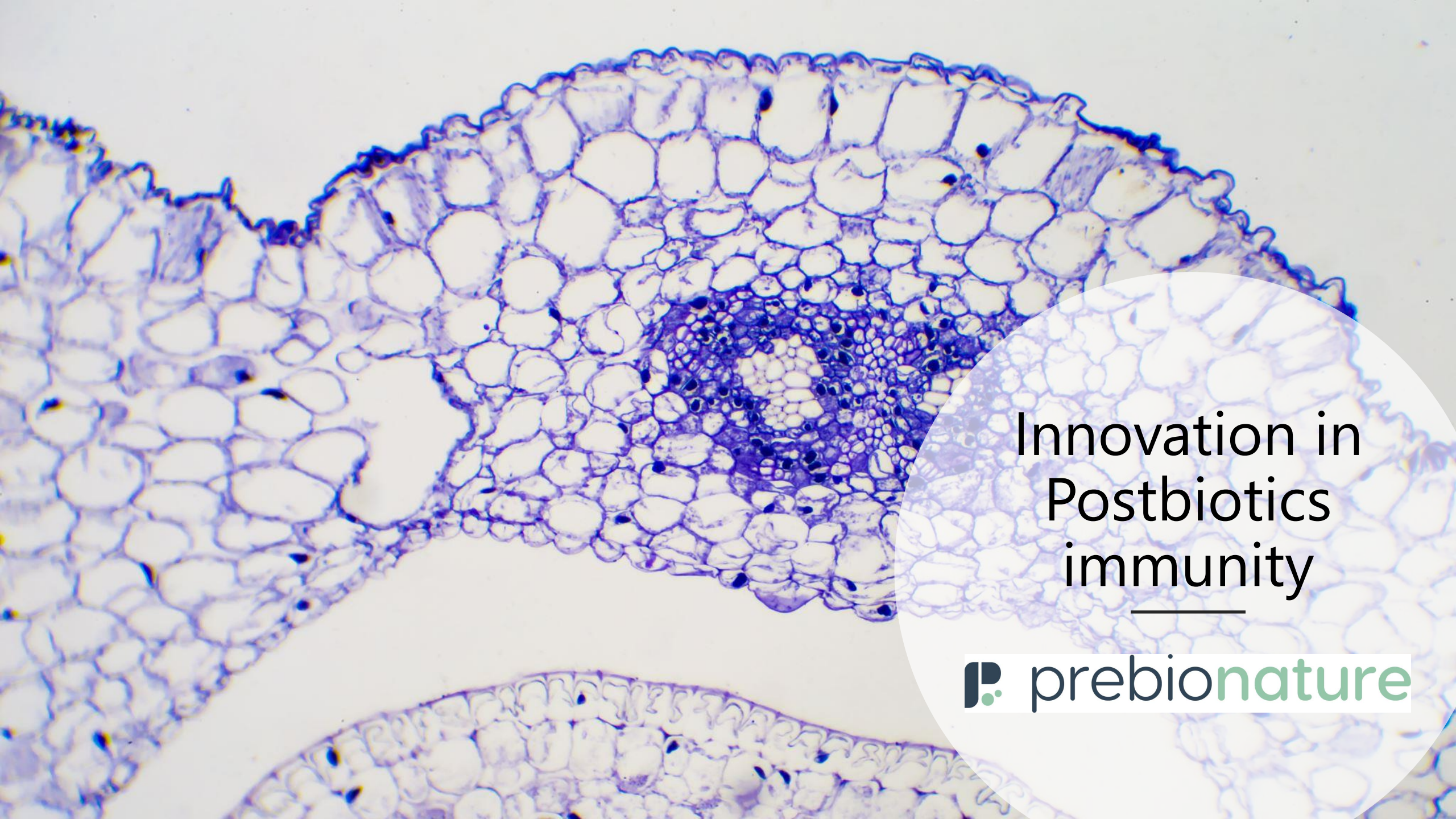


A microscopic image showing a cross-section of plant tissue, likely a root or stem. The tissue is stained with a purple/blue dye, highlighting the cellular structure. The outer layers consist of large, rectangular cells, while the inner part shows a more densely packed, vascular tissue region. A semi-transparent white circle is overlaid on the right side of the image, containing text and a logo.

Innovation in Postbiotics immunity

 prebionature

Postbiotic producing Probiotics

Bacteriocins that strengthen the ecological fitness of the gut microbiota

Probiotics demand has been growing due to increased personalization coming from strains, function in various microbiomes and format.

