



Immune health

Solutions for natural
immune support



The new opportunity in immunity

The trend towards proactively looking after our health continues to grow. The best medicine is preventative, and perhaps the prime example of this principle is our own amazing immune system.

Not surprisingly, consumer interest in immunity is at an all-time high, and as a result demand for supplements, ingredients and foods with apparent immunity-boosting properties is accelerating¹.

Prompted by consumer demand, the number of product launches featuring immune health claims has risen for several years in a row². The supplement market with immunity propositions has also grown significantly, with US sales increasing by 25% in 2020³.

These trends look set to accelerate in the wake of COVID-19.

At the same time, consumers are becoming more educated and discerning in what they buy to support their immunity. They will actively seek out scientific substantiation - in fact, almost half (47%) say they regularly research ingredients to help decide on their best options⁴.

This will lead to significant new opportunities for growth, as our increasing understanding of the human immune system leads to new solutions with scientifically validated benefits.

Biotis™ | Immune Health



Immunity market trends

IN 2019

53% of consumers stated they wanted to improve **their immune health**, but this rose to **70%** in 2020¹.



Products with **immune health** claims are rising with a CAGR of **15%**².

40%

stated they used more fortified drinks

whereas **16%** stated that they used more supplements to improve their **immune health**¹.



A consumer study shows that: **46%** of people who use supplements specific to immune health, with immunity-specific ingredients or claims, take them **daily**⁴.



There were far more launches of supplements in 2020 with **immune health claims** compared to food & drinks³.

Vitamin & mineral supplements show a CAGR of **18%**² and consumers show significant interest in ingredients like

omega-3 oils and minerals such as **iron, zinc & magnesium** to support the function of the immune system⁵.



Introducing Biotis™ Immune Health

Now FrieslandCampina Ingredients is launching Biotis™ Immune Health, the latest of three health benefit solution platforms under the Biotis™ brand. Like Biotis™ Gut Health and Biotis™ Brain Health, our immune health platform represents a whole new era of ingredient science.

We're opening up new opportunities for our customers by tapping into our many years of experience in this field. During this time, we've established ourselves as true world leaders in infant, performance and medical nutrition.

We are now turning our attention to the positive effects of dairy on the immune system across the entire adult life span. Already many ingredients isolated from dairy have been shown to form the basis of scientifically robust, immunity-supporting products, that we will develop for the market together with our customers.

The human immune system

The human immune system is a breathtakingly sophisticated and complex triumph of evolution.

