEQ ID NO 55
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 55

Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5 10

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<210> SEQ ID NO 56
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 56

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala
1 5 10

<210> SEQ ID NO 57
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 57

Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5 10

<210> SEQ ID NO 58
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 58

Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10

<210> SEQ ID NO 59
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 59

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp
1 5 10 15

<210> SEQ ID NO 60
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 60

Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10 15

<210> SEQ ID NO 61
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 61

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Xaa Phe Ala Asp Arg
1 5 10 15

<210> SEQ ID NO 62
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 62

Gln Lys Ile Pro Xaa
1 5

<210> SEQ ID NO 63
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 63

Lys Ile Pro Xaa Val
1 5

<210> SEQ ID NO 64
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 64

Ile Pro Xaa Val Arg

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1 5

<210> SEQ ID NO 65
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 65

Pro Xaa Val Arg Pro
1 5

<210> SEQ ID NO 66
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 66

Xaa Val Arg Pro Phe
1 5

<210> SEQ ID NO 67
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 67

Pro Gln Lys Ile Pro Xaa
1 5

<210> SEQ ID NO 68
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 68

Gln Lys Ile Pro Xaa Val
1 5

<210> SEQ ID NO 69
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 69

Lys Ile Pro Xaa Val Arg
1 5

<210> SEQ ID NO 70
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 70

Ile Pro Xaa Val Arg Pro
1 5

<210> SEQ ID NO 71
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 71

Pro Xaa Val Arg Pro Phe
1 5

<210> SEQ ID NO 72
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 72

Xaa Val Arg Pro Phe Lys
1 5

<210> SEQ ID NO 73
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 73

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Ile Pro Gln Lys Ile Pro Xaa
1 5

<210> SEQ ID NO 74
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 74

Pro Gln Lys Ile Pro Xaa Val
1 5

<210> SEQ ID NO 75
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 75

Gln Lys Ile Pro Xaa Val Arg
1 5

<210> SEQ ID NO 76
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 76

Lys Ile Pro Xaa Val Arg Pro
1 5

<210> SEQ ID NO 77
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 77

Ile Pro Xaa Val Arg Pro Phe
1 5

<210> SEQ ID NO 78
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 78

Pro Xaa Val Arg Pro Phe Lys
1 5

<210> SEQ ID NO 79
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 79

Xaa Val Arg Pro Phe Lys Gln
1 5

<210> SEQ ID NO 80
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 80

Lys Ile Pro Gln Lys Ile Pro Xaa
1 5

<210> SEQ ID NO 81
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 81

Ile Pro Gln Lys Ile Pro Xaa Val
1 5

<210> SEQ ID NO 82
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 82

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Pro Gln Lys Ile Pro Xaa Val Arg
1 5

<210> SEQ ID NO 83
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 83

Gln Lys Ile Pro Xaa Val Arg Pro
1 5

<210> SEQ ID NO 84
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 84

Lys Ile Pro Xaa Val Arg Pro Phe
1 5

<210> SEQ ID NO 85
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 85

Ile Pro Xaa Val Arg Pro Phe Lys
1 5

<210> SEQ ID NO 86
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 86

Pro Xaa Val Arg Pro Phe Lys Gln
1 5

<210> SEQ ID NO 87
<211> LENGTH: 9
<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 87

Gln Lys Ile Pro Gln Lys Ile Pro Xaa
1 5

<210> SEQ ID NO 88
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 88

Lys Ile Pro Gln Lys Ile Pro Xaa Val
1 5

<210> SEQ ID NO 89
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 89

Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5

<210> SEQ ID NO 90
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 90

Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5

<210> SEQ ID NO 91
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

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<400> SEQUENCE: 91

Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5

<210> SEQ ID NO 92
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 92

Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5

<210> SEQ ID NO 93
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 93

Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5

<210> SEQ ID NO 94
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 94

Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5

<210> SEQ ID NO 95
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 95

Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa
1 5 10

<210> SEQ ID NO 96
<211> LENGTH: 10

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 96

Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val
1 5 10

<210> SEQ ID NO 97
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 97

Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5 10

<210> SEQ ID NO 98
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 98

Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5 10

<210> SEQ ID NO 99
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 99

Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5 10

<210> SEQ ID NO 100
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

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<400> SEQUENCE: 100

Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5 10

<210> SEQ ID NO 101
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 101

Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5 10

<210> SEQ ID NO 102
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 102

Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10

<210> SEQ ID NO 103
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 103

Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys
1 5 10

<210> SEQ ID NO 104
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 104

Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser
1 5 10

<210> SEQ ID NO 105

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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 105

Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa
1 5 10

<210> SEQ ID NO 106
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 106

Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val
1 5 10

<210> SEQ ID NO 107
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 107

Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5 10

<210> SEQ ID NO 108
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 108

Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5 10

<210> SEQ ID NO 109
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)

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<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 109

Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5 10

<210> SEQ ID NO 110
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 110

Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5 10

<210> SEQ ID NO 111
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 111

Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5 10

<210> SEQ ID NO 112
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 112

Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10

<210> SEQ ID NO 113
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 113

Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys
1 5 10

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<210> SEQ ID NO 114
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 114

Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser
1 5 10

<210> SEQ ID NO 115
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 115

Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu
1 5 10

<210> SEQ ID NO 116
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 116

Pro Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa
1 5 10

<210> SEQ ID NO 117
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 117

Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val
1 5 10

<210> SEQ ID NO 118
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature

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<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 118

Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5 10

<210> SEQ ID NO 119
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 119

Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5 10

<210> SEQ ID NO 120
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 120

Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5 10

<210> SEQ ID NO 121
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 121

Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5 10

<210> SEQ ID NO 122
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 122

Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5 10

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<210> SEQ ID NO 123
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 123

Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10

<210> SEQ ID NO 124
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 124

Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys
1 5 10

<210> SEQ ID NO 125
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 125

Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser
1 5 10

<210> SEQ ID NO 126
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 126

Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu
1 5 10

<210> SEQ ID NO 127
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 127

Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala
1 5 10

<210> SEQ ID NO 128
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 128

Met Pro Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa
1 5 10

<210> SEQ ID NO 129
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 129

Pro Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val
1 5 10

<210> SEQ ID NO 130
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 130

Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5 10

<210> SEQ ID NO 131
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 131

Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5 10

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<210> SEQ ID NO 132
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 132

Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5 10

<210> SEQ ID NO 133
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 133

Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5 10

<210> SEQ ID NO 134
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 134

Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5 10

<210> SEQ ID NO 135
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 135

Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10

<210> SEQ ID NO 136
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 136

Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys
1 5 10

<210> SEQ ID NO 137
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 137

Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser
1 5 10

<210> SEQ ID NO 138
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 138

Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu
1 5 10

<210> SEQ ID NO 139
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 139

Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala
1 5 10

<210> SEQ ID NO 140
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 140

Xaa Val Arg Pro Phe Lys Gln Arg Ser Lys Leu Ala Ile

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1 5 10

<210> SEQ ID NO 141
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 141

Met Pro Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg
1 5 10 15

<210> SEQ ID NO 142
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 142

Pro Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro
1 5 10 15

<210> SEQ ID NO 143
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 143

Pro Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe
1 5 10 15

<210> SEQ ID NO 144
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 144

Pro Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys
1 5 10 15

<210> SEQ ID NO 145
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 145

Gln Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln
1 5 10 15

<210> SEQ ID NO 146
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 146

Lys Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10 15

<210> SEQ ID NO 147
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 147

Ile Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys
1 5 10 15

<210> SEQ ID NO 148
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 148

Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser
1 5 10 15

<210> SEQ ID NO 149
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 149

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Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu
1 5 10 15

<210> SEQ ID NO 150
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 150

Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala
1 5 10 15

<210> SEQ ID NO 151
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 151

Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala Ile
1 5 10 15

<210> SEQ ID NO 152
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 152

Pro Xaa Val Arg Pro Phe Lys Gln Arg Lys Ser Leu Ala Ile Arg
1 5 10 15

<210> SEQ ID NO 153
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Xaa is serine or phosphoserine

