

LP GLOBAL NETWORK



Laminine FAQ and Summary of 11 Clinical Research



INTRODUCTION

CONGRATULATIONS! If you are reading this material, you have a keen interest in leading a healthy life, and helping your love ones and friends do the same.

The human body is a complex mechanism operated with thousands of interdependent biological chemical and electrochemical reactions. Efforts to understand these mechanisms are constantly producing new and exciting information to help us "fight" the consequences of aging. At the very least, most people desire a healthy life, regardless of the length.

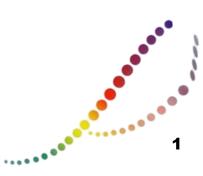
It is no secret that important hormones for essential bodily and mental functions are secreted and regulated from major organs due to signals originating within the brain. In a perfect world of exacting diets and nutrition, the brain would get the stimuli from the foods, environment and other sensory inputs, order the appropriate organs to create and regulate the hormones, enzymes and other chemicals required for bodily and mental functions.

Unfortunately this is far from the scenario in the real world. Our modern life puts immense amounts of stress on our brains and bodies and we certainly recognize the effects. The imbalances created by these factors manifest themselves in the form of depression, fatigue, memory loss, etc.

Compounding the effect from stress and physical activity, is our increasing consumption of harmful chemicals either by simply breathing the air around us, or by succumbing to the convenience of preserved foods, massproduced meats, fish vegetables and fruits. The impact of the dietary changes are not completely understood, but more and more is being discovered everyday. Examples can include use of flavor enhancers and artificial sweeteners, which upset the balance of the amino acids responsible for exciting neurons in our brain. While commercially successful, these products have a profound effect on the long term functioning of the brain.

Eating "healthy" has become a trend, but most people do not recognize the caveats usually associated with healthy eating. There are thousands of examples of modern day foods, which do not provide the same nutrition they did in the days gone by. An example is that of a farmed fish. You may think you are eating healthy by eating salmon. However, most salmon consumed today is farmed, and is much lower in Omega-3 oils (among many things, low level of Omega-3 are linked to Alzheimer's) than wild salmon.

Why? Farmed fish are fed low cost soy and other plant foods to increase their fat content. Salmon is a camivorous fish in the wild, and the Omega-3 oils for which it is famous for are produce not from a vegetarian diet, but by a camivorous diet. Additionally, farmed fish is typically contaminated with chemicals from the water, such as PCBs. To lower the effect of the chemicals, you must cook it in ways that eliminates what little Omega-3 oils it did happen to make.



How do we encounter the constant attacks on our body, especially from our diets and stress? Much has been written about what type of foods to eat, enough to make one paranoid about eating anything at all. Manufacturers are constantly changing names of ingredients, which become infamous. Take for example MSG (Monosodium Glutamate) a flavor enhancer. Due to all the negative publicity from MSG, it is now labeled as "hydrolyzed oat flour", "autolyzed yeast", "sodium caseinate", etc. All these ingredients pass the scrutiny of an average person having all the intent of eating healthy.

It seems the best defense to these attacks, first, to do your best at eating healthy, and then supplement your diet with something that actually helps regulate the body functions by working in a coherent manner with the brain.

This mini booklet is designed to help introduce you to the phenomenal health benefits of an almost miraculous formulation of amino acids, oligopeptides and growth factors. The explanations and definitions that follow will give you a logical path to actually living a healthier life, even if you are currently extremely conscious about your diet.

What is Laminine? The philosophy and story of the formulation.

Fundamental to any problem solving approach is answering the questions:

1.) Has something similar it been solved successfully before?

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2.) What are the similarities, and what part of our problem statement may be unique and require additions to the prior solution?

When Pendura Lifestyles started down the path of providing it's customers a solid, proven nutritional supplement to aid the brain in regulating the body, we searched for an amino acid and oligopeptide combination which had all the required nourishment for the task at hand. We found numerous studies for the causes and effect of individual amino acids, peptides and hormones, not to mention an equal number of products touting high dosages of one over another as beneficial for consumption.

What was not clear was how many companies had developed and proven the right "combination" of amino acids, peptides and growth factors that the brain requires?

It didn't surprise us to find there were none. So we embarked on our own research project. We looked for balanced amino acid/peptide blend in nature, which could meet our need with minimal additions.

That is when we discovered that in 1929 a Canadian doctor, Dr. John Ralston Davidson, theorized than an injected extract from fertilized hen eggs could be helpful for a number of his cancer patients. In fact, he spent well over a decade developing and researching his theory. However, when Dr. Davidson passed away in 1943, his research on fertilized hen eggs quickly and quietly came to a halt.

It wasn't until almost 50 years later that the pursuit of fertilized hen egg extract was revived by Norway's foremost expert on egg research, Dr. Bjodne Eskeland.

Dr Eskeland also hypothesized that partially incubated, fertilized hen eggs contained a special combination of amino acids peptides and protein fractions that could help provide an incredible array of health benefits when consumed by humans. In theory, these partially incubated, fertilized eggs - specifically 9-day-old fertilized eggs, contain all the nutrients required to start a new life. This includes vitamins, minerals and protein, as well as important defense factors, growth factors, hormones and other biologically active components. While not much was known about the growth factor at the time, the high level of oligopeptides (small peptides) gave credence to research we had done on the necessity of rapid transport across the digestive membrane in order to derive effective benefits from amino acids.

We felt this could be the best "base" ingredient for our formulation. A patented process extracts the critical nutritional fluid from the white of an egg at the protoembryonic stage, so we called it ProtoEmbryonic Stage Extract (PESE). The extract not only provided a mechanism of rapid transport of very critical nutrients, but also contained Basic Fibroblast Growth, which is most probably responsible for the amino acids and peptides to be utilized in the right manner, by "directing" so as to say the path. The growth factor is also responsible for nurturing the body's own stem cells both differentiated, and undifferentiated. Common amino acid formulations do not contain this growth factor, and may not be utilized by the brain in the most efficient manner.

Next, we looked at the symptoms caused most by our diets and environment, so we can "super charge" the PESE for modern day use. Skin and hair health, moods (depression), memory loss, fatigue and cardiovascular health are most affected by today's lifestyle. These individual symptoms and how Laminine addresses them are covered later in the booklet.

Having a perfectly balanced, natural transport mechanism, with a strong "director" we knew that we were assured of the added amino acids will not only find their way to the right spots, but will be guided properly to perform their function efficiently. We then added the amino acids most critical for the health of skin, hair, memory function, cardiovascular health and restoration of energy, from natural plant protein and marine protein.