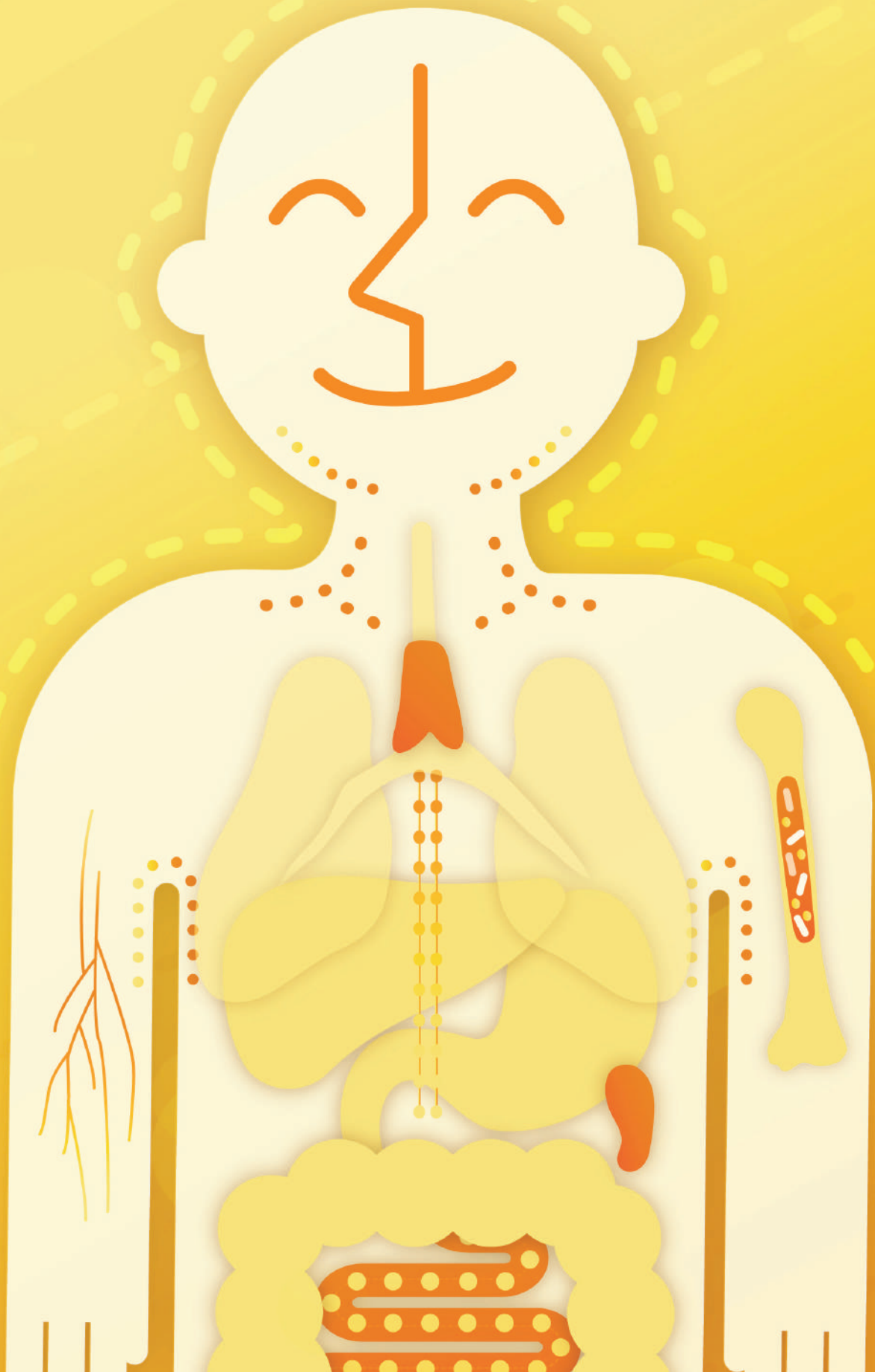
Our body seeks to maintain a state of physical and biochemical harmony and balance (called 'homeostasis'), but this desirable state is constantly being threatened by invasion from disease-causing microbes such as bacteria and viruses.

These can enter our bodies through what we eat, through our skin (especially via wounds) and via the air that we breathe.

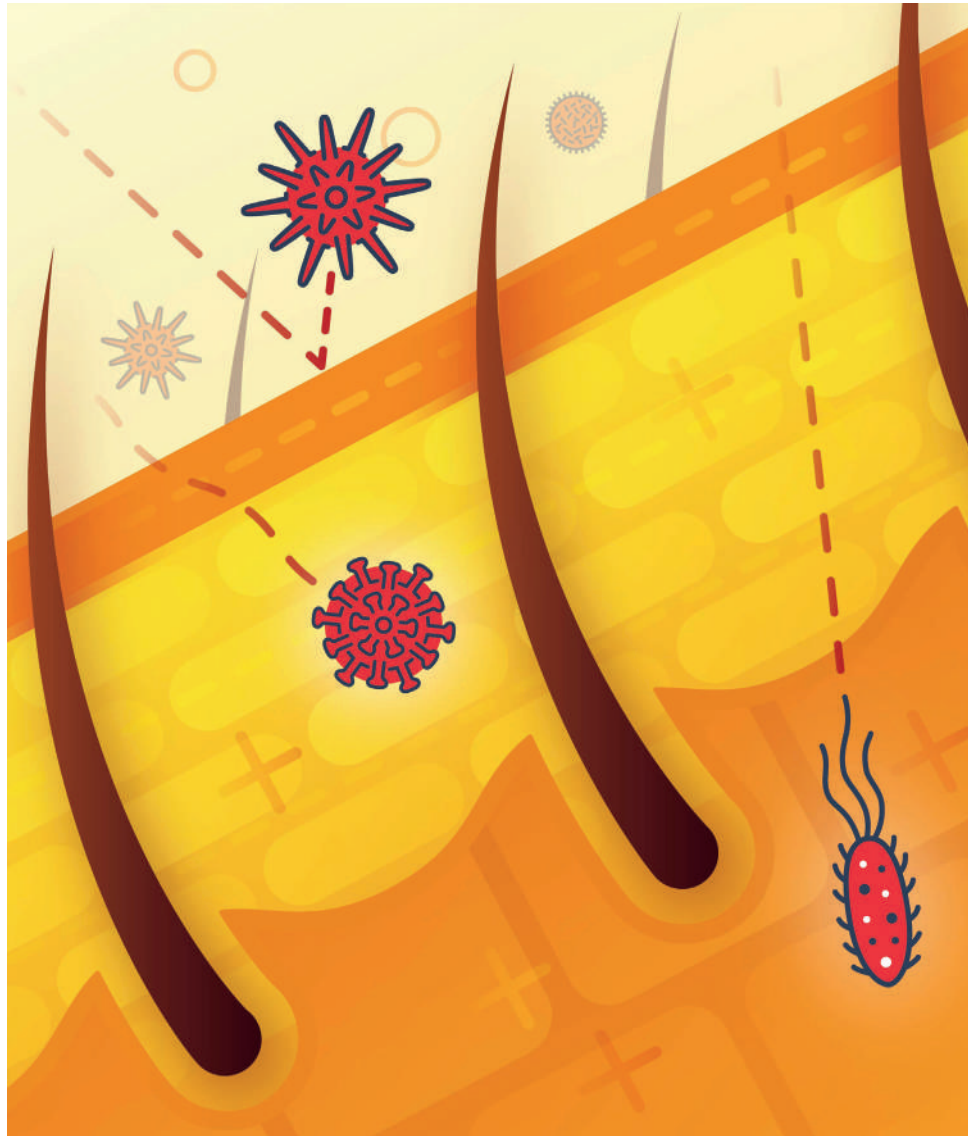
The immune system consists of dozens of different types of agents - specialist cells and biochemicals - whose sole job is to track down, identify and kill these pathogens.

