

# **The Effect of a Colostrum Extract of Proline Rich Polypeptides (PRP) on Immune Status in Guinea Pigs and Its Implications on the Potential of PRP in Aging Humans**

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# Objectives

- To promote an understanding of the active immune peptides in colostrum called Proline Rich Polypeptides (PRP)
- To demonstrate the immune modulating potential of PRP in the animal hypersensitivity model
- To relate the potential immune modulating power of PRP to the health of humans who experience neuroendocrine / immune imbalance related to:
  1. high cortisol levels found in stress and with aging.
  2. Low GH levels found in stress and aging

# Introduction

- Proline Rich Polypeptides (PRP) are active immune modulating peptides found in all mammalian colostrum.
- In particular PRP are thought to :
  1. modulate thymus function,
  2. specifically the T helper 1 / T helper 2 (Th1 / Th2) balance.
- Th1 and Th2 are classified on the basis of the cytokines they produce.

# Introduction (cont.)

- To demonstrate the efficacy of PRP in lessening Th2 over-activity an experiment was performed on guinea pigs sensitized to egg protein.
- Exposure to egg protein resulted in development of acute phase bronchial spastic reaction in 100% of animals, 50% of whom died from suffocation.
  1. The duration of acute phase in the three surviving animals was 5 minutes on average.
  2. Introduction of PRP prior to egg protein inhalation resulted in death of only 2 animals out 7 (28.6%).
  3. Development of acute bronchial spastic reaction on exposure to the antigen was completely blocked by PRP in the remaining 5 animals.

# Introduction ( cont.)

- In humans the thymus is very sensitive to *stress hormones* (cortisol) which also promote Th2 over activity, favoring tumor growth, and lessens Th1 immunity, favoring infection. Cortisol / DHEA ratios favor cortisol over DHEA with aging.
- Further, *thymopoiesis* is diminished with diminishing Growth Hormone (GH) secretion, which itself is diminished with aging.
- This study supports the hypothesis that an understanding of the potential of PRP from or in colostrum to modulate thymus / immune function in humans may be of import to the antiaging health professional interested in maintaining *optimal immune function* in the aged, especially in the *distressed*.

# Colostrum: Nature's Prime Zoonutrient!

- Just as certain fruits and vegetables are naturally rich in special health promoting chemicals called *phyto-nutrients*, certain animal sourced foods are rich in special health promoting compounds called *zoo-nutrients* (pronounced zoo' -o-nutrients). The richest of all zoonutrients is the “first meal” of all mammals, called *colostrum*.

# Colostrum: Nature's Super Zoonutrient! (cont.)

- Colostrum provides a *macro and micro nutrient* dense “super food”.
- This “first meal” for all mammals is also rich in cell signaling messengers that support the immune system both actively and passively, while promoting rapid growth via growth factors, passive immune factors and active immune system modulating peptides.
- These are the *zoonutrients*

# Zoonutrients defined

- Zoonutrients may be defined as compounds found in foods derived from animal beyond the usual macronutrients (fat, protein, carbs) and micronutrients (vitamins and minerals) foods that nonetheless have a salubrious effect on physiology.
- Examples: peptides, enzymes, glycoconjugates, special amino acid bonds

# What are the main components in Colostrum ?

- Nutritional Components
- Growth Factors
- Immune Factors
- Other Health Related Components
- Proline-Rich Polypeptides (PRPs)

# Nutritional – Vitamins

- Thiamin (Vitamin B1)
- **Riboflavin (Vitamin B2)**
- Pantothenic Acid ( B5)
- Pyroxidine (Vitamin B6)
- **Folic Acid (B9)**
- Vitamin B12
- Vitamin E
- Vitamin A (from beta-carotene)
- Retinoic Acid
- Vitamin C

# Nutritional – Minerals

- **Calcium**
- Chromium
- Iron
- Magnesium
- Phosphorus
- Potassium
- Sodium
- Zinc

# Nutritional - Fats

- Milk Fat
  - Provides essential fatty acids for cell development and acts as an energy source. Colostrum's milk fat profile is similar to that of "spring milk" in that it contains a higher percentage of **unsaturated fatty acids**.
- Milk Fat Globule Membrane (liposomes)
  - Contains compounds, such as sphingomyelin, cephalin, phos. choline and phos. serine that assist in development of the mucosal barrier, liver function, brain function, and immune function