Thus the symbiotic formulation we proudly call **lominine** was born.

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What are amino acids?

Amino acids are critical to life, and have many functions in metabolism. One particularly important function is as the building blocks of proteins, which are linear (straight) chains of amino acids. Amino acids are linked together in varying sequences to form a vast variety of proteins. Amino acids are also important in may other biological molecules and due to this central role in biochemistry, they are very important in nutrition.

Amino acids join together to form short polymer chains called peptides or longer chains called either polypeptides or proteins.

Twenty-two amino acids are naturally incorporated into polypeptides and are called proteinogenic or standard amino acids. Of the twenty-two standard amino acids, eight are called essential amino acids because the human body cannot synthesize them from other compounds at the level needed for normal growth, so they must be obtained from food. The amounts required also depend on the age and health of the individual so it is hard to make general statements about the dietary requirement for some amino acids.

What are peptides?

Peptides are short polymers formed the linking, in a defined order, of a-amino acids. Hence depending on the number of amino acids, peptides are called di-peptides, tri-peptides, oligopeptides, etc. Proteins are multi peptide chains.

Small amino avid chain peptides (such as contained in Laminine), commonly known as oligopeptides, are very easily transported through the intestinal, membrane. They are sometimes used as transport mechanisms for drugs.

Protein must be broken down to smaller and smaller peptides, and eventually an amino acid to perform its functions. Dietary intake of peptides and amino acids, which can reach their destination, therefore, can be extremely beneficial.

Peptides are the most abundant compounds in the hypothalamus of the brain, and perform vital functions of communication sensory impulses to the endocrine system (hormone producing glands) Peptide based hormone-releasing agents from the hypothalamus use the anterior pituitary to signal the thyroid gland, the adrenal cortex, the mammary gland, the ovaries & testicles and the growth hormone.

Understanding the mechanisms of the effect of peptides, and the types of peptides is a complex field, and is being studied extensively. Unfortunately, these studies are done in isolation and disregard the wholistic picture of the complex mechanisms, which exist in our marvelous bodily electrochemical system. Further, the studies are focused on a particular amino acid, peptide or other neurotransmitter. While the result identify the final activity with the amino acid/peptide, the mechanism of transport of such critical amino acid/peptides to the final destination is a subject of major arguments. These arguments cast a shadow on the importance of nutritional supplements. Most doctors will tell you nutritional supplements "cannot hurt", but stop short of endorsing them. The reason is the lack of evidence that the active ingredients have been formulated in the correct form, that is, intermediates or ligands that can make the active ingredient available to the nervous or endocrine system of the brain.

What exactly is PESE, and how much is known about it's benefits?

Proto Embryonic Stage Extracts is the name we have given the ingredient in Laminine that is derived from the partially incubated (9 days) fertilized hen eggs. PESE contains the most potent and balanced combination of not only amino acids in short peptide chain form, but also other known (and unknown) factors such as Fibroblast Growth Factor. We believe amino acids (in the form of di and tripeptides) derived from such fluids combines with the growth factors are able to enhance brain function because they are "precisely" engineered to support the most complex stage of birth of a living creature, the beginning; just like the take off is the most complex function in flying an airplane, or the foundation and construction is the most complex function in the life of a building.

The health benefits of the hen egg have been known for centuries. Recently, further investigation of the mechanism of the development of an embryo in an egg during incubation revealed the scientific equivalent of the "miracle of life". In earlier studies, whilst monitoring weight gain of the embryo during the incubation period, scientists (1) found very little gain in the first 9-10 days (7.5%), and then a sharp increase (1,190% by end of incubation), suggesting rapid development of a body.

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The potency of the nutrients available to the embryo at this stage has always been assumed to be high, but it was only recently that the chemical structure of the original egg solids for these critical stages was obtained. During the blastodermal to protoembryonic stages of embryogenesis, oligopeptides with small molecular weights were identified. These short chains of amino acids are able to cross the digestive barrier without breaking down or changing the ratios and proportions (5). Peptides are far more potent than other neurotransmitters, requiring only small amounts to produce a profound effect.

Additional, the uptake of the Fibroblast Growth Factor (FGF) (present in PESE) by the embryo sharply increase between days 11 & 12. These embryonic peptides and the FGF have been isolated through a patented process (US Patent 5,641,517) precisely at the right stage of incubation, extracted and freeze dried to bring the *"miracle of life"* benefits to humans.

Extracting PESE before the peptides and FGF are "used up" to build organs and bones, allows us to provide this building, repairing, maintenance mechanism of perfectly balanced amino acids, peptides and growth factors to humans.

How is FGF helpful to humans?

The precise blend of oligopeptides may be seen as building blocks, without a bridge, or a director. The role of such a director is fulfilled by a growth factor known as the Fibroblast Growth Factor, or FGF. FGF is prolific in PESE, as well as in the human placenta. On the *11th* day of the incubation cycle of a chicken egg, the embryonic tissue shows a steep increase in the FGF, with the appropriate peptides to form the solid organs and bones (A1). A detailed day-by-day study was performed in 1988 (A4, A11). Discovered only in the seventies, and also a peptide, this FGF is critical in the development of embryos, including humans. However, it is not found to be circulating in the human adult bodies.

FGF is responsible for building the lining in the blood vessels, creating the infrastructure for the nutrients to flow to critical areas of the brain and organs. Research credits FGF with the potential to directly affect many neuro disorders because of clear result of the ability of FGF to affect the growth of neuritis (A2). Neurites are signal senders (Axons) and signal receivers (dendrites) attached to the brain neurons.

Research (A7) has also shown clearly that new cell cultures show a dramatic increase in peptide and amino acid uptake in the presence of FGF. This result gives credence to the hypothesis that embryonic growth is influenced by a very precise mechanism, which combines unique combinations of amino acids, peptides and FGF.

Since FGF is not circulating in adults, multiple research projects on the effects of FGF serums to cure neuro disorders have been carried out.

Fundamental to the research is the fact discovered by Altman, J. in 1962 (26) that neural STEM cells are formed by the body in response to abnormalities, and are resident in certain zones of the brain. The brain is therefore ready to repair the damage, and these cells have shown to differentiate into a wide range of neurons (A27). Neurons derived from such neural stem cells to FGF permits direct differentiation into the required neural cells (A14, A25).

What else is added to PESE and what benefits does that provide?

To the PESE, we add two important sources of targeted amino acids.