At the same time these agents must ignore friendly bacteria and, of course, avoid over-reaction - attacking the body and its organs by mistake.

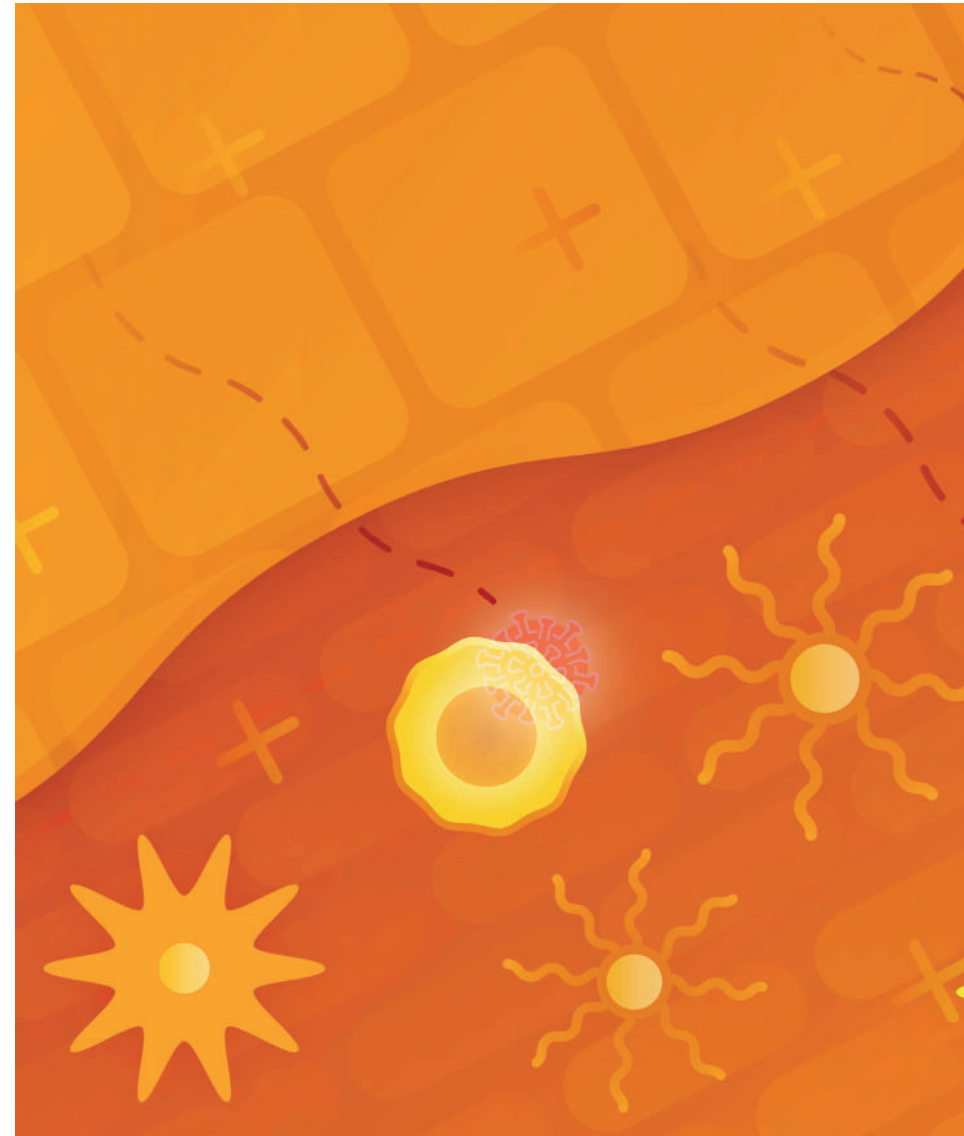
The myriad ways in which our immune system keeps us safe can be thought of in terms of three separate 'lines of defence'.