<400> SEQUENCE: 153

Met Pro Pro Pro Gln Lys Ile Pro Xaa Val Arg Pro Phe Lys Gln Arg
1 5 10 15

Lys Ser Leu Ala Ile Arg
20

<210> SEQ ID NO 154

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<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

<400> SEQUENCE: 154

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
1 5 10 15

<210> SEQ ID NO 155
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

<400> SEQUENCE: 155

Met Pro Pro Pro Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg
1 5 10 15

Lys Ser Leu Ala Ile Arg
20

<210> SEQ ID NO 156
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Ser is Phosphoserine

<400> SEQUENCE: 156

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
1 5 10 15

Cys

<210> SEQ ID NO 157
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

<400> SEQUENCE: 157

Met Pro Ser Asp Arg Pro Phe Lys Gln Arg Arg Ser Phe Ala Asp Arg
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Cys

<210> SEQ ID NO 158
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Ser is Phosphoserine

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Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg Cys

-continued

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1               5                   10


<210> SEQ ID NO 159
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic peptide

<400> SEQUENCE: 159

Gln Lys Ile Pro Ser Val Arg Pro Phe Lys Gln Arg Cys
1               5                   10
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1. An isolated APG8 peptide comprising an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18) wherein X is serine or phosphoserine, and with the proviso that the peptide is not a full-length APG8 protein.

2. An isolated APG8 peptide of claim **1** wherein the peptide does not comprise a sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, or SEQ ID NO:9.

3. The isolated APG8 peptide of claim **1**, which comprises an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), MPSDRPFKQRRXFADR (SEQ ID NO:61), QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVRPFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID

NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

4. The isolated APG8 peptide of claim **1**, which comprises an amino acid sequence selected from the group consisting of MPSDRPFKQRRXFADR (SEQ ID NO:61) and MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153).

5. The isolated APG8 peptide of claim **1**, wherein X is serine.

6. The isolated APG8 peptide of claim **1**, wherein X is phosphoserine.

7. A method for producing an antibody to an APG8 polypeptide, which method comprises:

(a) introducing an isolated APG8 peptide of claim **1** to a mammal in an amount sufficient to produce an antibody to said APG8 peptide; and

(b) recovering said antibody from said mammal.

8. The method of claim **7**, wherein the X in the isolated APG8 peptide is serine and the method is used to produce an antibody to a nonphosphorylated APG8 polypeptide.

9. The method of claim **7**, wherein the X in the isolated APG8 peptide is phosphoserine and the method is used to produce an antibody to a phosphorylated APG8 polypeptide.

10. The method of claim **9**, which further comprises a step of removing an antibody that binds to an isolated APG8 peptide of embodiment 1 wherein X is serine.

11. The method of claim **7**, wherein the isolated APG8 peptide is conjugated to a carrier to enhance the peptide's immunogenicity.

12. The method of claim **7**, wherein the isolated APG8 peptide is comprised in an immunogen of embodiment 10 or a MAP of embodiment 12.

13. An antibody to an APG8 polypeptide produced by the method of claim **7**.

14. An isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPSDRPFKQRRXFADR (SEQ ID NO:61), wherein X is serine or phosphoserine.