# Nutritional - Carbohydrates

- Lacto-oligosaccharides
  - promote the growth of good bacteria in the intestine.
- Sialyl-oligosaccharides and sialyl-glycoconjugates
  - have an immune function in the intestine,
  - are involved in brain and nerve development,
  - and in cell to cell recognition

# Growth Factors

- Growth factors help signal *growth, repair and regeneration* of tissue.
- For example, colostrum is known in the cosmetic industry as a natural source of Epithelial Growth Factor, which is thought to enhance the regeneration of skin and maintenance of skin elasticity.
- Similarly, colostrum is believed to enhance the regeneration of stomach and gut cells, and reduce the intestinal permeability to bacteria and viruses associated with *leaky gut syndrome*.

# Growth Factor Peptides

- Growth hormone (GH)
- Insulin type growth factor (IGF-1)
- Insulin type growth factor (IGF-2)
- Transforming growth factor (TGF-alpha)
- Transforming growth factor (TGF-beta)
- Epidermal-GF
- Fibroblast-GF
- Platelet-derived-GF

# Passive Immunity Factors – Ig Antibodies

- Immunoglobulin type G (IgG1)
- Immunoglobulin type G (IgG2)
- Immunoglobulin type A (IgA)
- Immunoglobulin type M (IgM)
- Immunoglobulin type D (IgD)
- Immunoglobulin type E (IgE)
- secretory IgA
- IgA specific helper

# Bio-Active Immune Modulators: Proline-Rich Polypeptides

- PRPs are short chains of amino acids, called polypeptides, with a molecular weight of 500-5000 Da, with a high concentration of the amino acid proline.
- PRPs are also known as info-peptides, info-proteins, cytokine precursors, or immune-modulators.
- They support the regulation of the thymus, the gland responsible for the normal development of immunologic function in the body.
- They are generally characterized by PRP1 thru PRP5, with PRP2 and PRP3 most active.

## PRP % Concentration in colostrum

- The concentration of PRPs in whole colostrum powder is between 1-3% of the total powder weight.
- Specially fortified whole colostrum contains 5-6 % PRPs!
- Most manufacturers of colostrum powders remove the PRP fraction, lactose, minerals and water, using ultrafiltration technology, to elevate the protein / IGG content of the powder.
- This then reduces the *active* immune modulating effectiveness of the colostrum powder.



## APS-18FI -Biopharma (BP)

### Description and Suggested Applications

APS-18FIBP is an instantized whole colostrum powder, with PRPs coated with a Biopharma's Liposome binder. This product is a custom product for Biopharma. It is produced from flash pasteurized colostrum liquid collected only from the first two milkings after birth. APS-18FIBP is processed both at low pressures and temperatures and is spray dried using indirect steam to maintain maximum bio-activity. The colostrum used to produce APS-18FIBP is from antibiotic free sources. The solubility is excellent. It is also lactose-free <0.4% on a wet-basis.

Suggested applications include: immune system enhancement, nutritional supplement, digestive health improvement, protein supplement and alternative treatment for general health.

### Analytical and Microbiology Analysis\*

	<u>Specification</u>	<u>Typical</u>	<u>Method</u>
Protein % (Nx6.38) db	45.0 min	50.0	Kjeldahl
Immunoglobulins %	15.0 min	18.0	HPLC (dry basis)
Lactoferrin %	0.5 min	1.75	HPLC (dry basis)
Moisture %	5.5 max	4.5	CEM
Ash %	9.0 max	7.0	Mass Spec.
Fat %	25.0 max	22.0	Mojonnier
Lactose %	1.0 max	0.4	HPLC
Proline Rich Polypeptide	5.50min	6.1	HPLC
Liposome %	0.50min	0.55max	By weight.
Sediment	B	A	Pad
pH	6.5 < 7.5	7.0	10% sol., 20C
Bulk density	0.3 < 0.5	0.35	grams / cc
Standard Plate Count (CFU/g)	50,000 max	10,000	Standard**
Yeast and Mold (CFU/g)	10 max	<10	Standard**
Coliform (CFU/g)	10 max	<10	3M Petrifilm
E.Coli (CFU/g)	10 max	<1	3M Petrifilm
Salmonella sp.	Neg. / 200g	Neg.	ELISA
Listeria sp.	Neg. / 25g	Neg.	ELISA
Antibiotics	Neg.	Neg.	CHARM
Pesticides	Neg.	Neg.	DELVO