Our three lines of immune defence



1. Physical barriers such as the skin, and the mucous membranes of the mouth, respiratory tract, gastrointestinal tract and urinary tract, all help prevent pathogens from entering the body.



2. The innate immune system provides an immediate but non-specific response by an army of leukocytes (white blood cells) as well as other agents. These cells identify and eliminate pathogens, and are also important mediators in the activation of the third line of defence.



3. The adaptive immune system is activated by the innate response. Its role is to learn to recognise the pathogen, orchestrate a specific attack on this pathogen and then creating an 'immunological memory' that allows faster and stronger attacks when this pathogen is encountered again.

A delicate balance

Innate and adaptive immunity are processes that need 'just right' levels of precision. The objective is to clear an infection without collateral damage to the body itself.

This is why an immune response can sometimes be too weak (allowing infections and even cancers to thrive), or too strong (leading to autoimmune diseases or allergic reactions), caused by (over-) inflammation.

Certain components of our diet have very specific roles in the development and maintenance of an effective immune system throughout life, or in reducing chronic inflammation.

There is a great deal of research interest in whether specific nutrient interventions can further enhance immune function in sub-clinical situations, and so prevent the onset of infections or chronic inflammatory diseases¹.

¹Childs et al., *Nutrients* 2019; 11(8): 1933.



Dairy, health and immunity

For centuries, dairy, health and immunity have gone hand in hand. Dairy products provide fuel and help to build muscles but are also packed full of friendly substances that protect us from disease.

Because the creation of immunity begins at birth, milk has a central role, and so it isn't surprising to find that many of the ingredients within dairy can help maintain a healthy immune system¹⁻³.