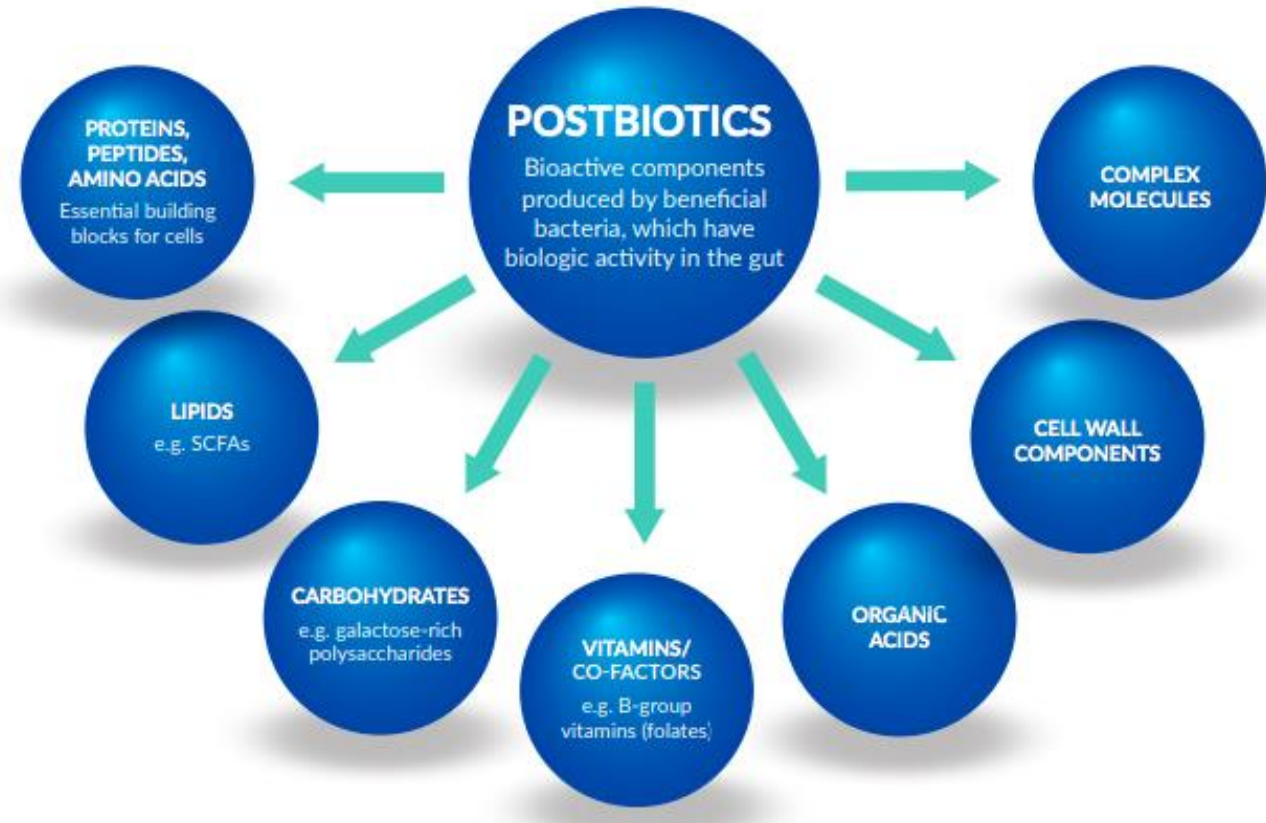
Selective prebiotics feed commensal bacteria to improve diversity and better gut-driven mechanisms via the production of postbiotics.

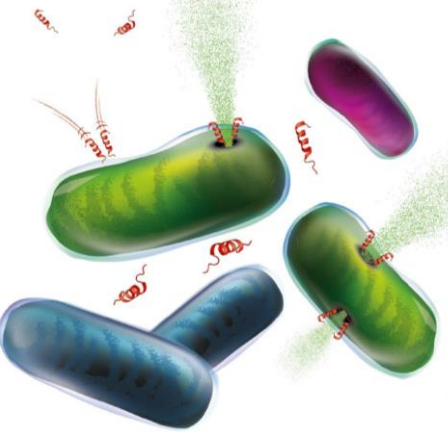
Postbiotic-producing probiotics are a growing subsegment as technology improves to ensure cultivated cells retain their active function.

Bacteriocins stand out thanks to their antimicrobial actions and promote gut microbiota diversity and stability.