<u>Adding specific, targeted vegetables protein ingredients</u>: Vegetable protein, specifically certain legume proteins, have an essential amino acid profile, which is very close to that of the ideal protein for human nutrition (FAO/WHO 1985 and 2002). For **Lominine**, a patented process further isolates such a protein to eliminate the compounds, which neutralized the benefits of the essential amino acids. The result is an ingredient, which is high in Glutamic acid, (further enhancing the cognitive function of the brain) branched chain amino acids (to counter insomnia), Lysine (to control release of serotonin, controlling moods) and Arginine (promoting NO and growth hormone formation).

<u>Adding Marine Protein</u>: The high level of Glycine in the specifically marine protein, combined with a significant amount of hydroxyproline to stabilize the glycine, make it a primary candidate fro brain food. By itself, Glycine is a neurotransmitter and an important component in memory function, along with glutamate, the salt form of glutamic acid (see vegetable protein above).

Health Benefits of laminine?

Mood Enhancement, controlling depression:

Some 20 million people around the world suffer from depression severe enough to be prescribe medication. Depression is caused by many external factors, including stress. In the brain, the serotonin uptake and release mechanism is affected. Laminine contains the amino acid Lysine; derived from PESE and the vegetable protein. The combination delivers a higher level of Lysine than either ingredient by itself. Lysine is known to regulate serotonin levels in the brain.

Fatigue & Energy:

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Laminine combines the Leucine and Isoleucine (known as branched chain amino acids) from the PESE with an added dose from the vegetable protein extract. Leucine and Isoleucine provide ingredients for the manufacturing of other essential biochemical components in the body, some of which are utilized for the production of energy stimulants to the upper brain and helping you to be more alert.

Memory function is controlled by a well-balanced joint effect of glutamate (salt of glutamic acid) and Glycine. The most pronounced effect of artificial sweeteners and MSG is to interfere with this synergistic performance. We therefore decided to address this issue in the Laminine formulation.

Both these amino acids act together to play a critical role in the ability of the neurons to connect, a cellular mechanism for learning and memory. PESE is low in these amino acids. Therefore, Laminine enhances the levels by the addition of isolated vegetable protein to provide extra glutamic acid and with marine protein extract to provide extra Glycine.

PESE is used to provide the FGF in the aid of memory. FGF is known to build neuritis, the bridges between the neurons and the receptors/transmitter of signals. Research shows FGF also inhibits and destroys mutant protein genes, in this case, quite possibly blocking the genes responsible for memory loss.

In 1962, it was discovered that the neuro stem cells reside in certain parts of the brain, when there is a malfunction. It is also proven that FGF feeds and nurtures these stem cells to help heal any scarred tissue. Lately, compelling arguments have been made to inject FGF directly to cure Huntington's disease, Schizophrenia, OCD and Autism.

The synergistic effect of building the neuritis, nurturing the stem cells, having the most relevant amino acids and factors to guide where the amino acids are to go makes Laminine perform extremely well in memory enhancement.

Cardiovascular Health, Libido Enhancement:

The PESE and vegetable protein provide a very potent dose of Arginine. Arginine is a precursor of nitric oxide, which is one of the few gaseous signaling molecules known, playing a role in a variety of biological processes. The (inner lining) of blood vessels uses intric oxide to signal the surrounding smooth muscle to relax, thus resulting in increased blood flow. Effects include modulation of the hair cycle, and increased libido (through its ability to increase blood flow). Sildenafil Citrate, popularly known by the trade name Viagra, stimulates erections primarily by enhancing signaling through the nitric oxide pathway in the penis.

NO (nitric oxide) is know fro growth hormone formation, increasing defense of the organs against effects of aging.

Skin and Hair:

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Memory:

PESE contains Cysteine, which is a precursor to glutathione, a powerful anti oxidant receiving much attention nowadays for healthier looking skin. The added potent dose of Glycine, (another precursor to glutathione) from our marine protein further enhances the anti aging effect of glutathione.

Glycine from the marine protein also builds collagen, making the skin healthier and less wrinkled.

What is the recommended dosage of Laminine?

We recommend 2 capsules , twice a day for the first two weeks, and 1 capsule, twice a day thereafter.

How is the PESE potency assured?

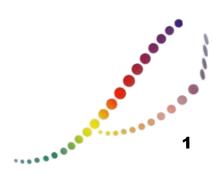
The PESE used in Laminine is derived from eggs, which come from free range hens. There is no confinement or other stressful environment factors, which affect the natural path to the essential life giving ingredients.

Is there any significant cholesterol in the PESE?

No. The egg consumes all the cholesterol during the protoembryonic and early stages. The PESE is derived from egg whites, not yolks.

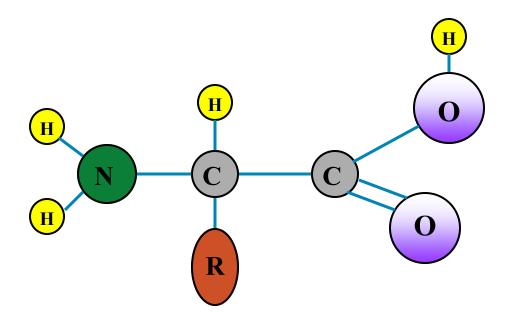


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Summary Of Clinical Research For lominine

Amino Acids are molecules containing an amine group (NH2), a carboxylic acid (COOH) group and a side chain that varies. In a alpha amino acid, the amino and carboxylate groups are attached to the same carbon atom, which is called the *a*-carbon. The various alpha amino acids differ in which (R group) is attached to their alpha carbon.



These side chains can vary in size from just a hydrogen atom in Glycine to a methyl group in Alanine through to a large heterocyclic group in Tryptophan.

Amino Acids are critical to life, and have many functions in metabolism. One particularly important function is as the building blocks of proteins, which are linear (straight) chains amino acids. Every protein is chemically defined by this primary structure, while its unique sequence of amino acid residues, in turn define the three dimensional structure of the protein. Amino acids are linked together in varying sequences to form a vast variety of proteins. Amino acids are also important in many other biological molecules, and due to this central role in biochemistry, they are very important in nutrition.

Amino acids join together to form short polymer chains called peptides or longer chains called either polypeptides or proteins. These polymers are linear and un-branched, with each amino acid within the chain attached to two neighboring amino acids. Twenty-two amino acids are naturally incorporated into polypeptides and are called proteinogenic or standard amino acids. Of the twenty-two standard amino acids, eight are called essential amino acids because the human body cannot synthesize them from other compounds at the level needed for normal growth, so they must be obtained from food. How ever the situation is quite complicated since Cysteine, Taurine, Tyrosine, Histidine and Arginine are semi-essential amino acids in children, because the metabolic pathways that synthesize these amino acids are not fully developed.

