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LACTOFERRIN, A TRULY VERSATILE ENZYME

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Lactoferrin is mostly recognized as a milk protein that also contains a significant amount of iron, but it is much more than that. It is a natural protein found throughout the body that can play many roles. The protein can act as an enzyme, as an active immune system protein, and as a regulatory protein. Its functionality can be altered by pH, binding, and the degree and type of metal saturation. Lactoferrin can even change its function and activity by being degraded into its separate lobes or by releasing protein fragments through auto catalysis. It serves so many versatile functions that some people refer to it as the "Swiss army knife" of proteins.

Lactoferrin is an integral part of the first line of defense at many of the entry points to the body. It is present in most, if not all of the fluids of the body, including blood, urine, sweat, tears, saliva, milk, gastric fluid, intestinal lumen, vagina fluid, and nasal secretions. It is also present in many cells of our body. This includes the neutrophil granulocyte white blood cells which release it along with other defensive peptides when they de-granulate. Receptor sites for lactoferrin have been found on a wide variety of cell types in the body.

There are numerous citations in the scientific literature concerning the antibacterial properties of human and bovine lactoferrin. These include intensive comparative studies of the human and bovine forms that conclude that they are essentially functionally bioequivalent. Lactoferrins can inhibit both gram positive and gram negative bacteria by multiple mechanisms. They can bind to the surface of cells, inhibiting the entry of the pathogen. They can bind to the endotoxic membrane of the pathogen, disrupting the membrane. This disruption makes the pathogen susceptible to other antimicrobial agents that may be present such as antibiotics, antibodies, bacteriophages, lysozymes, peroxidases, or other microbes. Lactoferrin can also penetrate the pathogen and inhibit its function and development from within by binding to and/or hydrolyzing both DNA and RNA. It may also release protein fragments of itself into the pathogen that can disrupt the inner workings of the cell resulting in the death of the pathogen. Some common types of bacterial pathogens with documented inhibition either in vitro and/or in vivo include E. coli, Listeria, Clostridium, Streptoccus, Staphylopcoccus, Shigella, Helibacter, and C. difficile.

Lactoferrin can also inhibit pathogens indirectly by tipping the intestinal balance in favor of non-pathogenic bacteria such as the Lactobacillus and Bifidobacterium probiotics. These bacteria are adapted to a low iron environment, and by binding iron lactoferrin helps to maintain low iron levels in the intestines. Most pathogenic bacteria require more iron.

The probiotics are also more resistant to the antimicrobial effects of lactoferrin. Combined with the iron effects, under normal circum-

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(LACTOFERRIN, A TRULY VERSATILE ENZYME *cont.*)

stances the competitive advantage favors the probiotics. When this balance is disrupted, supplementary lactoferrin can help support the restoration of this balance.

Lactoferrin also has several studied properties that help it to inhibit viruses. It binds to the surface of many cells that are viral targets, inhibiting viral entry. Lactoferrin can also bind to the envelope proteins of some viruses disrupting the defenses of the virus. The protein can also penetrate some viruses and proteolytically hydrolyze their RNA, disabling the functioning of the virus. It can also bind to the DNA or RNA of the virus, preventing or slowing the growth and replication of the virus. Anti-viral properties of lactoferrin have been identified for both the human and bovine form. No significant differences in biological function have been reported. Common viruses that are known to be susceptible to inhibition by lactoferrin either in vitro or in vivo include HIV, herpes simplex, all major subtypes of influenza including the H5N1 avian variety, Hepatitis C, adeno virus, SARS virus and cytomegaloviruses.

Both human and bovine lactoferrin also has anti-fungal and anti-parasitic properties. These proteins inhibit numerous strains of Candida both in vitro and in animal models. Both forms are also active against spore forming parasites such as Giardia, Eimeria, Encephalitozoon and Toxoplasma.

In addition to its effect on living pathogens, lactoferrin also has an effect on the endotoxins released after they die. Lactoferrin has very strong binding sites for endotoxins, as well as enzyme activity that can help degrade them. In addition, it has antioxidant and anti-inflammatory properties that further protect the body from the toxins released when the cells die. These properties limit the toxic effects and helps clear the toxins from the body.

While its anti-pathogen properties are impressive, it also plays a key role in the overall immune response. Lactoferrin supports the transition from the innate to the adaptive immune system. It is released at the point of insult by the innate immune system along with other immune system proteins and inflammatory cytokines for the initial isolation and dismantling of the source of the insult. After the threat is isolated and neutralized, lactoferrin inhibits the inflammatory cytokines at the mast cells, slowing and modulating the inflammation cascade. This allows the adaptive immune system to begin to take over, transitioning the immune response and helping to bring the inflammatory system back to its normal state of readiness. Lactoferrin can also chelate many oxidative metals and can act directly as an antioxidant, reducing the levels of oxidative stress in the body.

Lactoferrin's role in modulating inflammation and oxidative stress makes it an important factor in maintaining health. Scientific research has correlated low levels of plasma lactoferrin in humans with altered glucose tolerance, low insulin sensitivity, high blood sugar, obesity, coronary artery stenosis, high plasma free fatty acid levels and altered lipid metabolism. Plasma levels of lactoferrin also

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decrease with age. Neutrophil white blood cells taken from diabetics also express less lactoferrin in comparison to non-diabetics. All of these correlations have led some researchers to suggest that "decreased circulating lactoferrins may play a role in chronic low level inflammation associated insulin resistance".

Because of its role in so many critical systems of the body, much scientific research involving supplementation with lactoferrin has been conducted in human clinical trials. Some highlights include reductions periodontis and oral biofilms. Additional human clinical trials showed a reduction H. pylori infections, the stomach ulcer associated bacterium. In nursing home patients, C. difficile infections were reduced. In children routinely exposed to Giardia, a reduction in the rate of infection and improvement in growth rates were reported. An additional study also demonstrated a reduction in post-antibiotic associated diarrhea with oral supplementation.

Beyond pathogens and parasites, other human studies showed additional benefits. One demonstrated oral supplementation could result in a reduction in skin lipid concentrations. Skin lipid concentrations are an important factor in acne. Another human clinical trial showed an increase in neutrophils in the blood with oral supplementation, and modulation of the pro-inflammatory cytokines TNF-alpha and IL-6. In women runners, an additional study demonstrated improved blood levels of iron when taken with lactoferrin, as well as reduced levels of blood lactate after a 3000 meter run.

There are many more in vitro and animal studies suggesting additional areas for research such as bone growth, eye support, immune support, lipid and blood sugar metabolism, urinary tract support, vaginal support, liver support, digestive support, wound healing support, and recovery support. With such a versatile range of functions, nutritional supplementation with lactoferrin has the potential to have significant and broad ranging health support benefits on par with any supplement ingredient currently available. Given the breadth of existing and emerging research in all of the most popular supplement categories, this underappreciated and often unrecognized enzyme has the potential to become one of the most supplemented nutritional ingredients. ●

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