Postbiotics are the soluble metabolites produced by live bacteria once in the gut:

Short-chain fatty acids, Peptides, Enzymes, Vitamins and Bacteriocins – the tool-kit for total health.





Proacticin™ Z

Physiologically-active nisin-Z produced by *Lactococcus lactis* MJC18

- **Proacticin™ Z** is a new concept of a probiotic strain *Lactococcus lactis* MJC18 producing Nisin-Z, which has broad-spectrum antimicrobial action and is GRAS approved.
- Nisin-Z is endowed with many biological properties, from the inhibition of bacterial growth to the induction of an immune protection against viral infections.
- Nisin-Z induces the production and secretion of molecular immune system regulators called chemokines such as TNF-alpha which play a critical role in immune responses, especially in the gut-lung axis homeostasis.
- Nisin Z is a cationic peptide made with rare amino acids bearing a positive charge. This physico-chemical feature can lead to electrostatic interactions with viral capsids or envelopes and could be one of the antiviral mechanisms of nisin Z
- Nisin Z switches on an important arm of our immune system preparing neutrophils in the fight of a viral infection without contributing to the inflammatory process.
- *Lactococcus lactis* MJC18 survives a gastro-intestinal tract modeled environment and maintains the ability to produce Proacticin™ Z.
- Applications include
 - (1) protection against food and airborne pathogens;
 - (2) People with weakened immune systems such as IBS/IBD sufferers
 - (3) Providing a daily protection of the microbiota

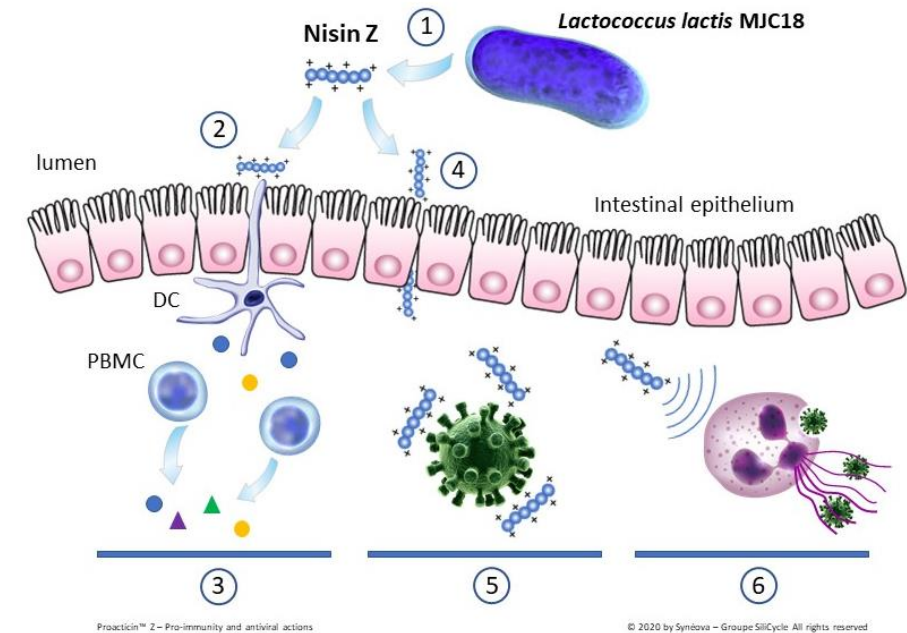
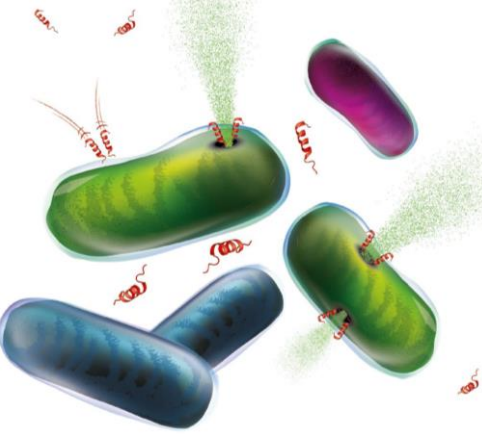


Figure 1: Pro-immune and antiviral actions of nisin Z and *Lactococcus lactis* MJC18 – Proacticin™ Z.