### Mineral Analysis\* and Physical Properties

<u>Minerals</u>	<u>Specification mg/100gm</u>	<u>Typical mg/100gm</u>	<u>Heavy Metals</u>	<u>Properties</u>
Sodium	150 < 300	250	Lead <1ppm	Solubility: Good
Calcium	250 < 500	350	Nickel <1ppm	Color: Soft yellow
Phosphorus	250 < 400	300	Mercury <1ppm	Flavor: Clean & Bland
Potassium	450 < 750	500	Arsenic <0.2ppm	Odor: Clean
Magnesium	30 < 60	50		Appearance: Free flowing
Chloride	< 200	50		& non-caking

### Packaging, Shipping and Storage

APS-18FIBP powder is packaged in color labeled bleached corrugated boxes with a polyethylene liner. The box is 20 in. x 15.5 in. x 14.5 in. Each box holds 15 kg net. There are 24 boxes per pallet. Colostrum proteins are hygroscopic and can absorb odors. Temperatures below 75 degrees F, relative humidity below 65% and an odor free environment will extend storage life. Stocks should be used in rotation and preferably within three years from date of manufacture.

## Description and Suggested Applications

APS-18FI is a pasteurized, 100% whole colostrum powder produced from raw colostrum collected only from milkings within 16 hours after birth. APS-18FI is processed both at low pressures and temperatures and is spray dried using indirect steam to maintain maximum bio-activity. The colostrum used to produce APS-18FI is from antibiotic free sources. APS-18FI is encapsulated with a milk bio-lipid coating to help the colostrum transfer into the upper intestine without denaturing.

Suggested applications include: immune system enhancement, nutritional supplement, digestive health improvement, protein supplement and alternative treatment for general health.

## Major Active Component Analysis

	<u>Specification</u>	<u>Typical</u>	<u>Method</u>
Protein % (Nx6.38) db	45.0 min	50.0	Kjeldahl
Total Immunoglobulins %	18.0 min	22.0	HPLC (dry basis)
Immunoglobulins (Type G1 & G2) %	15.0 min	18.0	HPLC (dry basis)
Immunoglobulins (Type A) %	2.0 min	2.60	HPLC (dry basis)
Immunoglobulins (Type M) %	0.75 min	1.40	HPLC (dry basis)
Immunoglobulins (Type D) %	0.15 min	0.20	HPLC (dry basis)
Immunoglobulins (Type E) %	0.10 min	0.15	HPLC (dry basis)
Lactoferrin %	0.5 min	0.75	HPLC (dry basis)
Transferrin (mg/g)	3.0 min	4.50	HPLC (dry basis)
Lactoperoxidase-thiocyanate %	0.3 min	0.45	HPLC (dry basis)
Proline-Rich Polypeptides (PRPs) %	3.0 min	4.0	HPLC (dry basis)
Insulin Growth Factor (Type 1) µg/g	1.0 min	2.3	ELISA (dry basis)
Insulin Growth Factor (Type 2) ng/g	100 min	140	ELISA (dry basis)
Derived Platelet Growth Factor ng/g	3.5 min	4.2	HPLC (dry basis)
Epidermal Growth Factor µg/g	0.8 min	1.1	ELISA (dry basis)
Fibroblast Platelet Growth Factor ng/g	4.0 min	5.0	ELISA (dry basis)
Transforming Growth Factor Alpha ng/g	15.0 min	22.0	ELISA (dry basis)
Transforming Growth Factor Beta mg/g	0.15 min	0.21	ELISA (dry basis)
Nerve Growth Factor ng/g	8.0 min	11.0	ELISA (dry basis)
Leptin ng/g	35.0 min	50.0	ELISA (dry basis)