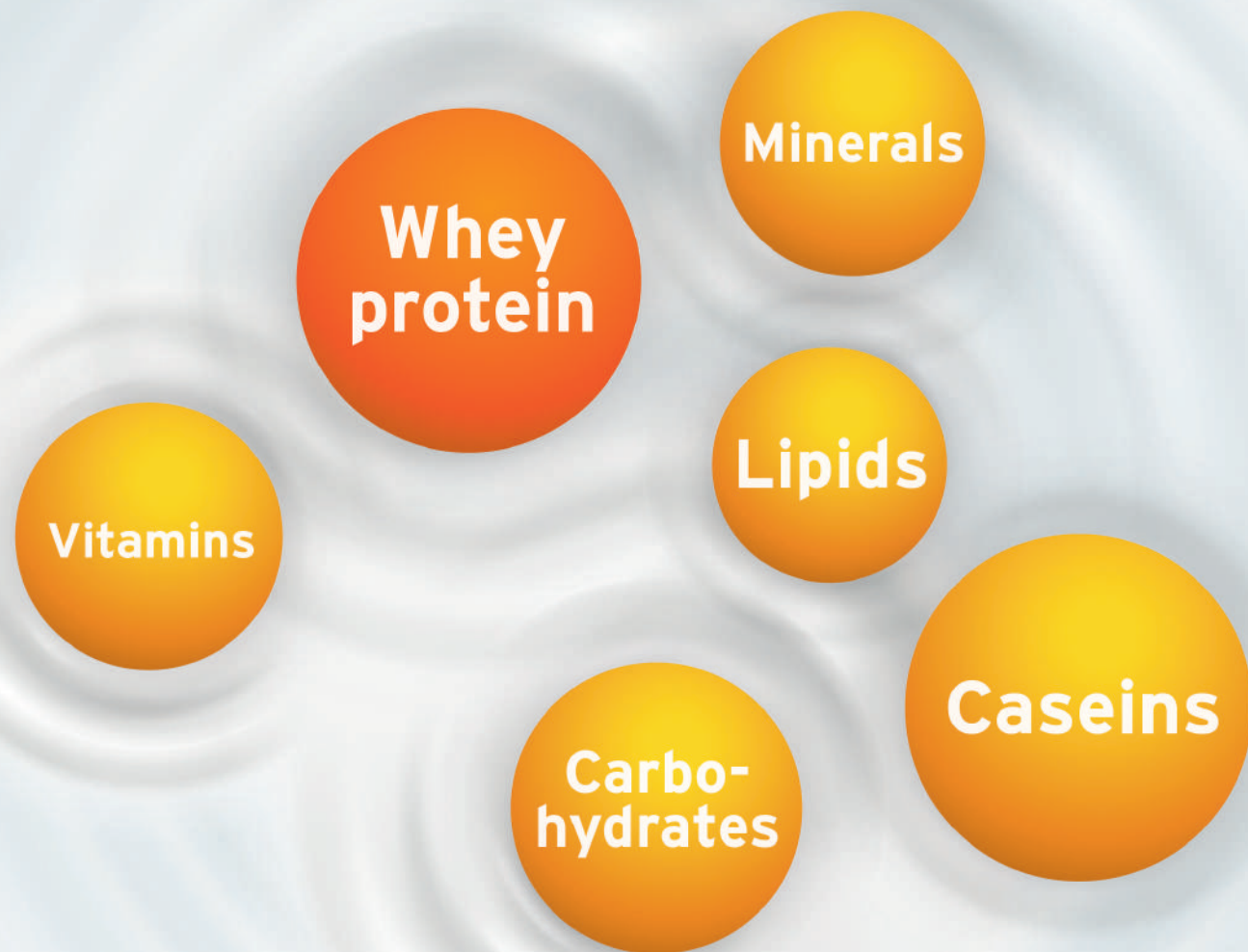
Dairy can both help our immune system to stay active, but also prevent it becoming hyperactive⁴.

Many of the minor components in breast milk are also present in cow's milk, for example Vitamins B2 and B12, zinc and selenium. These are linked to numerous health benefits.

With specific regard to immunity, both human⁵ and cow's milk⁶ have been shown to contain antigens, immune modulators, prebiotics⁷ and antimicrobials.

¹Meyer et al., *Ann Nutr Metab* 2006;50(3):282-9; ²Olivares et al., *J Dairy Res* 2006;73(4):492-8; ³Ebringer et al., *Folia Microbiol (Praha)* 2008;53(5):378-94; ⁴Perdijk et al., *Front Immunol* 2018;9:143; ⁵Hosea Blewett et al., *Advances in Food and Nutrition Research* 2008; 54:45-80; ⁶van Neerven et al., *J Allergy Clin Immunol* 2012;130:853-8; ⁷ISAPP (International Scientific Association for Probiotics and Prebiotics); Gibson et al., 2017; Substrates that are selectively utilized by host microorganisms conferring a health benefit.





Whey's importance in nutrition

Whey protein is known to be a high quality protein source for muscle protein synthesis, as it contains all nine essential amino acids, has a high leucine level and is easily digestible.

In addition, many of the components in whey protein, including lactoferrin and immunoglobulins, have been shown to play an active role in supporting immunity¹.

¹Ng et al., Applied microbiology and biotechnology 99.17 (2015): 6997-7008.

The promise of lactoferrin

Lactoferrin is a globular glycoprotein found in human and bovine milk, which has been shown to provide multiple beneficial effects for immune health.

Antiviral

Lactoferrin has strong antiviral activity against a broad spectrum of both naked and enveloped DNA and RNA viruses¹.

Antibacterial

Lactoferrin has also been shown to protect against bacteriological infection, both by competing with siderophilic bacteria for ferric iron², and by various other mechanisms independent of its iron-binding ability³.

Iron regulation

With its very specific iron-binding properties, lactoferrin is emerging as an important regulator of iron homeostasis, avoiding iron accumulation in tissues and secretions - which causes iron deficiency in blood⁴.

