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(54) **UTILISATION DE LA SECRETINE POUR LE TRAITEMENT DE  
L'AUTISME ET D'AUTRES TROUBLES DU  
COMPORTEMENT, TROUBLES NEUROLOGIQUES OU  
IMMUNOLOGIQUES**

(54) **USE OF SECRETIN FOR THE TREATMENT OF AUTISM AND  
OTHER NEUROLOGICAL, BEHAVIORAL AND  
IMMUNOLOGICAL DISORDERS**

(57) L'invention concerne l'utilisation de la sécrétine et de compositions de sécrétine pour le traitement des troubles neurologiques, immunologiques ou troubles du comportement. Ces procédés consistent à administrer une quantité efficace de sécrétine à un patient. L'invention traite également de divers procédés et de compositions permettant d'administrer une quantité efficace de sécrétine.

(57) Secretin and secretin compositions are used for the treatment of neurological, behavioral, and immunological disorders. The methods include administering an effective amount of secretin to a patient. Various methods and compositions for administering an effective amount of secretin can be used.

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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/US99/13061  <b>(22) International Filing Date:</b> 9 June 1999 (09.06.99)  <b>(30) Priority Data:</b> 60/088,575           9 June 1998 (09.06.98)           US 09/229,208       13 January 1999 (13.01.99)       US  <b>(71) Applicant:</b> REPLIGEN CORPORATION [US/US]; 117 Fourth Avenue, Needham, MA 02194 (US).  <b>(72) Inventors:</b> BECK, Victoria; 11 McIntosh Lane, Bedford, NH 03110 (US). RIMLAND, Bernard; 4758 Edgeware Road, San Diego, CA 92116 (US).  <b>(74) Agent:</b> FASSE, J., Peter; Fish & Richardson, P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).		<b>(81) Designated States:</b> AU, CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
<b>(54) Title:</b> USE OF SECRETIN FOR THE TREATMENT OF AUTISM AND OTHER NEUROLOGICAL, BEHAVIORAL AND IMMUNOLOGICAL DISORDERS  <b>(57) Abstract</b>  <p>Secretin and secretin compositions are used for the treatment of neurological, behavioral, and immunological disorders. The methods include administering an effective amount of secretin to a patient. Various methods and compositions for administering an effective amount of secretin can be used.</p>		

## USE OF SECRETIN FOR THE TREATMENT OF AUTISM AND OTHER NEUROLOGICAL, BEHAVIORAL AND IMMUNOLOGICAL DISORDERS

5

Background of the Invention

Autism is a disabling neurological disorder that affects thousands of Americans and encompasses a number of subtypes, with various putative causes and few  
10 documented ameliorative treatments. The disorders of the autistic spectrum may be present at birth, or may have later onset, for example, at ages two or three. There are no clear cut biological markers for autism. Diagnosis of the disorder is made by considering the  
15 degree to which the child matches the behavioral syndrome, which is characterized by poor communicative abilities, peculiarities in social and cognitive capacities, and maladaptive behavioral patterns.

A number of different treatments for autism have  
20 been developed. Many of the treatments, however, address the symptoms of the disease, rather than the causes. For example, therapies ranging from psychoanalysis to psychopharmacology have been employed in the treatment of autism. Although some clinical symptoms may be lessened  
25 by these treatments, modest improvement, at best, has been demonstrated in a minor fraction of the cases. Only a small percentage of autistic persons become able to function as self-sufficient adults.

Although much controversy exists about the causes  
30 and treatments of autism, a few established biomedical findings have been made. Many individuals with autism experience intestinal difficulties, often including the inability to digest gluten and casein. Abnormalities have also been found in the metabolism of the  
35 neurotransmitter serotonin and in various parameters of



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immune system functions, for example, elevated Measles, Mumps and Rubella (MMR) titers. Prior to the discovery of the present invention, however, no useful links had been made between these biomedical findings, nor had any  
5 successful treatments been derived therefrom, as disclosed in various articles incorporated herein by reference. Priven, J. (1997), "The biological basis of autism." Current Opinion in Neurobiology, 7, 708-712; Rapin, L. & Katzman, R. (1998), "Neurobiology of autism,"  
10 Ann. Neurology, 43, 7-14; Wing, L. (1997), "The autistic spectrum," The Lancet, 350, (Dec. 13), 1761-1765.