## Vitamin Analysis\*

Vitamin B6 µg/g	10.0 min	15.0	Mass spec. (wet basis)
Vitamin B12 µg/g	0.10 min	0.16	Mass spec. (wet basis)
Vitamin E µg/g	0.15 min	0.20	Mass spec. (wet basis)
Vitamin A µg/g	15.0 min	20.0	Mass spec. (wet basis)
Vitamin C µg/g	0.25 min	0.40	Mass spec. (wet basis)
Vitamin D µg/g	1.00 min	1.20	Mass spec. (wet basis)
Thiamin (Vitamin B1) µg/g	100.0 min	150	Mass spec. (wet basis)
Folic Acid µg/g	2.0 min	2.3	Mass spec. (wet basis)
Pantothenic Acid µg/g	2.0 min	2.3	Mass spec. (wet basis)
Riboflavin (Vitamin B2) µg/g	50.0 min	60.0	Mass spec. (wet basis)
Beta-carotene µg/g	180 min	220	Mass spec. (wet basis)
Glycoconjugates µg/g	2.0 min	2.4	Mass spec. (wet basis)
Glycogen µg/g	40.0 min	56.0	Mass spec. (wet basis)
Retinoic Acid µg/g	5.0 min	8.0	Mass spec. (wet basis)

# Unique PRP Enriched Colostrum

- PRP enriched colostrum is unique in that it only uses:
- whole colostrum, extra rich in PRPs, from pasture feed cows that are antibiotic, growth hormone, steroid and pesticide free;
- taken from the first two milkings,
- in the first 24 hours.
- This does not prevent the newborn calf from getting its colostrum!



# What are PRPs functions?

- promoting proper response to microbial invaders, toxins, or allergens through immune and cytokine modulation, and Natural Killer Cell (NK) Activity.
- To provide anti-viral, anti-allergy, and anti-inflammatory functions, especially by:
- stimulating T helper lymphocytes type 1 (TH1) responses to infections and tumors and
- lowering T helper lymphocytes type 2 in TH2 dominated hypersensitivity related inflammatory conditions.

# PRPs Stimulate Natural Killer T-Cell Activity

- NK cells, large lymphocytes that circulate in plasma, comprise of 10-15% of the lymphocytes in human blood.
- Of all the immune system's soldiers, NK cells are the most aggressive.
- NK Cells provide the front line of defense and as such are specially equipped to locate and kill diseased cells.
- NK cells attach to the surfaces of foreign substances, and inject a chemical “grenade” (granule) into the interior.
- They are your first line of defense against mutant and virus infected cells like
  1. Severe Acute Respiratory Syndrome (SARS) or
  2. Bird Flu Virus.

# TH1 helper/TH2 helper paradigm

- T helper lymphocytes develop along two lines of cell populations, TH1 and TH2.
- TH1 cells, which modulate **cell-mediated immunity**, produce the cytokines: IL-2, IFN-gamma, and TNF-alpha.
- TH2 cells, which modulate **humoral immunity, or antibody production**, produce IL-4, IL-5, IL-6, IL-10, and IL-13
- PRPs tend to stimulate TH1 and lower TH2 **if** these are in imbalance; i.e., PRP modulate TH1/TH2.
- This is known as the “**TH2 to TH1 shift**”.

# T helper lymphocytes Type 1 (TH1)

- TH1 helper responses are important in defense against viruses, fungi, parasites, cancer and intracellular organisms.
- Cell-mediated immunity can be tested by delayed hypersensitivity skin testing, response to non-specific or specific mitogens (lymphocyte transformation) and allo-antigens (self-recognition).

# T helper lymphocytes Type 2 (TH2)

- If one has a TH2-dominated condition, with decreased *cellular* immunity and heightened *humoral* immunity, the conditions that tend to prevail are:
- allergies, chronic sinusitis, atopic eczema, **asthma**;
- systemic autoimmune conditions such as SLE and mercury-induced autoimmunity, vaccination-induced reactions
- malaria, parasite infestations, chronic giardiasis and candidiasis, viral infections, hepatitis C, AIDS
- Certain cases of autism, **hyper-insulinism**, **hyper-cortisolism**, **cancer**, ulcerative colitis

# Allergy Pathophysiology

- Allergy is the result of a complex immune cascade leading to the dys-regulated production of Th2 cytokines, the generation of allergen-specific IgE-producing B cells and the subsequent activation and degranulation of mast cells upon allergen challenge.