The amount required also depend on the age and health of the individual, so it is hard to make general statements about the dietary requirement for some amino acids.

Non-protein functions of Amino Acids : Besides building proteins, many amino acids are used to synthesize other molecules, for example: <u>Tryptophan</u> is a precursor of the neurotransmitter *serotonin*. Almost 80% of the serotonin in a human body is found in the gut, where it is secreted and absorbed into the blood platelets, and help regulate critical functions like blood cotting and wound healing. The remainder is synthesized in serotonergic neurons in the Central Nervous System, where it has various functions, including the regulation of mood, appetite, sleep, muscle contraction, and some cognitive functions including memory and learning.

Glycine is a precursor of *porpyrins*, which is the red pigment in blood.

<u>Arginine</u> is a precursor of *nitric oxide*, which is an important signaling molecule in Mammals. NO is one of the few gaseous signaling molecules known. It is a key vertebrate biological messenger, playing a role in a variety of biological processes. The (inner lining) of blood vessels uses nitric oxide to signal the surrounding smooth muscle to relax, thus resulting in what is called vasolidation which increase blood flow. Nitric oxide is highly reactive (having a lifetime of a few seconds), yet diffuses freely across our body's membranes. These attributes make nitric oxide ideal as a signaling molecule between adjacent cells as well as within a single cell. Effects include vasodilatation, modulation of the hair cycle, and penile erections (though its ability to vasolidate). Sild enafil Citrate, popularly known by the trade name Viagra, stimulates erections primarily by enhancing signaling through the nitric oxide pathway in the penis.

Nitric oxide (NO) contributes to vessel homeostasis by inhibiting vascular smooth muscle contraction and growth, platelet aggregation, and leukocyte adhesion to the endothelium. Humans with atherosclerosis, diabetes or hypertension often show impaired NO pathways.

Glycine and glutamine are precursors of nucleotides. Nucleotides are molecules that, when joined together, make up the structural units of RNA and DNA. In addition, nucleotides play central roles in metabolism. In that capacity, they serve as sources of chemical energy (adenosine triphosphate and guanosine triphosphate). Participate in cellular signaling.

PEPTIDES:

Peptides are short polymers formed form the linking, in a defined order, of *a*-amino acids. Hence depending on the number of amino acids, peptides are called di-peptides, tri-peptides, oligopeptides, etc. Proteins are multi peptide chains.

Small amino acid chain peptides, commonly known as oligopeptides are very easily transported through the intestinal, membrane. They are sometimes used as transport mechanisms for drugs. Protein must be broken down to smaller and smaller peptides, and eventually an amino acid to perform its function. Dietary intake of peptides and amino acids, therefore, can be extremely beneficial.

Peptides are the most abundant compounds in the hypothalamus of the brain, and perform vital functions of communicating sensory impulses to the endocrine system (hormone producing glands). Peptide based hormones-releasing agents from the hypothalamus use the anterior pituitary to signal the thyroid gland, the adrenal cortex, the mammary gland, the ovaries & testicles and the growth hormone.

Understanding the mechanisms of the effect of peptides, and the types of peptides is a complex field, and is being studied extensively. Unfortunately, these studies are done in isolation and disregard the wholistic picture of the complex mechanisms, which exist in our marvelous bodily electrochemical system. Further, the studies are focused on promoting a particular amino acid, peptide or other neurotransmitter.

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While the result identify the final activity with amino acid/peptide, the mechanism of transport of such pritical amino acid/peptides to the final destination is a subject of major arguments. These arguments cast a shadow on the importance of nutritional supplements. Most doctors will tell you nutritional supplements "cannot hurt", but stop short of endorsing them. The reason is the lack of evidence that the active ingredients have been formulated in the correct form, that is, intermediates or ligands that can make the active ingredient available to the nervous or endocrine system of the brain.

At Pendura, we take a different approach. Our goal is to maximize benefits, not profits. We strongly believe that it is not enough to understand the discrete <u>end points</u> of the mechanisms of neurotransmission and regulate of bodily functions. If we are to supplement this complex chemistry machine, we must try and duplicate the entire path to the end result. We are not arrogant enough to claim that we (or the medical community) understand this complex path to the end reaction. Our approach therefore is to use the "natural PATH", (not just isolated natural components) to supplement the role of the amino acids in regulating the complex electrochemical machine we call the human body.

How do we achieve this? Simple : Nature puts the most potent and balanced combination of not only amino acids in short peptide chain form, but also other known (and unknown) factors such as Fibroblast Growth Factor in blastodermal to protoembryonic fluids preceding the formation of the crucial organs and embryo. We believe amino acids (in the form of di and tripeptides) derived from such fluids combined with the growth factors are able to enhance brain function because they are "precisely" engineered to support the most complex stage of birth of a living creature, the beginning; just like the off is the most complex function in the life of a building.

The health benefits of hen egg have been known for centuries. Recently, further investigation of the mechanism of the development of an embryo in an egg during incubation revealed the scientific equivalent of the "*miracle of life*". In early studies, whilst monitoring weigh gain of the embryo during the incubation period, scientists (1) found very little gain in the 9-10 days(7.5%), and then a sharp increase (1190% by end of encubation), suggesting rapid development of a body. The potency of the nutrients available to the embryo at this stage has always been assumed to be high, but it was only recently that the chemical structure of the original egg solids for these critical stages, termed blastodermal to protoembryoinic stages was obtained. During the blastodermal to protoembryonic stages of embryogenesis, oligopeptides with molecular weights from 0.5 to 1.0 kD were identified. Oligopeptides are compounds, which have 2 to 20 amino acids joined by a peptide bond. *These short chains of amino acids are able to cross the digestive barrier without breaking down or changing the ratios and proportions (5). Peptides are far more potent that other neurotransmitters, requiring only small amounts to produce a profound effect.*

Additionally, the uptake of the Fibroblast Growth Factor (FGF) (present in the protoembryonic fluid) by the embryo sharply increase between days 11 & 12. These embryonic peptides and the FGF have been isolated through a patented process (US Patent 5,641,517) precisely at the right stage of incubation, extracted and freeze dried to bring the "miracle of life" benefits to humans. The extract is termed Blastodermal & Protoembryonic stage Extract (BPE).