Similar to autistic spectrum disorder, many other behavioral, neurological and immunological disorders have been equally difficult to understand and to effectively  
15 treat. Such disorders include depression, obsessive-compulsive disorder, Alzheimers, allergies, anorexia, schizophrenia, as well as other neurological conditions resulting from improper modulation of neurotransmitter levels or improper modulation of immune  
20 system functions, as well as behavioral disorders such as ADD (Attention Deficit Disorder) and ADHD (Attention Deficit Hyperactivity Disorder), for example.

Accordingly, a need exists for a method and composition for the treatment of autism and other  
25 behavioral, neurological and/or immunological disorders.

The hormone secretin is a polypeptide hormone secreted by the mucosa of the duodenum and upper jejunum when acid chyme enters the intestine. The hormone secretin stimulates the pancreatic acinar cells to  
30 release bicarbonate and water, which are excreted into the duodenum and change the pH in the gut from acid to alkaline, thereby facilitating the action of digestive enzymes. Secretin is always used and indeed is intended only to be used in diagnostic tests given to patients

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with gastrointestinal disorders to stimulate the release of pancreatic juices for testing purposes.

### Summary of the Invention

The present invention features methods and compositions  
5 for the treatment of neurological, immunological, and  
other disorders in a patient. The methods include the  
step of stimulating the secretion of pancreatic juices in  
the patient. In one embodiment, stimulating the  
secretion of pancreatic juices comprises the step of  
10 administering to the patient an effective amount of  
natural or synthetic secretin. One method of the present  
invention is for the treatment of autistic spectrum  
disorder.

According to one method of administering secretin,  
15 the secretin is administered by infusion and the  
effective amount is generally 2 clinical units (CU) per  
kilogram (kg) of body weight given intravenously within 1  
minute. In another method, the secretin is administered  
transdermally by applying a transdermal carrier  
20 substance, such as dimethyl sulfoxide (DMSO) to the skin,  
applying crystalline secretin in an effective amount onto  
the carrier substance, and rubbing the composition into  
the skin. One example of an effective amount of secretin  
administered transdermally includes about 15 CU of  
25 crystalline secretin.

Other methods of administering secretin include,  
but are not limited to, administering secretin  
transdermally with a gel (e.g., a Pluronic-Lecithin-  
Organogel (PLO) gel), lotion or patch; administering  
30 secretin with a suppository; administering secretin  
orally, as tablet, capsule or lozenge; administering  
secretin by inhalation (e.g., as an aerosol) either  
through the mouth or the nose; administering secretin  
intranasally (e.g., as a snuff); and administering



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secretin using acoustic waves to permeate the skin. The present invention also contemplates other physiologically acceptable carriers or excipients for carrying an effective amount of secretin into the patients body.

5 In another embodiment, the method for stimulating the secretion of pancreatic juices comprises the step of causing the body to secrete secretin in an effective amount to at least ameliorate and preferably treat autism and other neurological and/or immunological disorders.

10 This method includes, for example, stimulating or otherwise causing the duodenum and upper jejunum to secrete the hormone secretin for one or more of the purposes described herein.

The present invention also features compositions  
15 for use according to the above methods. In one embodiment, a pharmaceutical composition, according to the present invention includes an effective amount of secretin together with a suitable volume of sodium chloride for dissolving the secretin and carrying the  
20 secretin into the body by infusion. In another embodiment, a composition according to the present invention includes an effective amount of secretin and a transdermal carrier substance, such as DMSO or PLO gel for carrying the secretin into the body transdermally.  
25 Other compositions include an effective amount of secretin together with physiologically acceptable carriers or excipients for carrying the secretin into the patients body. The present invention contemplates the use of both natural and synthetically produced secretin.

30 Description of the Preferred Embodiments

The present invention will be better understood from the following examples which are given by way of illustration and not by way of limitation. The patient, the same in both examples, is a boy with symptoms of

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autism. Although only two examples of treatment are presented on the same patient, the present invention has been tried on a number of children in accordance with the method of the first example with similar satisfactory  
5 results.

The patient in the present examples developed normally until about fourteen months of age, with the exception of gastrointestinal problems (i.e., chronic diarrhea and constipation) which began at about six  
10 months. At about thirteen months, when whole milk was introduced into his diet, the patient began having reoccurring ear infections. At about fourteen months, the patient appeared to lose the ability to process language, first receptively (at about 14 months) then  
15 expressively (at about 16 months). The patient also experienced episodes of shivers that appeared to be intermittent seizures.