Human thymic stromal lymphopoietin: a novel epithelial cell-derived cytokine and a potential key player in the induction of allergic inflammation Vassili Soumelis<sup>1</sup> and Yong-Jun Liu<sup>2</sup> (1) Department of Hematology, Necker Hospital, Paris, France(2) Department of Immunology, M.D. Anderson Cancer Center, Houston, Texas, USA Received:

1 September 2003 Accepted: 15 September 2003 Published online: 29 November 2003

## Assessment of anti-allergic properties of Liquid Colostrum Extract on systemic anaphylaxis in guinea pigs

- A poster presentation at the Fourth International Conference on Mechanisms of Action of Nutraceuticals, "The Science Behind Nutraceuticals: Medical and Dietary Opportunities", in Tel-Aviv on October 21 - 24, 2007.
- This study for BioPharma was conducted by Krylov A, et. al., Institute of General Pathology and Pathophysiology, Moscow, Russia.
- Also presented at the Scripps Integrative Medical Conference in San Diego in Jan 2008

## Material and methods

- Study has been conducted in guinea pigs, both males and females.
- Egg Protein (ovalbumin) and histamine were used as antigens.
- Egg protein and histamine were injected into animals by using compressor nebulizer.
- The effect of pre-treatment PRP was measured upon repetition of both challenges.

## **Active Sensitization** (*P. Anderson Method, 1980*)

- Guinea pigs (250-300 g) were sensitized by a one time injection of 10 g Ovalbumin (OA) and 100 mg aluminum hydroxide (Al(OH)<sub>3</sub>) in 1ml total volume: 0.2 ml intramuscularly in thigh, on two sides, and 0.6ml intra-abdominally.
- Experiment began 5 weeks after sensitization, when IgE antibodies were formed in high enough quantities.
- Bronchial spasms in animals are developed after injection of permissive dose of antigen.

# Experimental Design

1. Measurements of bronchial spastic duration time after histamine introduction - internal control.
2. Introduction of PRP 24 hours after internal control, repeated histamine inhalation and evaluation of the duration of bronchial spastic reaction, acute and sub acute.

## ***Histamine model - induced bronchial spasm***

- 0.2% **histamine solution** containing 0.9% of NaCl was inhaled by Guinea pigs, until first signs of bronchial spastic reaction. Duration time of this reaction was measured. (Table 1)
- **Histamine model repeated with prior introduction of PRP by spray 5 or 10 times into animal mouth-throat 30 minutes before histamine introduction. (Table 1a)**
- Bronchial spastic reaction is characterized by 2 phases:
  - 1) *acute phase* > guinea pigs lie on their side, deep breath, frequency of breathing 10-15 per minute;
  - 2) *sub-acute phase* > sitting position, increase of chest muscular activity, more frequent breathing 40-50 per minute.

Table 1. Effect of **histamine-induced** bronchial spasm in sensitized guinea pigs.

*Control*

<u>Animals</u>	<u>Duration of Acute Phase</u>	<u>Sub-acute Phase</u>
#1	205 (sec)	360 (sec)
#2	245	480
#3	220	600
#4	230	540
#5	205	360
#6	150	300
<b>M ± m</b>	<b>225 ± 8.4</b>	<b>495 ± 51,0</b>

Table 1a. Effect of PRP spray on **histamine-induced** bronchial spasm in sensitized guinea pigs.

*Treated Group PRP*

<u>Animals</u>	<u># PRP-CE sprays</u>	<u>acute phase</u>	<u>sub-acute phase</u>
#1	5	290 (sec)	300 (sec)
#2	5	120	420
#3	5	225	420
#4	10	240	480
#5	10	230	540
#6	10	140	420
<b>M ± m</b>		<b>207.5 ± 50.4</b>	<b>430.0 ± 53.1</b>

## *Model of Egg protein-induced bronchial spasm*

- Experiment was conducted on guinea pigs actively sensitized by egg protein which induced a bronchial spastic reaction.
- Animals were been dived in two groups, one pre-treated with PRP and one not.
- Egg protein in dose of 2.5 g/kg has been given to animals of each group.
- This egg albumin, dissolved in 1 ml of 0.9 % NaCl solution, was inhaled during 3 min with nebulizer with following assessment of acute and sub-acute bronchial spasm. (Table 2)
- Animals in the experimental group have received PRP 30 min prior to egg protein challenge. PRP was delivered by the spray into mouth-throat in the amount of 10-12 portions.
- Antiallergenic effect was evaluated on the basis of difference in extent of bronchial spasms between experimental and control groups.