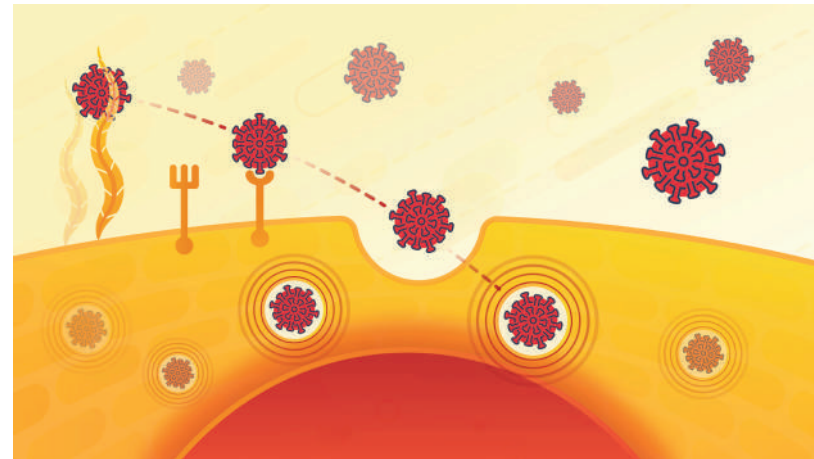
The postulated mechanisms for lactoferrin's antiviral properties are highlighted on the following page.



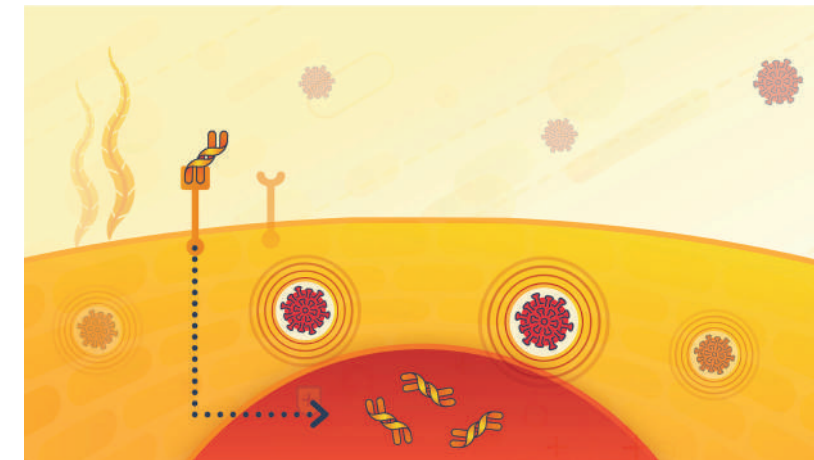
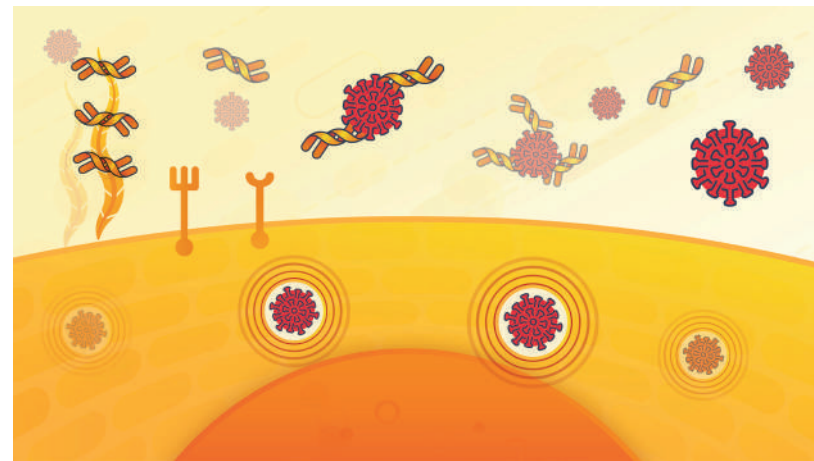
At Biotis™ Immune Health, we are researching and developing the potential consumer benefits of lactoferrin, as well as exploring other complementary dairy ingredients and solutions in this rapidly growing area.

How lactoferrin inhibits viral infection¹⁻⁷

Viruses that enter the body look for specific receptors on the surface of our cells, so they can attach themselves and enter the cell where they replicate.



But when lactoferrin is present, it can help prevent the virus from finding the receptor it needs, either by 'binding' the virus directly or by binding to the receptor the virus uses to gain access.



Lactoferrin can also trigger an immune response directly. First, it binds to a specific receptor, which induces signalling that prepares the cell to act; then lactoferrin is transported to the cell nucleus.



Here it acts directly on the DNA to initiate the production of cytokines inside the cell.



Released from the cell into the surrounding tissue, cytokines warn nearby cells to heighten their antiviral defences and also activate immune cells - such as macrophages and natural killer cells.