After consulting with numerous neurologists, pediatricians, child development specialists,  
20 audiologists, endocrinologists, allergists, and other medical professionals, no consistent diagnosis had been reached. Although not clinically diagnosed with autism, the patient exhibits a number of behavioral symptoms of autism and pervasive developmental disorder (PDD) in  
25 general. The term autism is used herein for reference purposes only, and this invention is intended to apply to any number of pervasive developmental disorders as well as neurological and immunological disorders.

Prior to receiving the treatment with secretin, a  
30 single photon emission computed tomography (SPECT) scan of the brain revealed a decreased perfusion in the right hemisphere and left temporal lobe, with the most severe decrease in the right parietal occipital region. Also, steady state auditory evoked responses recorded in  
35 response to rapid amplitude and frequency modulations of



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a 1 kHz tone were abnormal, suggesting disturbances of neural mechanisms responsible for frequency and amplitude modulation analysis. Further, the patients secretin cells prior to receiving treatment, measured at a level of 9, are far below the normal limit in the range of 20-70.

#### EXAMPLE 1

When the patient was three years old, the secretin was administered by way of an infusion as part of an upper gastrointestinal endoscopy. The secretin was used in this diagnostic procedure at the request of the patients parents, one of which is an inventor of the present invention. The secretin used in this procedure is known as Secretin-Ferring available from Ferring Laboratories, Inc., Suffern, New York (See Appendix A). The secretin was dissolved in a 7.5 solution of sodium chloride and administered in a dosage of 2 clinical units (CU) per kilogram (kg) body weight by intravenous injection over one minute. (I.E. 30 IU IV for approximately 15 kilograms of body weight.)

Immediately after the administration of the secretin, the diagnostic testing revealed that the patients pancreas responded, quite surprisingly, with an unusually large amount of pancreatic juice being released (approximately 10 ml/min compared to a usual rate of 1-2 ml/min). The diagnostic tests performed on the patient during this procedure also indicated gastric inflammation. Within days after the administration of secretin, the patients chronic abnormal bowel movements became normal, although no changes had been made in the patients diet. Within weeks after the treatment, the patient was able to make normal eye contact, language appeared for the first time in two years, and other behavioral and developmental problems improved



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remarkably. The following Table I summarizes the improvements observed in the patient within 3 weeks after the infusion of secretin.

Table I

5	<u>Symptoms Before Secretin Infusion</u>	<u>Progress within 3 Weeks After the Secretin Infusion</u>
	Two words	100's of words - will repeat approximation of any word requested.
	No sentences	Short sentences - such as; "I love you", "I want juice", "Good night mommy", "Thank you, daddy".
	No flash cards	40 - 50 flash cards.
	No focus on requested tasks	Will sit and watch carefully. Will perform most tasks after watching once or twice. For instance, will sort by color or category. Will construct more complicated puzzles. Will respond appropriately to questions.
10	Diapers only	Completely potty trained.
	Watch Videos	Now, gets "involved" interactively with his videos. He will imitate the hand motions, sing the songs or dance to the music.
15	Consistent sleeping problems. Although these were much worse when he was 18-24 months, prior to the procedure he was still up numerous times each night.	Has slept through almost every night entirely.
	Infrequent (1-2 times/week) "spinning" episodes.	No spinning episodes.
	Abnormal bowel movements.	Normal bowel movements.
20	Excessive water consumption approximately 50 cups per day.	Excessive water consumption - no change approximately 50 cups per day.

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Table I (continued)

	<u>Symptoms Before Secretin Infusion</u>	<u>Progress within 3 Weeks After the Secretin Infusion</u>
5	Limited Diet Preferences (French Toast, bananas, French Fries, pancakes, crackers, cookies, raisins, chocolate, chicken nuggets).	No Change.
10	No apparent connections made between language and objects.	Many connections made between new language learned and objects. Recites names he has learned on flash cards when he sees the same on computer game or video.
	No response to request for gestures.	Responds to all kinds of things such as, "blow a kiss", "Wave bye bye", "Say bye bye", etc. Will often now spontaneously say these things himself.
	No interest in drawing.	Wants to draw constantly. Will draw complete face and name the parts as he draws.
	Did not imitate commands.	Will imitate almost any multi-step command.
15	Minimal eye contact.	Eye contact 75% of the time.

