The Physiological Functions of Proline Rich Polypeptides (PRP)

Proline Rich Polypeptides are extremely small chains of 10 amino acids or less, notably proline, that nonetheless have a very powerful effect in initiating and balancing our immune responses.

Proline Rich Polypeptides, also known as PRP, enhance the ability of thymus gland to release factors that help regulate immune functions in the body. Specifically, certain T cells, called TH1 helper cells, are antagonist to the activity of TH2 helper cells that promote certain functions of B lymphocytes. PRP can induce a shift from a predominantly humeral immune response to a more protective cellular response described as a "*TH2 to TH1 shift*". Doing so may assist the immune system in more effectively fighting chronic viral and bacterial infections while simultaneously inhibiting the initiation of inappropriate inflammatory cascades associated with allergy, chemical sensitivity and auto-immune responses.

A more detailed list of the physiological functions of proline rich polypeptides follows.

- Modulate the immune system - PRP promote T-lymphocyte function[1] and can either stimulate the lymphocytes to become helper T-cells or suppressor T-cells[2,3]. Helper T-cells activate B-lymphocytes by presenting an antigen (such as a viral protein) to the B-cell, which then produces antibodies to that protein[4]. Helper T-cells also help produce memory T-cells which retain the "memory" of the antigen to shorten the response time in case of new infection[5]. Suppressor T-cells deactivate other lymphocytes, effectively turning off the immune response to avoid damage to healthy tissue[6]. PRP also stimulate the production of a whole range of cytokines, particularly the pro-inflammatory cytokines TNF-α and INF-γ[7] and the anti-inflammatory cytokines IL-6 and IL-10[8].

- Act as molecular signaling devices - PRP work through specific receptors on cell surfaces[2].

- Stimulate undifferentiated lymphocytes in thymus to become either helper T-cells or suppressor T-cells - PRP from ovine (sheep) colostrum act as a hormone in the thymus gland by stimulating thymocytes (immature lymphocytes) to differentiate and become activated as either helper T-cells (CD4+) or suppressor T-cells[9]. Helper T-cells are a vital part of the immune response which stimulate the production and differentiation of cytotoxic T-cells and B-cells, attract white blood cells, and stimulate macrophages to engulf and destroy pathogens. Suppressor T-cells inhibit the production of cytotoxic T-cells to prevent tissue damage and suppress the immune response when no longer needed.

- Promote growth and differentiation of B-cells- PRP promote the growth and differentiation of B-cells, a type of lymphocyte which produces antibodies to antigens, including viral antigens[10].

- Stimulate Natural Killer cell (NK cell) activity - PRP stimulate the activity of NK cells up to 10 times, far greater than any other known substance. NK cells, along with cytotoxic T-cells, are the cells which actually attack and kill pathogens. NK cells also attack and kill cancerous cells[11].

- Stimulate the production of tumor necrosis factor-alpha (TNF-α) and interferon-gamma (INF-γ)- PRP stimulate production of pro-inflammatory cytokines TNF-α and INF-γ, the two major pro-inflammatory cytokines, in white blood cells[12], peritoneal cells[13], and placental and amniotic membranes[14].

- Promote the proliferation of leukocytes (white blood cells)[15]

- Stimulate production of cytokines by peripheral blood cells -The types of cytokines stimulated by PRP depend on the antigenic stimulation present or the activity state of the immune system (underproductive or overproductive). In one study, mice exposed to Herpes simplex virus (HSV) were stimulated to produce large amounts of IL-2 and INF-γ and small amounts of IL-10, while mice which had been given transfer factor (PRP) prior to infection responded to HSV by secreting

INF-γ but no IL-2[16]. PRP stimulates the production of TNF-α, INF-γ, IL-6 and IL-10 in blood cell cultures[17].

- Induce differentiation and maturation of monocytes and macrophages[18]

- Increase the permeability of blood vessels in the skin - Part of the inflammatory response to infection is an increase in the permeability of blood vessels in the skin to allow the passage of blood cells and cytokines into the connective tissue to combat the infection. PRP is known to initiate this inflammatory response[19].

- Produce immunity to certain viruses- PRP has been experimentally shown to provide immunity to several viruses, including herpes viruses[20,21,22], Epstein-Barr virus[23], HIV[24], measles[25], vesicular stomatitis virus[26] (a close relative of the rabies virus which is used in experimental systems to study the properties of Rhabdoviruses), and others[27,28].

- Inhibit viruses known to be associated with autoimmune diseases- Epstein-Barr virus and human herpes virus-6 (HHV-6) have been associated with chronic fatigue syndrome, an autoimmune disorder. PRP inhibits the replication of both viruses[29,30].

- May help down regulate the "cytokine storm" seen in bird flu - Influenza A virus subtype H5N1 sets off a so-called "cytokine storm" which usually results in an often fatal respiratory disease in those infected with the virus. Research has indicated that the storm is caused by cytokine dysregulation which allows pro-inflammatory cytokines to be produced in large numbers, setting off a potentially fatal inflammatory response[31]. As PRP is known to down regulate an overactive immune system, it potentially could be used to put a stop to the overproduction of cytokines and restore homeostasis to the body, preventing a fatal outcome. In one case in Thailand, four patients were diagnosed with bird flu. Only one survived – that person had been taking colostrum powder (which contains PRP) prior to infection.

- Increase T-cell count in AIDS to normal or near-normal levels- In clinical studies conducted in the nations of Nigeria, Kenya and Zambia in Africa, where AIDS is a particularly devastating disease, PRP oral spray products were shown to boost T-cell (CD4+) levels to normal or near-normal levels (median 502, none less than 300) in AIDS patients whose T-cell levels prior to treatment were well below normal (median 275). Along with the increase in T-cells came a remission of AIDS symptoms within two days of start of treatment, including nausea, vomiting and diarrhea. In the Nigerian study, weight gains of 5% were recorded. Patients taking the PRP spray fared much better in terms of quality of life than did patients on anti-retroviral drugs[32]. Thus the ability of PRP to stimulate the immune response when it is insufficient by inducing the production of new helper T-cells appears to enable the immune system of AIDS patients to recover sufficiently so that it is able to fight the HIV on its own.

Proline Rich Polypeptides are not species specific. PRP from bovine milk works on all mammals, including humans, dogs and cats[33]. As PRP is produced by all mammals and is an entirely natural product, it is generally thought to be safe for all ages. However, lactose is usually associated with PRP and therefore those with *milk intolerance* may need to proceed with caution. The addition of lactase, the milk sugar digesting enzyme, may ameliorate *lactose intolerance*.

Also, delicate immune system changes occur following conception and during pregnancy. Specifically, there is a shift to TH2 dominance to inhibit the mother's immune system from over responding to the different DNA of the new life now inside her. Although there are no known reports of colostrum's interference with full and normal gestation, until further investigation assures safety, BioPharma suggests pregnant women and women hoping to conceive should avoid PRP rich colostrum products unless suggested by their doctor.

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