¹Kell et al., *Front. Immunol.* 2020;11:1221; ²Chang et al., *Int. J. Antimicrob. Agents*;56 (3):106118;
³Liao et al., *Biochem. Cell Biol.* 2012;90(3):476; ⁴Suzuki et al., *Cell. Mol. Life Sci.*2005;62(22)2560;
⁵Ashida et al., *Biometals* 2004;17(3):311; ⁶Jiang, Lönnnerdal, *Int. J. Biochem. Cell Biol.* 2012;44(1):91;
⁷Mirabelli et al., *BioRxiv* 2020; 05.27.117184.

Lactoferrin - in demand globally

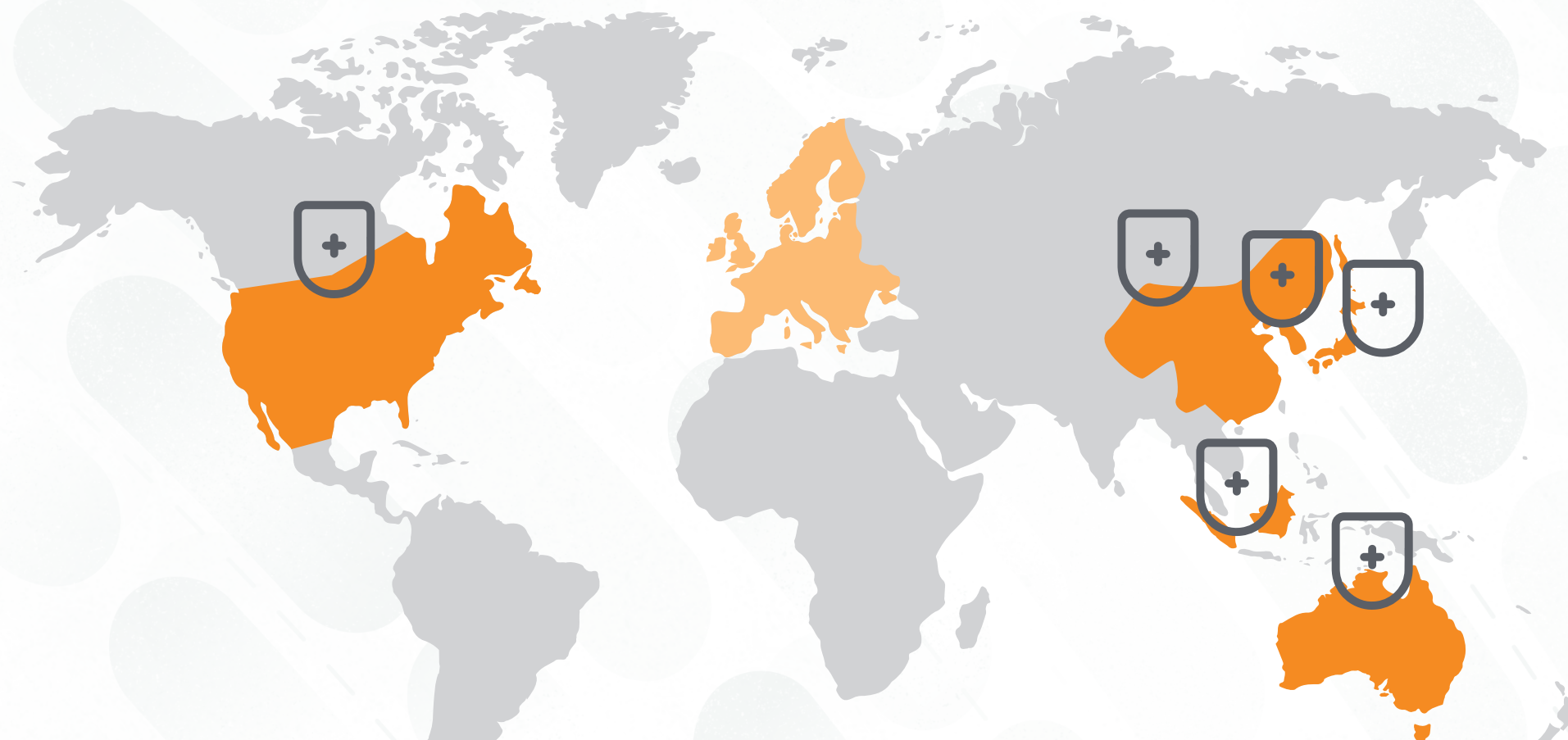
Lactoferrin is already widely known as a bioactive ingredient in many parts of the world.

