"Lactoferrin and its capacity as an iron transporter and distributor"

| | V |
|----------|----------------------------------|
| |) |
| | \mathbf{O} |
| Ο | $\mathbf{\overline{\mathbf{V}}}$ |
| \frown | |

What is lactoferrin?

Lactoferrin is a protein present in milk as well as in many human and mammalian bodily fluids and cells. In terms of the innate immune system, it plays an important role inhibiting bacteria, viruses, even some fungal pathogens and also by regulating inflammation.

It is breast-fed newborns who benefit primarily from the lactoferrin in mothers milk which both protects them from harmful germs whilst at the same time promoting the development of beneficial gut microbiota.

Adults can also benefit from these properties due to the fact that lactoferrin is easily digestible and quite safe. Due to the fact that it contains no lactose, the protein can also be taken in case of lactose intolerance.



Simplified model of lactoferrin; iron atoms marked in red

Lactoferrin is fundamentally a protein and more specifically a Glycoprotein. This means that it is composed of a single chain of amino acids, typical for proteins, with attached carbohydrate chains. Human lactoferrin comprises 691 amino acids and has a molecular mass of approximately 80 kDa.

Role of lactoferrin

Lactoferrin is integral to the newborn's immune system. It also plays a role in the immune response of adults. Lactoferrin is released by some of our leukocytes - more specifically it is present in the secondary granules of neutrophils - and is part of our innate immune system.^[1] Lactoferrin was named after its occurrence in milk (lat. lacteus). It can be found, highly concentrated, in breast milk but also in other bodily fluids and in cow's milk.

Lactoferrin is a component of the nonspecific defence system against various pathogens. The body, wishing to prevent bacteria multiplying and invading the organism, enriches our bodily fluids, for example tears, saliva or sweat, with lactoferrin. However, the quantity of lactoferrin produced naturally in our bodies appears to be insufficient in response to today's stress and modern lifestyle.

Fortunately, human and bovine lactoferrin (from cow's milk) are almost identical and fulfill the same function. Therefore, purified lactoferrin from cow's milk is also well-suited to support the human immune system.

The properties of lactoferrin

One of the best researched properties of lactoferrin is its ability to bind iron. Lactoferrin belongs to the group of transferrins which is why it is also referred to as lactotransferrin. Lactoferrin's affinity for iron is up to 300 times greater than other transferrins.^[2] Lactoferrin is able to bind ferrous ions from its surroundings making it a perfect transporter and distributor of iron and also enabling a higher absorption of iron into the intestines.^[3]

Iron is an essential trace element, not only for the human body (which contains approximately 3 to 4 grammes of iron), but also for bacteria.

artgerecht



Iron plays an essential role in microbial metabolism especially as a co-factor for several enzymes. In the absence of iron, bacteria die.^[4] As a result, these bacteria have developed their own strategy to absorb iron by secreting compounds like enterobactin.^[5] Lactoferrin competes with such compounds for iron, thus inhibiting the bacteria from absorbing it.

In addition to its ability to bind iron, lactoferrin has a further range of beneficial functions. It attacks the cell membrane of bacteria directly, prevents viruses attaching to human cells and has a negative effect on the spread of fungal infections. In addition, it promotes the growth of natural gut microbiota and ensures an immunomodulating effect. Lactoferrin also prevents the build-up of free radicals in the enterocytes lining the small and large intestines, which would normally result from the oxidation of Fe2+.

Lactoferrin is like a Swiss Army Knife for our immune system in that it boasts a whole range of different functions.

Unique composition of IRON

The unique combination of high purity Lactoferrin CLN[®], herbal curry leaf iron, and vitamin C from rose hip extract ensures that it is well tolerated and quickly available to the body.

In addition to 3 mg of elemental iron from the leaves of the curry leaf tree, one capsule of IRON contains 100 mg Lactoferrin CLN[®]. This combination means that the iron can be directly absorbed into the small intestine via the lactoferrin receptor.^[6]

The 20 mg of vitamin C per capsule increases the capacity to absorb iron into the intestines and, due to its antioxidant properties, prevents the oxidation of bioavailable Fe2+ to insoluble Fe3+.^[7] Lactoferrin CLN[®] and vitamin C in IRON work synergistically to ensure the maximum absorption capacity of the available iron.

This composition makes IRON particularly suitable for iron malabsorption issues and iron salt intolerances.

In particular, a symptomatic iron deficiency can result from chronic, inflammatory disorders like inflammatory bowel disease, where iron absorption and distribution is low. This can also be the result of stress, immune and lifestyle deficiencies.^[8]

The inferior distribution of iron as a result of a chronic inflammation results in a higher production of interleukin, particularly IL6 as an indicator of the degree of inflammation, which results, via the Hepcidin-Ferroportin mechanism, in the transport of iron from intestinal and liver cells being inhibited. Lactoferrin CLN[®] is a natural immunomodulator which can manage the inflammation and take care that iron is distributed better throughout the organism.

Initial research of patients with iron deficiency (measured in terms of Ferritin) and high infection levels who took IRON over a 30 day period show a 23 % reduction of Interleukin-6 and, on average, a 5 times increase in Ferritin.

Ferritin Growth after 30 days of IRON



Interlukin-6 Growth after 30 days of IRON



4 Rosa, L.; Cutone, A.; Lepanto, M. S.; Paesano, R.; Valenti, P. Lactoferrin: A Natural Glycoprotein Involved in Iron and Inflammatory Homeostasis 2017, Int. J. Mol. Sci, 18(9), 1985

8 Furman et al. Chronic inflammation in the etiology of disease across the life span. Nature Medicine, 2019, 25, 1822-1832

¹ Sanchez, L.; Calvo, M.; Brock, J. H. Biological Role of Lactoferrin. Archives of Disease in Childhood 1992, 67 (5), 657-66

² Baker, H. M.; Baker, E. N. Lactoferrin and Iron: Structural and Dynamic Aspects of Binding and Release. BioMetals 2004, 17 (3), 209–216

³ Lepanto, M. S.; Rosa, L.; Cutone, A.; Conte, M. P.; Paesano, R.; Valenti, P. Efficacy of Lactoferrin Oral Administration in the Treatment of Anemia and

Anemia of Inflammation in Pregnant and Non-Pregnant Women: An Interventional Study. Frontiers in Immunology 2018, 9

⁵ Saha, P.; Xiao, X.; Yeoh, B. S.; Chen, Q.; Katkere, B.; Kirimanjeswara, G. S.; Vijay-Kumar, M. The Bacterial Siderophore Enterobactin Confers Survival Advantage to Salmonella in Macrophages. Gut Microbes 2018, 10 (3), 412–423

⁶ Jiang, R.; Lopez, V.; Kelleher, S. L.; Lönnerdal, B. Apo- and Holo-Lactoferrin Are Both Internalized by Lactoferrin Receptor via Clathrin-Mediated Endocytosis but Differentially Affect ERK-Signaling and Cell Proliferation in Caco-2 Cells. Journal of Cellular Physiology 2011, 226 (11), 3022–3031

⁷ Yoshino, M.; Murakami K. Interaction of Iron with Polyphenolic Compounds: Application to Antioxidant Characterization, Analytical Biochemistry 1998, 257, 40-44