①. Nisin Z and post-biotic metabolites could stimulate the systemic immune system through interactions with microbiota-sensing immune cells (DC: dendritic cells, PBMC: T cells) ②. A cascade of immune regulators can impact the trafficking and polarization of distant subsets of T cells thereby tailoring the systemic immune system ③ (also Grainger, 2018). Nisin Z can diffuse through an intact intestinal barrier ④ towards target organs exerting a direct antiviral effect through electrostatic interactions ⑤. Another pro-immune mechanism induced by nisin Z occurs via neutrophils. Indeed, nisin Z induces NET formation and phagocytosis leading to the trapping, internalization and inactivation of viral particles ⑥.



Proacticin™ PA

Physiologically-active Pediocin PA-1 produced by *Pediococcus acidilactici* UL5

- **Proacticin™ PA** is a new concept of a probiotic strain *Pediococcus acidilactici* UL5 producing and secreting an active bacteriocin pediocin PA-1.
- Canadian discovery and funded research development
- Pediocin PA-1 remains active and inhibits *Listeria* sp. growth throughout the gastro-intestinal tract without affecting the integrity of the microbiota.
- Proacticin™ PA survives a gastro-intestinal tract modeled environment
- The strain *Pediococcus acidilactici* UL5 maintains the ability to produce the bacteriocin pediocin PA-1, in situ, in a gastro-intestinal tract modeled environment
- The bacteriocin pediocin PA-1 is active against pathogenic *Listeria* sp.
- Proacticin™ PA does not affect the ileal microbiota
- Applications include
 - (1) protection against foodborne *Listeria*;
 - (2) People with weakened immune systems such as IBS/IBD sufferers
 - (3) Occasional and frequent travelers
 - (4) Providing a daily protection of the microbiota



In situ visualization of the cytoplasmic emptying of a *Listeria* bacterium through a pore created by the bacteriocin pediocin PA-1





Experts in Probiotics and
Gut Health Solutions



Quality bacteria for your formulation

Prebionature works with reputable and experienced manufacturers of strains to ensure highest quality and supply

Strains are chosen based on formulation requirements such as

- strain diversity and CFU quantity
- delivery format (capsule, chewable tablet, liquid)
- Addition of bioactives such as a plant extracts
- shelf stability and climate zone



Clinical strains for your probiotics

- Prebionature has a series of unique clinically-studied strains in its portfolio to build superior formulations aimed at:
 - Food-borne pathogens like *Salmonella*, *Campylobacter*, *E coli* 0157, *Clostridium*, *Listeria* sp.
 - Antibiotic and *C. difficile* associated diarrhea
 - Prenatal / Postnatal women's health
 - Infant and Toddler health
- *Pediococcus acidilactici* UL5
- *Lactococcus lactis* MJC5
- *Lactococcus lactis* MJC18
- Howaru™ Protect *Lb acidophilus* NCFM™ + *Bf lactis* BI-07
- Howaru™ Protect Early Life *Lb rhamnosus* HN001
- *Bifidobacterium breve* M-16V™
- *Bifidobacterium bifidum* BB-536™
- *Lactobacillus acidophilus* L92™
- Howaru™ Transit *Bifidobacterium lactis* HN019™





R&D is at the heart of our success

- A complete team with PhDs, Masters and technicians
- Solid oral, liquid and vaginal formulations
- Topical formulations
- Regulatory support



Our clients love our
Quality

Prebionature has put in place a complete Total Quality Program with Standard Operating Procedures (SOPs).

All Manufacturing stages are verified, guaranteeing the conformity and integrity of the product.

Our clients are assured to receive products of the highest quality.



Manufacturing Quality Probiotics

- 70,000 sq ft of manufacturing and packaging
- Over 2000 sq ft of dedicated refrigerated and freezer space for strain storage and tempering
- Pharmaceutical grade facility, environmental controls (temp, RH, contamination controls)
- UL, FDA (21CFR111), Health Canada approved; EcoCert organic certified
- Site produces NDC (US) and DIN (Canada) products
- Over 300 million doses produced annually
- No recall or product incident on record



Manufacturing Quality Probiotics

Multiple format capabilities

Oral dosage : capsules, tablets, organic SR tablets, microtablets, ODTs, chewables, wafers, ovules, powders, DuoCaps (liquid/solid cap in cap)

Liquid: plant-based oil bases

Combination products with other bioactives

Topicals

Over 20 years of experience sourcing/formula development

Significant production flexibility

Low cost manufacturing – Canadian cost position

Stable workforce

Existing and future capacity options

Strict Health Canada manufacturing standards on all supplements

Regular audits and certifications

Integrated API – R&D – Production capabilities

Our Manufacturing Advantages

Over 100 Active Private Label Products

United States
Canada and
International





 prebionature

Experts in Probiotics and Gut Health Solutions