(Table 2a)

Table 2. Effect of **Egg Protein-induced** bronchial spasm in sensitized guinea pigs.

*Control*

<b>Animals</b>	<b>Duration: latent period</b>	<b>acute phase</b>	<b>sub-acute phase</b>
#1	300 (sec)	240 (sec)	960 (sec)
#2	140	Death	-
#3	260	Death	-
#4	193	Death	-
#5	160	340	380
#6	185	360	300
<b>M ± m</b>	<b>206,3±25.0 (sec)</b>	<b>313.3±37.1 (sec)</b>	<b>546.7±208.0 (sec)</b>

Table 2a. Effect of **Egg Protein-induced** bronchial spasm in sensitized guinea pigs.

*Treatment Group PRP*

<u># Animal</u>	<u># PRP Sprays</u>	<u>latent period</u>	<u>Acute Phase</u>	<u>Sub Acute phase</u>
1	10	240	0	0
2	10	225	Death	-
3	10	230	Death	-
4	10	240	0	0
5	10	240	0	0
6	12	240	0	60
7	12	240	0	20
	<b>M ± m</b>	<b>236,4 ± 2.4</b>		<b>16.0 ± 11.7</b>

# CONCLUSIONS

- PRP didn't affect on the development of systemic anaphylaxis induced in sensitized guinea pigs by *exogenous* histamine.
- PRP showed clear anti-allergic activity and inhibited the development of systemic anaphylaxis, induced in sensitized guinea pigs by egg albumin.

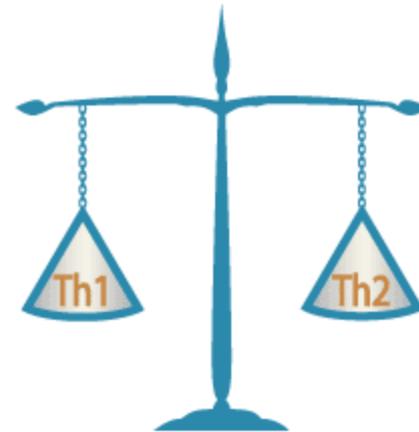
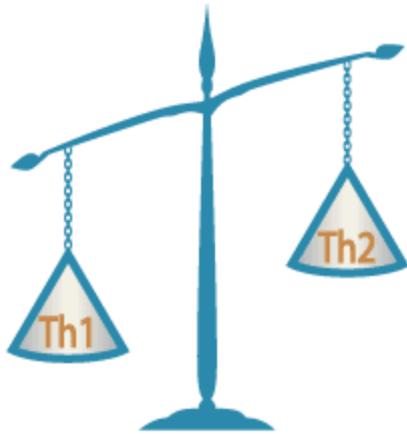
# Discussion

- It is proposed that egg protein sensitization lead to an over activity of Th2 as seen in asthma, for example.
- It is clear that PRP do not act as anti-histamine
- The dramatic increase in survival rates and decrease in both acute and sub acute hypersensitivity reactions supports the purported ability of PRP to modulate immune function, specifically the a “shifting” down of Th2.

# Th1/ Th2 Shift

- When our immune systems do not react strongly enough to infectious agents, or are overwhelmed by them, we have a “Th-1” immune imbalance. When our immune systems are over- reactive we have a “Th-2” imbalance and we may manifest allergies, chemical sensitivities and even auto-immune disease.
- Proline Rich Polypeptides, abbreviated PRP’ s, do not treat any symptoms or diseases. Rather they send signals to the thymus to help the immune system regain its proper balance.