Biomedical changes were also measured in the patient. A SPECT scan of the patient indicated that the perfusion of the right posterior parietal and right temporal lobes was improved. Blood tests taken after the treatment also indicated a rise in serotonin levels, and the patients rubella titers dropped from 5.8 to 2.3.

Although the behavioral improvements continued, the rate of the patient's progress appeared to decrease at about 5 weeks. At the request of the patient's parents, a second infusion of secretin was performed about 9 months after the first infusion, and a third infusion of secretin was performed about three months after the second infusion. The second and third infusions of secretin achieved the same results in the patient.



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EXAMPLE 2

At the time of this treatment, the patient was about 4 years old. Secretin was administered transdermally using pharmaceutical grade dimethyl sulfoxide (DMSO) (generally 5 99.9% pure) available from Clinic Service Co., Box 2512, Hemet CA 92543. The secretin (Secretin-Ferring) was administered daily in a dosage of about 75 CU over a five day period (i.e., about 15 CU daily). For each treatment, about 4 drops of DMSO were placed onto the 10 skin of the patient, about 15 CU of the crystalline secretin was placed onto the DMSO, and the composition was rubbed into the skin.

The administration of secretin transdermally on a daily basis in this way has resulted in even more 15 dramatic and significant improvements in the patient. Within a period of about 6 months, the patient has progressed to spontaneous and conversational language. When the daily dose of secretin is stopped, the autistic behavioral symptoms return.

20 It is important to note that similar results have been seen in numerous other autistic children using an intravenous administration of secretin in accordance with the teachings of the present invention, in order to validate the findings of the present invention.

25 Although the present invention is not limited by theory, it is believed that some autistic spectrum disorders are caused by a secretin deficiency resulting in a dysfunction of the pancreas. One function of the hormone secretin is to stimulate the pancreas to release 30 bicarbonate and water, which change the pH in the gut from acid to alkaline, thereby facilitating the action of digestive enzymes. The gastrointestinal disorders, such as an inability to digest gluten and casein, in autistic

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patients is possibly caused by this failure of the pancreas to release enzymes.

One possibility is that abnormal opioid peptides in the gut create problems in the brain. These abnormal  
5 opioid peptides have been found to diminish on a casein free and gluten free diet.

The gastric inflammation observed in the patient in the above EXAMPLE 1 suggests that the improper pH resulting from this dysfunction of the pancreas may be a  
10 cause of the digestive problems and malabsorption of essential minerals and nutrients found in many individuals with autism. The unusual secretion by the pancreas in response to the secretin, as observed in EXAMPLE 1, further suggests that this dysfunction of the  
15 pancreas is caused by a secretin deficiency.

In addition to this effect on the digestive function, secretin also appears to improve the abnormal brain activity in individuals having symptoms of autism. The increased blood flow in the brain detected during a  
20 SPECT scan after administering secretin in EXAMPLE 1 supports this theory. While causing pancreatic secretions, secretin also stimulates the production of cholecystokinin (CCK). Deficiencies in CCK have been linked to other neurological disorders, such as  
25 schizophrenia, and CCK production has been found to be related to levels of the neurotransmitter serotonin. Thus, secretin may be indirectly related to the body's natural production of serotonin. The increase in serotonin levels in the blood after the procedure in  
30 EXAMPLE 1 supports this relationship between secretin and serotonin.

Without proper modulation of neurotransmitter levels (i.e., serotonin) in the brain, the brain will not function properly. The inability to modulate  
35 neurotransmitter levels has been found to be related to



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other neurological conditions as well as autism. Thus, a secretin deficiency may cause an imbalance or improper modulation of neurotransmitter levels that results in autistic spectrum disorder or other neurological disorders. Administering secretin to patients with these disorders will modulate the neurotransmitter levels and correct the behavioral symptoms, such as the inability to process language and other maladaptive behavioral patterns. The secretin may also correct abnormalities in immune system functions, as indicated by the reduction of measles, mumps and rubella antibodies in the patient after the secretin administration in EXAMPLE 1.