Extracting the protoembryonic fluid before the peptides and FGF are "used up" to build organs and bones, allows us to provide this building, repairing, maintenance mechanism of perfectly balanced amino acids, peptides and growth factors to humans.

But is a balanced peptide combination sufficient to show such drastic effects as described in testimonials from Laminine users? Nature has devised an extremely versatile mechanism to provide nutrition with miraculous precision to the embryo of living creatures.

The precise blend of oligopeptides may be seen as building blocks, without a bridge, or a director. The role of such a director is fulfilled by a growth factor known as the Fibroblast Growth Factor, or GFG. FGF is a prolific in protoembryonic liquid as well as the human placenta. On the 11th days of the incubation cycle of a chicken egg, the embryonic tissue shows a steep increase in the FGF, with the appropriate peptides to form the solid organs and bones (A1). A detailed day-by-day study was performed in 1988 (A4,A11). Discovered only in the seventies, and also a peptide, this growth factor is critical in the development of embryos, including humans. However, it is not found to be circulating in the human adult bodies.

FGF is responsible for building the linings in the blood vessels, creating the infrastructure for the nutrients to flow to critical areas of the human brain and organs. Research credits FGF with the potential to directly affect many neuro disorders because of clear results of the ability of FGF to affect the growth of neuritis (A2). Neurites are signal senders (Axons) and signal receivers (dendrites) attached to the brain neurons.

Research (A7) has also shown clearly that new cell cultures show a dramatic increase in peptide and amino acid uptake in the presence of FGF. This result gives credence to the hypothesis that embryonic growth is influenced by a very precise mechanism, which combines unique combinations of amino acids, peptides and FGF. *Since FGF is not circulating in adults, multiple research projects on the effects of FGF serums to cure neuro disorders have been carried out.*

Fundamental to the research is the fact discovered by Altman, J in 1962 (A26) that multipotent neural STEM cells are formed by the body in response to abnormalities, and are resident in the Subventricular, subepyndymal and hippocampal subgranular zones. The brain is therefore ready to repair the damage, and these cells have shown to differentiate into a wide range of neurons (A27). Neurons derived from such neural stem cells are capable are capable of migrating to various regions of the Central Nervous System. Over a decade of work, both in vivo and ex vivo has revealed that exposure to such neural stem cells to growth factors such as FGF permits direct differentiated as well as undifferentiated in adult brains as well as organs can be nourished if the growth factor were present with the correct balance of peptides and amino acids, becomes the heart of the Laminine story. At Pendura, we have had faith that the natural serum contained in BPE MUST have all the factors (known and unknown) needed for embryo nourishment, because millions of years of flawless reproduction is proof. However, we also feel it is important for us to understand (to the best of "human" abilities) the "known" mechanisms and explain them to our customers. Our explanation should make it clear that simulating nature is not a n easy task, and though the natural route to neuro nutrition is more expensive, we prefer that route to approach our competitors take formulating the "known" components.

The BPE in Laminine provides a natural, evolved base of low molecular weight oligopeptides of precise proportions with rapid transport through the digestive tract and neurotransmitter functions. Along with the peptides, the Fibroblast growth factor is also extracted at an optimum time, giving an extremely potent combination of nourishment to the existing stem cells in the adult body, as if the placenta was made available to them in adulthood.

Having found the mechanism and dominating factors, Pendura looked at the compatibility of modern day stress with embryonic nourishment. Modern life puts pressures on our mental health which evolution has not caught up with. *Laminine takes the extraordinary blend of benefits from BPE and complements the amino acids with a precise formulation of balancing and enhancing peptides to "turbo charge" the effects from BPE related to brain activity.* Having nature provide us with the mechanisms to transport and direct the amino acids, peptides and FGF required to deal with the modern life, <u>Laminine provides benefits like no other nutritional supplement.</u>

Adding specific, targeted vegetables protein ingredients: Vegetables protein, specifically certain legume proteins, have an essential amino acid profile, which is very close to that of the ideal protein for human nutrition (FAO/WHO 1985 and 2002).

For Laminine, a patented process further isolate such a protein to eliminate the compounds, which neutralize the benefits of the essential amino acids. The result is an ingredient, which is high in Glutamic acid, (further enhancing the cognitive function of the brain), branched chain amino acids (to counter insomnia), Lysine (to control release of serotonin, controlling moods) and Arginine (promoting NO and growth hormone formation). The specially isolated protein therefore adds a synergistically potent composition to enhance brain activity.

Adding Marine: The high levels of Glycine in the specially extracted marine protein, combined with a significant amount of hydroxyproline to stabilize the glycine, makes it a primary candidate for brain food. By itself, Glycine is a neurotransmitter, primarily utilize by the brain to control glutamate levels. As a combination with BPE, it becomes a powerful force to enhance memory function in the brain.

Based on the testimonials received by consumers of Laminine and placebo studies done on individual components of Laminine, we were inspired to investigate the mechanisms that affect the positive results reported, specially the neurological effects. We found multitudes of studies, which point to either the amino acids/peptides or FGF as isolated causes of similar, but less significant result. Unfortunately, in our opinion, the two different paths of research have not connected the relevance of the two components working in harmony and cohesion. At Pendura, we believe working together, these nutrients produce far more potent results, and our custumers' testimonials are proof.

We therefore present the research on these ingredients in a bifurcated manner, combined with proof that cell cultures have a sharp increase in uptake of amino acids and peptides (A7), it should be obvious that the optimal way to nourish one's brain function is by a combination of FGF and oligopeptides.

Increased workout ability due to rapid healing of stressed (wounded) muscles. Di-peptide Carnosine (a peptide containing amino acids alanine and histidine) has been found to improve healing of wounds (1). Unhealed wounds are a constant source of inflammatory mediators and a substrate for infection. As such, they prolong the recovery of injured patients and may lead to multiple organ failure and death. It is believed that oligopeptides generated from dietary intake play a role in optimizing growth and healing. These peptides ay directly stimulate cells involved in the growing or healing process or may act directly by augmenting the production of growth factors. Indeed FGF2 has been shown to heal wounded tissue and organs effectively. FGF2 is produced by the body in response to an external injury, to provide nutrition to the new stem cells for repair. (A28, A13).