# Th1/ Th2 Shift



# Endocrine-Immunology network

- Distress pathophysiology:
- CRH ↑ = Vasopressin ↑ + oxytocin ↑ =  
Cortisol ↑ (adrenaline ↑) = Th2 ↑ + Th1 ↓
- (Th2 dominance profile).

## Distress endocrine/ immune pathophysiology

- Corticosteroids ↑ =
- macrophage progenitors ↓
- differentiation of the monocyte cell line to macrophage cell line ↓
- and granulocyte progenitors ↑ .

This is the same profile registered during acute and chronic distress situations.

# Distress endocrine/ immune pathophysiology (cont.)

- These cortisol effects on the immune system are mediated by the thymus, mainly.
- This profile favors anti-inflammatory activity of Th2 and decreased Th1 surveillance of tumor-producing agents.
- Cortisol induces:
  1. thymic apoptosis of the immune cells (immature **T** lymphocytes)
  2. but not of immature **B** cells.

This explains why corticosteroids favor *humoral* (Th2) immunity, and interfere with Th1 *cell-mediated* immunity.

# Distress endocrine/ immune pathophysiology (cont.)

- Distress= GH ↓ = Thymopoiesis ↓ = Naïve T Cells ↓ (memory T Cells↔)
- Growth hormone is not secreted during acute stress and chronic (uncontrollable or uncoping) *dis*-stress situations.
- Progressive reduction of GH secretion by the hypophysis is observed with aging.
- GH is a thymopoietic factor.

# GH, Colostrum and Thymopoiesis

- Both the thymus and GH fade progressively with aging, resulting in fewer naive T cells (memory T cells remain normal).
- GH is able to trigger *thymopoiesis* in adults and elder people. This favors reappearance of naive T cells.
- GHRH and GH have been used in the treatment of many stress-associated (Th2) diseases.
- Colostrum active peptides (PRPs) promote thymopoiesis of naïve T Cells and modulate Th2.

# Stress, Aging and Immune Function

- It is amply accepted that neuro-hormonal disorders (cortisol, adrenaline, free serotonin, etc.) registered during uncontrollable distress are important factors which favor tumor progression and metastasis.
- It is also amply accepted that with age GH secretion diminishes and cortisol rises.
- Therefore, we might expect to see the following in the senior population, especially when under distress.

# Hormonal and Immune Functional Relations in Aging

- Age ↑ = CRH ↑ = Cortisol ↑ = Th2 ↑ + Th1 ↓ (Th2 dominance profile).
- Age ↑ = GH ↓ = Thymopoiesis ↓ = Naïve T Cells ↓ = Tumor Surveillance ↓

# Hormone ↔ Immune Relations

- Alteration in the function of the neuro-endocrine glands effect cortisol and GH levels which effect the structure and function of the thymus gland
- Conversely, the thymus gland and thymic hormones contribute to human immunity and the neuro-endocrine system.
- Anti-aging health professionals may endeavor to effect immune function through:
  1. modulating the hormones of youth (GH) and
  2. the hormones of aging (Cortisol)to a more optimal and youthful balance.

# Direct Immune Modulation Support

- PRP have the potential to be used toward the same ends of modulating immune status, namely Th1/ Th2 balance,
  1. as a coincident therapy to hormone therapy
  2. as a more conservative and preventative stand alone nutraceutical support

# PRP as Nutraceuticals

- PRP's can be extracted from colostrum using ion exchange and nano-membranes.
- PRP's are small polypeptides that when separated from liposomes, GMP and protective anti-enzymes found in whole colostrum and whey may not survive the alimentary tract.
- PRPs can be taken sublingually. (< 6,000 Daltons)
- PRPs may be protected by liposomal delivery and allow better absorption orally.
- Presuming efficacy, whole colostrum and whey isolates/ concentrates can be fortified by PRP nano-encapsulated in liposomes for use pills and functional foods

# Conclusion

- Colostrum is rich in active immune peptides called Proline Rich Polypeptides (PRP)
- PRP demonstrate immune modulating potential in the animal hypersensitivity model
- PRP may well have potential as a immune modulator nutraceutical in those patients who experience neuro-endocrine / immune imbalance related to:
  1. high cortisol levels found in stress and with aging.
  2. Low GH levels found in stress and aging

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