Secretin has also been found to stimulate dopamine production through its precursor, tyrosine hydroxylase. Dopamine levels have been implicated in a variety of mental and behavioral disorders such as Parkinson's and Alzheimer's disease.

A secretin deficiency can therefore account for the gastrointestinal disorders as well as the behavioral symptoms found in many individuals with autistic spectrum disorder.

The therapeutic possibilities of the use of secretin appear to have been overlooked in the medical literature. For example, Guyton and Hall, in their widely used Textbook of Medical Physiology (9th edition, 1995-1997) mention briefly in passing that secretin can increase cellular utilization of insulin. Recent research suggests that insulin is required for normal brain functioning. (See also Science, vol. 280, April 24, 1998, p. 517-518). Furthermore, immunological disorders related to abnormally high levels of measles, mumps, and rubella (MMR) titers may also be treatable with secretin. Additionally, secretin is believed to stimulate antibodies to cows milk protein (and perhaps other proteins). Autism and other PDD's may be connected to

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protein intolerance and secretin may increase the body's tolerance to such protein(s). Secretin may also have histamine blocking capabilities.

Although the above examples use Secretin-Ferring, the present invention contemplates other forms of natural or synthetic (or recombinant) secretin, e.g., porcine or human. The present invention also contemplates using other types of transdermal carrier substances in addition to DMSO. Further, the present invention contemplates alternative ways of administering secretin including, but not limited to, administering secretin transdermally with a gel (such as Pluronic-Lecithin-Organogel (PLO gel, from Gallipot, Inc., St. Paul, MN) made of Pluronic® F127NF and a 1:1 mixture of soy lecithin:isopropyl palmitate, kept at a pH of 5 with a buffer, e.g., potassium sorbate), lotion or patch; administering secretin with a suppository; administering secretin orally, as tablet, capsule or lozenge; administering secretin by inhalation (e.g., as an aerosol) either through the mouth or the nose; and administering secretin intranasally (e.g., as a snuff). Such alternative methods of administering secretin are less invasive, do not have to be carried out by a doctor at a medical facility, and are less expensive. In addition, the level or dose of administration of secretin can be varied from those examples stated herein including, for example, intravenous administration over a period of time of several hours instead of several minutes and/or a smaller, maintenance or daily dose administered intramuscularly, transdermally or by other methods as disclosed herein or their equivalent.

A further alternative method of transdermally administering secretin includes the use of acoustic waves to permeate the skin. For example, acoustic waves generated using ultrasound or a shockwave from a pulsed



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laser have been found to make the skin temporarily permeable. A few minutes of low-frequency ultrasound (sound greater in frequency than 20 kilohertz) creates tiny cavities through which the secretin (alone or  
5 combined with another transdermal carrier substance) can be diffused.

Accordingly, the methods of treating autism by administering secretin and/or causing the body to naturally secrete required amounts of secretin corrects  
10 the secretin deficiency, improving the digestive functions in autistic patients previously experiencing intestinal difficulties and improving communication, cognition, and socialization capabilities of autistic patients. Since other neurological disorders, such as  
15 depression, obsessive-compulsive disorder, Alzheimer's, allergies, anorexia, bulimia, schizophrenia, also involve abnormal modulation of neurotransmitter levels, these disorders can also be treatable with secretin and/or the stimulation of pancreatic juices. Further, other  
20 disorders related to serotonin and dopamine may also be treatable with secretin.

Modifications and substitutions by one of ordinary skill in the art are considered to be within the scope of the present invention which is not to be limited except  
25 by the claims which follow.

What is claimed is:

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1. A method for treating an individual exhibiting a symptom of a neurological or immunological disorder, the method comprising administering to the individual an amount of secretin effective to improve one  
5 or more symptoms of the disorder.

2. The method of claim 1, wherein the neurological or immunological disorder is selected from the group consisting of depression, obsessive-compulsive disorder, Alzheimer's, allergies, anorexia, bulimia,  
10 schizophrenia, Attention Deficit Disorder (ADD), and Attention Deficit Hyperactivity Disorder (ADHD).

3. The method of claim 1, wherein the effective amount of secretin is administered by infusion.

4. The method of claim 3, wherein administering  
15 the effective amount of secretin by infusion includes the step of intravenously infusing secretin in an amount of about 2 clinical units (CU) per kilogram (kg) of body weight.