15. The isolated antibody of claim **14**, wherein the epitope is comprised of an amino acid sequence selected from the group consisting of KQRRX (SEQ ID NO:19), QRRXF (SEQ ID NO:20), RRXFA (SEQ ID NO:21), RXFAD (SEQ ID NO:22), XFADR (SEQ ID NO:23), FKQRRX (SEQ ID NO:24), KQRRXF (SEQ ID NO:25), QRRXFA (SEQ ID NO:26), RRXFAD (SEQ ID NO:27), RXFADR (SEQ ID NO:28), PFKQRRX (SEQ ID NO:29), FKQRRXF (SEQ ID NO:30), KQRRXFA (SEQ ID NO:31), QRRXFAD (SEQ ID NO:32), RRXFADR (SEQ ID NO:33), RPFKQRRX (SEQ ID NO:34), PFKQRRXF (SEQ ID NO:35), FKQRRXFA (SEQ ID NO:36), KQRRXFAD (SEQ ID NO:37), QRRXFADR (SEQ ID NO:38), RPFKQRRX (SEQ ID NO:34), RPFKQRRXF (SEQ ID NO:39), PFKQRRXFA (SEQ ID NO:40), FKQRRXFAD (SEQ ID NO:41), KQRRXFADR (SEQ ID NO:42), SDRPFKQRRX (SEQ ID NO:43), RPFKQRRXF (SEQ ID NO:39), RPFKQRRXFA (SEQ ID NO:44), PFKQRRXFAD (SEQ ID NO:45), FKQRRXFADR (SEQ ID NO:46), RPFKQRRXFA (SEQ ID NO:44), RPFKQRRXFAD (SEQ ID NO:47), PFKQRRXFADR (SEQ ID NO:48), MPSDRPFKQRRX (SEQ ID NO:49), PSDRPFKQRRXF (SEQ ID NO:50), SDRPFKQRRXFA (SEQ ID NO:51), RPFKQRRXFAD (SEQ ID NO:47), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXF (SEQ ID NO:53), PSDRPFKQRRXFA (SEQ ID NO:54), SDRPFKQRRXFAD (SEQ ID NO:55), RPFKQRRXFADR (SEQ ID NO:52), MPSDRPFKQRRXFA (SEQ ID NO:56), PSDRPFKQRRXFAD (SEQ ID NO:57), SDRPFKQRRXFADR (SEQ ID NO:58), MPSDRPFKQRRXFAD (SEQ ID NO:59), PSDRPFKQRRXFADR (SEQ ID NO:60), and MPSDRPFKQRRXFADR (SEQ ID NO:61).

16. The isolated antibody of claim **14**, wherein the epitope is comprised of an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

17. An isolated antibody that specifically binds to an epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine or phosphoserine.