In a 1997 study, immediately following surgery, (animal) subjects were randomized to receive either amino acid diet or peptide diet for 10 days and the strength of the wound was measured. Wound bursting pressure was found to be significantly higher in subjects receiving the peptides diets than in those just receiving amino acid diets. The authors suggest that dietary peptides may stimulate the production of growth factors such as growth hormone, insulin, or insulin growth factor (IGF-1). They also postulate that it is possible that the amino acid entry into the cell via peptide transporters is more efficient for stimulation of protein synthesis than entry in the form of just amino acids. Other possible mechanisms suggested by the authors for the increased wound healing with peptide versus non peptide diets include stimulation of collagen synthesis, increased blood flow to the wound, free radical scavenging, and generation of cytokine profiles which better support wound healing. ·····

Stress, weight gain and Cortisol: The body releases cortisol when under stress. Cortisol raises the sugar evel in the blood, increases blood pressure and performs a myriad of functions to help maintain balance. Unfortunately, evolution has not caught up with undue stress such as traffic jams, mean bosses, etc. and the cortisol released during such situation contributes to weight gain, blood pressure irregularities and hypertension. One of the mechanisms identified with the embryonic peptides contained in Laminine works via elevation of 17-ketosteroid levels in the adrenal glands, which improve anabolism through increased synthesis of androgens and a decrease in (the catabolic hormone) cortisol, which offer multiple health benefits (2). The elevation could be the result of a synergistic effect of the peptides with with FGF2, as explained in a 1977 paper (A32), in which FGF2 is described as working in cohesion with ACTH (main source or signal for cortisol production) to regulate cell production and inhibition.

Dementia/Alzheimer's and other neurodisorder symptoms: In a 1994 study (2), the pulvinar nuclei of nine patients with histologically confirmed Alzheimer's disease and twelve young (9-28 years of age) and age matched controls (without dementia and with non-Alzheimer's dementia) were examined using a battery of histopathalogical methods. All patients with Alzheimer's disease had numerous lesions, while control patients with and with out dementia had very few Alzheimer's lesions. If some of these lesions as well as many impaired organs and lesions within the brain could partially be considered wounds, they may be able to benefit from the rapid healing by carnosine explained above.

A compelling arguments has been made to use FGF as *a treatment for Huntington's Disease* and other degenerative neural diseases (A23). In 2005, the John Hopkins University School of Medicine conducted a study in which they used FGF2 as a neurogenesis factor, and found that the FGF increased proliferation of the stem cells by 5 times. We believe results could be even better if the right blend of amino acids and peptides were also available to the stem cells as nutrition when the FGF connects with the stem cells. Other studies have focused on the used of FGF for regulation of the Central Nervous System neurogenesis. A 2005 paper (A24) from University of Louisville, reviews what we consider to be Pendura's view. The review focuses on the emerging view among the medical community that localized and overlapping pathways of growth factors, metalloproteases, neurotransmitters, and hormones regulate different aspects of neurogenesis within the neurogenic niches. They suggest further elucidation of crucial molecular regulators and integration of their signaling cascades should lead to mor rational and effective approaches to harness the adult CNS neurogenesis. The story is similar to the neuro disorders:

Regarding autism, schizophrenia and OCD.

Flora M. Vaccarino, M.D., at the Yale School of Medicine, writes concerning Fibroblast Growth Factor 2: "The cerebral cortex controls higher cognitive functions. Connection between the cortex and basal ganglia control motor and cognitive programs, whereas connections between the cortex and the medial temporal region and amygdale mediate emotional behavior. Abnormalities in the development of the cerebral cortex and associated structures have been suggested to occur in several neuropsychiatric disorders, including schizophrenia, autism and obsessive compulsive disorder.

The human cortex is about 1000-fold greater than that of the mouse. This increase is largely due to an increase in surface area. Cortical surface area may be correlated with a higher capacity to perform increasingly complex cognitive operations.

Cerebral cortical neurons are generated during embryogenesis by the proliferation of cells situated around the lateral ventricles. Three factors can potentially influence the total number of cells generated and thus the final size of the cerebral cortex. These are the number of cortical progenitor cells presents before neurogenesis starts (the founder cell population), the number of proliferative cycles these cells undergo before differentiating, and the amount of cell death. ·····

Fibroblast growth factor 2 (FGF2), is a potent mitogen for cortical progenitor cells in vitro, particularly for the precursors og glutamatergic neurons (Vaccarino et al, Cerebral Cortex, 1995). The microinjection of FGF2 in the cerebral ventricle of rat embryos increases the proliferation of cortical progenitors in vivo, resulting in a dramatic expansion of cerebral cortical volume, total cell number and surface area (Vaccarino et al, Neuoscience Abstracts, 1995). FGF2 expands the size of the cortex by 50%, without altering its morphological features. These findings are of great interest from a development and evolutionary prospective and hold therapeutic promise as well, since FGF2 is one of the factors that is capable of maintaining the proliferation of stem cells in the adult mammalian brain.

Recovering from Stroke: Carnosine has recently been a focus of attention as a potential therapeutic agent for strokes have emerge from the demonstration of its neuro-protective capabilities. In a 2008 paper investigation (3) the role of carnosine as a potential therapeutic agent for stroke from demonstration of neuroprotective capabilities, cites a 2001 study (12) in which carnosine treatment reduces the infarct volume (infarct volume is a common index for a assessing the extent of brain injury) by 42.5% compared to treatment with other peptides. The authors state that their HPLC data suggests that exogenously administered carnosine results in increased cerebral levels. They prove that in response to a pMCAO (occlusion of the middle cerebral artery) carnosine immunoreactivity is enhanced in the brain.

In a separate study (A28), FGF2 was tested as a potent neurotrophic and angiogenic peptide. The rat with the FGF treatment showed decrease in infarct volume by 44%. FGF2 has also been shown by a study in 2005 (A23) to "block" cell death induced by mutant genes. They strongly suggest that FGF2 with the proper nutrients to back it up, first blocks further degeneration, and proceeds to heal neural tissue. FGF has also been shown to reduce toxicity in the neuron striatal cultures (A25).

Improved Vision: Depletion of glutathione has been proven to cause an uncoupling effect on retinal horizontal cells through oxidative stress. Glutathione is a a tripeptide thiol compound and is a substrate for scavenging reactive oxygen radicals or toxins through the enzymes glutathione peroxidase and glutathione reductase (4). In a 1999 study, Z.Y. ZHOU et al measured the retina effects of glutathione depletion in Carp by partially depleting it with glutathione inhibitor, L-buthionine sulfoximine (BSO). They measured the glutathione immediately after the electrophysiological experiments in each preparation. The glutathione was allowed to recover over 4-7 days. During this period, H1 cel response to red light was measured. The response measuring technique showed that 4 days after the injection of BSO, the response was much higher. It is postulated that glutathione serves as a physiological reductant to protect critical sulfhydryl groups from oxidation by hydrogen peroxide and other oxidants (13).