Of those who are aware of the health benefits of lactoferrin, **between 60 and 88 percent** of consumers in the US, China, Japan, Korea, Australia and Indonesia regularly seek out products that contain it.

These consumers believe that lactoferrin **reduces vulnerability to diseases** and improves overall health and recovery. They tend to buy products containing lactoferrin as part of their **daily health routine**, or when they feel that they may be getting a cold.

Lactoferrin is gaining popularity in Europe as various research groups have independently published expectations that lactoferrin might be effective **against COVID-19**¹⁻⁴.

Recent clinical findings in Italy¹ show that lactoferrin supplementation supports fast removal of the virus from the body. More controlled trials are ongoing to confirm efficacy.



¹Campione et al., *BioRxiv* 2020:1-33; ²Serrano et al., *Int J of Research in Health Sciences* 8(1):8-15;
³Lang et al., *PLoS One*. 2011;6(8):e23710; ⁴Mirabelli et al., *BioRxiv* 2020 bioRxiv. 2020 Jun preprint.

Why Biotis™ Lactoferrin?

Thanks to FrieslandCampina Ingredients' cutting-edge separation technique, Biotis™ Lactoferrin features the highest and most consistent quality level on the global market.

Our lactoferrin has a 96% purity level for total proteins, and a high iron binding capacity of approximately 80%.

FrieslandCampina Ingredients controls the entire supply chain for Biotis™ Lactoferrin, using our own raw milk for production, as well as gentle heat treatments to preserve nativity and immune bioactivity.

Biotis™ Lactoferrin is manufactured using a sophisticated spray-drying technology. This gives the product a very narrow particle size distribution, making it ideal for blending with other ingredients to deliver a homogenous, high-quality end product.

To serve the significant increase in demand that we envisage for lactoferrin across all adult life stages, we have invested in multiplying our production capacity, making us one of the world's largest producers.

Our applications

We work directly with our customers to help them deliver exciting new products and innovations to market, even connecting them with the right research partners or third-party manufacturers to fully realise their ambitions. We advise you all the way from concept to prototype to full product launch - a total solution.

Whilst Biotis™ Lactoferrin is available as a versatile spray dried powder at the highest purity and efficacy levels, ready for incorporation into multiple product formats, we also help customers to achieve novel product formats that offer innovation opportunities.

Chewable gummies is a potential area of application co-creation with Biotis™ Immune Health. Easy to chew, swallow and digest, such a product mimics the way we eat food, supplying the body with nutrients in the most natural way.

An oral application also delivers the active ingredient at a key 'frontline' of immune defence: the oral cavity, oropharynx, laryngopharynx and upper respiratory tract.



Human nutrition is a vast and multidimensional subject

Our knowledge, exploration and ongoing learning is supported by a network of research partners who share their findings and expertise with us.

We work closely with specialist universities and science centres, as well as influential associations, with one aim: to be your ideal partner for the development of immunity-supporting benefit solutions.

Let's work together to create innovative new products for better immune health globally.



Immune health

Solutions for natural immune support

The Netherlands

Stationsplein 4
3818 LE Amersfoort
The Netherlands

Tel: +31 (0)33 713 33 33

Asia-Pacific

3 Temasek Avenue
#11-01 Centennial Tower
Singapore 039190

Tel: +65 6580 8100

China

2506, West Tower of
Twin Towers
B12 Jianguomenwai Ave,
Chaoyang Dist.
Beijing 100022 China

Tel: +86 10 6566 6099

North America

61 S. Paramus Road,
Suite 535
Paramus, NJ 07652, USA

Tel: +1 551 497 7300

Latin America

Rua Fradique Coutinho
30 - 6° - Cj. 61
Condomínio Edifício WinWork
Pinheiros
05416-000 São Paulo, Brasil

Tel: +55 11 2395-1700

- This information is intended for B2B professionals only
- Potential consumer benefits are not to be considered as health claims. They should be considered as potential leads that might be developed into health claims complying with the local legal requirements.
- The information contained herein is, to the best of our knowledge, correct. The data outlined and

the statements are intended only as a source of information. No warranties, expressed or implied are made. On the basis of this information it is suggested that you evaluate the product on a laboratory scale prior to use in a finished product. The information contained herein should not be construed as permission for violation of patent right.

 Follow us on LinkedIn: **FrieslandCampina Ingredients**

 Follow us on Twitter: **Biotis_TM**

 Visit us at: **www.biotis.com**