5. The method of claim 1, wherein the effective  
20 amount of secretin is administered transdermally.

6. The method of claim 5, wherein administering the effective amount of secretin transdermally includes:



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applying a transdermal carrier substance to a portion of the skin of the individual; and

applying crystalline secretin in the effective amount onto the transdermal carrier substance.

5           7.    The method of claim 6, wherein the transdermal carrier substance comprises dimethyl sulfoxide (DMSO).

8.    The method of claim 5, wherein the effective amount of secretin includes between 5 and 20 clinical  
10 units (CU) of crystalline secretin per dose.

9.    The method of claim 5, wherein administering secretin transdermally includes administering the effective amount of secretin with a patch to be applied to a portion of the skin of the individual.

15           10. The method of claim 5, wherein administering secretin transdermally includes administering the effective amount of secretin using acoustic waves causing the secretin to permeate a skin surface of the individual.

20           11. The method of claim 1, wherein the effective amount of secretin is administered orally.

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12. The method of claim 11, wherein the effective amount of secretin is administered orally using an oral carrier selected from the group consisting of a tablet, capsule, or lozenge.

5           13. The method of claim 1, wherein the effective amount of secretin is administered using a suppository.

14. The method of claim 1, wherein the effective amount of secretin is administered by inhalation or intranasally.

10           15. The method of claim 1, wherein the effective amount of secretin includes an amount of secretin sufficient to increase serotonin levels in the brain of the individual.

16. Secretin for use in treating a neurological  
15 or immunological disorder.

17. The use of secretin for the manufacture of a medicament for the treatment of a neurological or immunological disorder.

18. A composition for treatment of a neurological  
20 or immunological disorder in an individual comprising an



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effective amount of secretin and a physiologically acceptable carrier.

19. The composition of claim 18, wherein the physiologically acceptable carrier includes a transdermal  
5 carrier substance.

20. The composition of claim 19, wherein the transdermal carrier substance comprises dimethyl sulfoxide (DMSO) or Pluronic-Lecithin-Organogel (PLO).

21. The composition of claim 18, wherein the  
10 effective amount of secretin comprises about 15 clinical units (CU) of crystalline secretin per dose.

22. The composition of claim 18, wherein the effective amount of secretin comprises about 2 clinical units (CU) per kilogram (kg) of body weight of an  
15 individual per dose.

23. The composition of claim 18, wherein the physiologically acceptable carrier comprises an oral carrier.

24. The composition of claim 18, wherein the  
20 physiologically acceptable carrier comprises an inhalable carrier.

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25. A method for treating an individual exhibiting symptoms of autism, the method comprising transdermally administering to the individual an amount of secretin effective to improve one or more criteria for  
5 autistic disorder.

26. The method of claim 25, wherein administering the effective amount of secretin transdermally includes the steps of:

applying a transdermal carrier substance to a  
10 priority of the skin of the individual; and

applying crystalline secretin in the effective amount onto the transdermal carrier substance.

27. The method of claim 25, wherein the transdermal carrier substance comprises dimethyl  
15 sulfoxide (DMSO).

28. The method of claim 25, wherein the effective amount of secretin includes about 15 clinical units (CU) of crystalline secretin per dose.

29. Secretin for use in treating symptoms of  
20 autism by transdermal administration.



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30. The use of secretin for the manufacture of a medicament for the treatment of symptoms of autism by transdermal administration.

31. A method for treating an individual  
5 exhibiting a symptom of a neurological or immunological disorder, the method comprising stimulating secretion of pancreatic juices in the individual.

32. The method of claim 31, wherein secretion of pancreatic juices is stimulated by administering to the  
10 individual an amount of secretin effective to improve one or more symptoms of the disorder.

33. The method of claim 31, wherein the secretin is administered by infusion.

34. The method of claim 31, wherein the secretin  
15 is administered transdermally.

35. The method of claim 31, wherein stimulating secretion of pancreatic juices increases a level in the individual of at least one of serotonin, dopamine, and CCK.

20 36. The method of claim 31, wherein stimulating secretion of pancreatic juices induces secretion of an

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amount of secretin in the individual effective to improve one or more symptoms of the disorder.

37. The method of claim 36, wherein secretion of secretin is induced by stimulating the duodenum of the  
5 individual.

38. The method of claim 31, wherein the disorder is autism.