Motivation/Depression: A double blind study has proven the powerful Glycine activity to elevate 17-ketosteroid levels in the adrenal glands, which improve anabolism through increased synthesis of androgens and a decrease in the catabolic hormone cortisol (6). Patients with mild to moderate mood disorders according to Hamilton ratingscale (Ham-D) and Beck Depression Inventory (BDI) were included in the study according to the protocol. The patients were randomly assigned to receive placebo, preventTM or Deprevent[™] Forte (commercial products with BPE) fro 12 weeks. The main outcome was change in the Ham-D total score from baseline to 12 weeks as well change in BDI from baseline to controls after 3, 6 and 12 weeks. 57 patients concluded the study. There was a significant effect in favor of the two active groups, however, it was no significant difference in the outcome measures, even if it was a weak tendency in favor of the Deprevent[™] Forte group. It was no reports of adverse effects in any of the groups during the study. Other studies have shown certain oligopeptides modify temporarily the inborn properties of the hypothalamics motivation centers (7,8).

7

In a 2006 study, several universities collaborated to publish a paper, which showed lack of FGF2 as a , major factor in depressed individuals brains.

<u>Blood Pressure Regulation</u>: In her Doctoral Thesis, Tina Jauhianen showed Tripeptides IPP (isoleucyl-prolyl-proline) and VPP (valyl-prolyl-proline) reduce hypertension (11) by inhibiting Angiotensin Converting Enzyme (ACE). ACE converts the body's Angiotensin I to Angiotensin II, which contracts blood vessels, resulting in high blood pressure.

The clearest result regarding the effect on blood pressure was achieved in 24-hour ambulatory blood pressure measurement; the difference between the group that received peptides and the placebo group in lowering systolic and diastolic blood pressure was statistically significant. The 24-hour ambulatory measurement method is considered the most reliable.

A 1998 study done in Germany showed that lack of FGF2 impaired cerebral cortex development, subsequently affecting the ability of the subject mice brains to regulate their blood pressure.

<u>Reduction in Arthritic Pain, Joint pain</u>: In the late eighties and nineties, several studies (A33,A34,A35) have proven that *FGF2 plays a major role in the process of balancing the synovial fluid* (joint fluid) and *growth of new bone cells through different pathways*. Bone growth *was observed on implants as well as natural bones*.

Summary:

We have outlined plausible explanation above for the benefits experienced by consumers of Laminine. As we move forward with this amazing product, we are certain there will be other testimonials with other benefits and will investigate the possible mechanisms for such benefits. An analysis of the Laminine formulation gives us an insight into the amino acids present. Tests also confirm these amino acids are present mostly as oligopeptides. FGF2 has been confirmed in chick embryos by many studies after day 11, and in the protoembryonic liquid (A1, A3, A4, A9, A10, A11). If the peptides and growth factors are available for the maintenance, repair or building of the neuro system, there should be sufficient reason to believe it has far more outreaching effects than what we have experienced so far. We feel this si just the beginning of our investigations.

REFERENCES:

- (1) Roberts, Pamela R, et al. Nutrition Vol. 14, No. 3, 1998
- (2) Kuljis, Rodrigo O. Jour. of Neuropathology & Exp. Neur., 1994
- (3) Jiangyong Min, et al. Jour. Of Neuroscience Res., 86:2984-2991 (2008)
- (4) Z.Y. Zhou, et al. Neuroscience, Vol. 90, No. 4, 1493-1499, 1999
- (5) Arvanitakis, Constantine. Am. Jour. of Physiology, Vol.231, No. 1, July 1976.
- (6) Kristoffer, ester S., ETC Research & Development, Oslo, Norway.
- (7) Zilov, V.G. et al, Byulleten' Eksperimental'noi Biologii I Meditsiny, Vol. 114, No. 11, pp 455-457, Nov. 1992.
- (8) Sudakov, K.V., Zhurnal Vysshei Nervnoi Deyatel'nosti imeni I.P.Pavlove, Vol.37, No.1, pp. 78-87, Jan-Feb 1987.
- (9) Mihaescu G, Olinescu R & Oancea F. Significant modification of lipid metabolism in aged persons following treatment with a nutritive supplement containing embryonary peptides-preliminary results. Rom J Inter Med 2005;43:133-139.
- (10) Physiological Ontogeny. A. Chicken Embryos, Henry A. Murray, Jr., Rockefeller Institute for Medical Research.

(1) Jauhianen, Tina et al. Journal of Nutrition, Vol 2010, Article # 287030.

(12)Rajanikant et al, 2007

(13) Meister, A.J.Bio. Chem. 263, 17,205-17,208

(A1) Joseph-Silverstein, Jacquelyn, et al (June 1989) Basic Fibroblast Growth Factor in the Chick Embryo: Immunolocalization to Striated Muscle Cells and Their Precursor.

The Journal of Cell Biology, 108:2459-2466.

(A2) Hatten, M. E., et al (1988) In Vitro Neurite Extension by Granule Neurons is Dependent upon Astroglial-Derived Fibroblast Growth Factor. Development Biology, 125:280-289.

(A3) Kardami, Elissavet, et al (1985) Selected Muscle and Nerve Extracts Contain an Activity which Stimulates Myoblast Proliferation and which is distinct from Transferring. Development Biology, 112: 353-358.

(A4) Seed, Jennifer, et al (1988) Fibroblast Growth Factor Levels in the Whole Embryo and Limb Bud during Chick Development. Development Biology, 128: 50-57.

(A5) Risau, Werner, Ekblom, Peter (September 1986) Production of a Heparin-binding Angiogenesis Factor by he Embryonic Kidney. The Journal of Cell Biology, 103:1101-1107.

(A6) Gospodarowicz, Denis, et al (December 1983) Bovine Brain and Pituitary Fibroblast Growth Factors: Comparison of Their Abilities to Support the Proliferation of Human and Bovine Vascular Endothelial Cells. The Journal of Cell Biology, 97:1677-1685.

(A7) Gospodarowicz, D, et al (1986) Molecular and Biological Characterization of Fibroblast Growth Factor, an Angiogenic Factor Which Also Controls the Proliferation and Differentiation of Mesoderm and Neuroectoderm Derived Cells. Cell Differentiation, 19: 1-17.