18. The antibody of claim **17**, wherein the epitope is comprised in an amino acid sequence selected from the group consisting of QKIPX (SEQ ID NO:62), KIPXV (SEQ ID NO:63), IPXVR (SEQ ID NO:64), PXVRP (SEQ ID NO:65), XVRPF (SEQ ID NO:66), PQKIPX (SEQ ID NO:67), QKIPXV (SEQ ID NO:68), KIPXVR (SEQ ID NO:69), IPXVRP (SEQ ID NO:70), PXVRPF (SEQ ID NO:71), XVRPFK (SEQ ID NO:72), IPQKIPX (SEQ ID NO:73), PQKIPXV (SEQ ID NO:74), QKIPXVR (SEQ ID NO:75), KIPXVRP (SEQ ID NO:76), IPXVRPF (SEQ ID NO:77), PXVRPFK (SEQ ID NO:78), XVRPFKQ (SEQ ID NO:79), KIPQKIPX (SEQ ID NO:80), IPQKIPXV (SEQ ID NO:81), PQKIPXVR (SEQ ID NO:82), QKIPXVRP (SEQ ID NO:83), KIPXVRPF (SEQ ID NO:84), IPXVRPFK (SEQ ID NO:85), PXVRPFKQ (SEQ ID NO:86), QKIPQKIPX (SEQ ID NO:87), KIPQKIPXV (SEQ ID NO:88), IPQKIPXVR (SEQ ID NO:89), PQKIPXVRP (SEQ ID NO:90), QKIPXVRPF (SEQ ID NO:91), KIPXVRPFK (SEQ ID NO:92), IPXVRPFKQ (SEQ ID NO:93), PXVRPFKQR (SEQ ID NO:94), PQKIPQKIPX (SEQ ID NO:95), QKIPQKIPXV (SEQ ID NO:96), KIPQKIPXVR (SEQ ID NO:97), IPQKIPXVRP (SEQ ID NO:98), PQKIPXVRPF (SEQ ID NO:99), QKIPXVRPFK (SEQ ID NO:100), KIPXVRPFKQ (SEQ ID NO:101), IPXVRPFKQR (SEQ ID NO:102), PXVRPFKQRK (SEQ ID NO:103), XVRPFKQRKS (SEQ ID NO:104), PPQKIPQKIPX (SEQ ID NO:105), PQKIPQKIPXV (SEQ ID NO:106), QKIPQKIPXVR (SEQ ID NO:107), KIPQKIPXVRP (SEQ ID NO:108), IPQKIPXVRPF (SEQ ID NO:109), PQKIPXVRPFK (SEQ ID NO:110), QKIPXVRPFKQ (SEQ ID NO:111), KIPXVRPFKQR (SEQ ID NO:112), IPXVRPFKQRK (SEQ ID NO:113), PXVRPFKQRKS (SEQ ID NO:114), XVRPFKQRKSL (SEQ ID NO:115), PPPQKIPQKIPX (SEQ ID NO:116), PPQKIPQKIPXV (SEQ ID NO:117), PQKIPQKIPXVR (SEQ ID NO:118), QKIPQKIPXVRP (SEQ ID NO:119), KIPQKIPXVRPF (SEQ ID NO:120), IPQKIPXVRPFK (SEQ ID NO:121), PQKIPXVRPFKQ (SEQ ID NO:122), QKIPXVRPFKQR (SEQ ID NO:123), KIPXVRPFKQRK (SEQ ID NO:124), IPXVRPFKQRKS (SEQ ID NO:125), PXVRPFKQRKSL (SEQ ID NO:126), XVRPFKQRKSLA (SEQ ID NO:127), MPPPQKIPQKIPX (SEQ ID NO:128), PPPQKIPQKIPXV (SEQ ID NO:129), PPQKIPQKIPXVR (SEQ ID NO:130), PQKIPQKIPXVRP (SEQ ID NO:131), QKIPQKIPXVRPF (SEQ ID NO:132), KIPQKIPXVRPFK (SEQ ID NO:133), IPQKIPXVRPFKQ (SEQ ID NO:134), PQKIPXVRPFKQR (SEQ ID NO:135), QKIPXVRPFKQRK (SEQ ID NO:136), KIPXVR-

PFKQRKS (SEQ ID NO:137), IPXVRPFKQRKSL (SEQ ID NO:138), PXVRPFKQRKSLA (SEQ ID NO:139), XVRPFKQRSKLAI (SEQ ID NO:140), MPPPQKIPQKIPXVR (SEQ ID NO:141), PPPQKIPQKIPXVRP (SEQ ID NO:142), PPQKIPQKIPXVRPF (SEQ ID NO:143), PQKIPQKIPXVRPFK (SEQ ID NO:144), QKIPQKIPXVRPFKQ (SEQ ID NO:145), KIPQKIPXVRPFKQR (SEQ ID NO:146), IPQKIPXVRPFKQRK (SEQ ID NO:147), PQKIPXVRPFKQRKS (SEQ ID NO:148), QKIPXVRPFKQRKSL (SEQ ID NO:149), KIPXVRPFKQRKSLA (SEQ ID NO:150), IPXVRPFKQRKSLAI (SEQ ID NO:151), and PXVRPFKQRKSLAIR (SEQ ID NO:152).

19. The antibody of claim **17**, wherein the epitope is comprised in an amino acid sequence selected from the group consisting of QRRX (SEQ ID NO:11), RRXF (SEQ ID NO:12), RXFA (SEQ ID NO:13), XFAD (SEQ ID NO:14), KIPX (SEQ ID NO:15), IPXV (SEQ ID NO:16), PXVR (SEQ ID NO:17), and XVRP (SEQ ID NO:18).

20. The antibody of claim **17**, wherein the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is serine.

21. The antibody of claim **17**, wherein the isolated antibody specifically binds to the epitope that comprises the amino acid residue X in the amino acid sequence MPPPQKIPXVRPFKQRKSLAIR (SEQ ID NO:153), wherein X is phosphoserine.

* * * * *