(A8) Gospodarowicz, D, et al (1986) Effect of Fibroblast Growth Factor and Lipoproteins on the Proliferation of Endothelial Cells Derived From Bovine Adrenal Cortex, Brain Cortex and Corpus Luteum Capillaries. Journal of Cellular Psychology, 127: 121-136.

(A9) Giussani, Dino A, et al (2007) The Role of Oxygen in Prenatal Growth: Studies in the Chick Embryo. The Physiological Society, 585.3:911-917.

(A10) Sutendra, Gopinath, Michelakis, Evangelos D (2007) the Chicken Embryo as a Model for Ductus Arteriosus Developmental Biology: Cracking into New Territory, the American Physiological Society, 292:R481-R484.

(A11) Seed, Jennifer, et al (1988) Fibroblast Growth Factor Levels in the Whole Embryo and Limb Bud during Chick Development. Development Biology, 128:50-57.

(A12) Gospodarowicz, D, et al (1986) Molecular and Biological Characterization of Fibroblast Growth Factor, an Angiogenic Factor Which Also Controls the Proliferation and Differentiation of Mesoderm and Neuroectoderm Derived Cells. Cell Differentiation. 19:1-17

(A13) Houchen, Courtney W, et al (1999) FGF-2 Enhances Intestinal Stem Cell Survival and its Expression is induced after Radiation Injury. The American Physiological Society.

(A14) La Spada, Albert R (December 2005) Huntington's Disease and Neurogenesis: FGF-2 to the rescue? Vo. 102

(A15) Barrett, Andrea Lynn (December 2007) A FGF-Hh Feedback Loop Controls Stem Cell Proliferation in the Developing Larval Brain of Drosophila Melanogaster.

(A16) ito, Tomoni, et al (2007) FGF-2 Suppresses Cellular Senescence of Human Mesenchymal Stem Cells by Down-Regulation of TGF-B2. Biochemical and Biophysical Research Communication, Vol. 359.

(A17) Gospodarowicz, D, et al (1986) Effect of Fibroblast Growth Factor and Lipoproteins on the Proliferation of Endothelial cells derived from Bovine Adrenal Cortex, Brain, and Corpus Luteum Capillaries. Journal of Cellular Physiology, 127: 121-136.

(A18) Hatten, M. E., et al (1988) In Vitro Nuerite Extension by Granule Neurons is Dependent upon Astroglial-Derived Fibroblast Growth Factor. Developmental Biology, 125:250-289.

(A19) Tropepe, Vincent, et al (1999) Distinct Neural Stem Cells Proliferate in Response to EGF and FGF in the Developing Mouse Telencephalon. Development Biology, 208:166-188.

(A20) Palmer, T.D., et al (1995) FGF-2 Responsive Neuronal Progenitors Reside in Prolifereative and Quiescent Regions of the Adult Rodent Brain. Molecular and Cellular Neuroscience, 6: 474-486.

(A21) Curtis, Maurice A, et al, (July 2003) Increased Cell Proliferation and Neurogenesis in the Adult Human Huntington's disease Brain, Vol.100.

(A22) Taylor, J. Paul, et al, (June 2002) Toxin Proteins in Neurodegenerative Disease. Science's Compass, Vol. 296.

(A23) Jin, Kunlin, et al (Dec. 2005) FGF-2 Promotes Neurogenesis and Neuroprotection and Prolongs Survival in a Transgenic Mouse Model of Hunting's disease, Vol.102.

(A24) Hagg, Theo (2005) Molecular Regulation of Adult CNS Neurogenesis: an Integrated View.

(A25) Bjugstad, K.B., et al (2001) IGF-1 and bFGF Reduce Glutaric Acid and 3-Hydroxyglutaric Acid Toxicity in Striatal Cultures.

(A26) Altman, J. (1962) Science 132:1127-1128.

(A27) Arlotta, P., et al (2003) Exp. Gerontol, 38:173-182.

(A28) Watanabe, Takuji, et al (2004) Postischemic Intraventicular Administration of FGF-2 Expressing Adenoviral Vectors Improves Neurologic Outcome and Reduces Infarct Volume after Transient Focal Cerebral Ischemia in Rats. Journal of Cerebral Blood Flow and Metabolism, 24:1205-1213.

(A29) Dono, Rosanna, et al (1998) Impaired Cerebral Cortex Development and Blood Pressure Regulation in FGF-2-Deficient Mice. The EMBO Journal, 17:4213-4225.

(A30) Neurology, The Lancet (December 2004) Vol. 3.

(A31) Gaughran, Fiona, et al (2006) Hippocampal FGF-2 and FGFR1 mRNA Expression in Major Depression, Schzophrenia and Bipolar Disorder. Brain Research Bulletin, 70:221-227.

(A32) Horsby, Peter J., Gill, Gordon N. (August 1977) Hormonal Control of Adrenocortical Cell Proliferation. The Journal of Clinical Investigation, 60:342-352.

(A33) Manabe, N, et al (1999) Involvement of Fibroblast Growth Factor-2 in Joint Destruction of Rhematoid Arthritis Patients. British Society for Rheumatology.

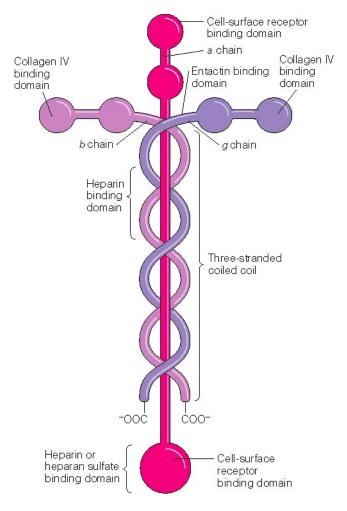
(A34) Sahmi, Malika, et al (1999) FGF Signaling Inhibits Chondrocyte Proliferation and Regulates Bone Development through the STAT-1 Pathway. Genes & Development, 13:1361-1366.

(A35) Takechi, Masaaki, et al (2008) Effect of FGF-2 and Melatonin on Implant Bone Healing: A Histomorphometric Study. Master Med, 19:2949-2952

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Colossian 1:15-17

He is the image of the invisible God, the firstborn of all creation. For by Him all things were created, in heaven and on earth, visible and invisible, whether thrones or dominions or rulers or authorities-all things were created through Him and for Him. And He is before all things, and in HIM all things HOLD TOGETHER.