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Immune evolution:
Forming a **new** foundation

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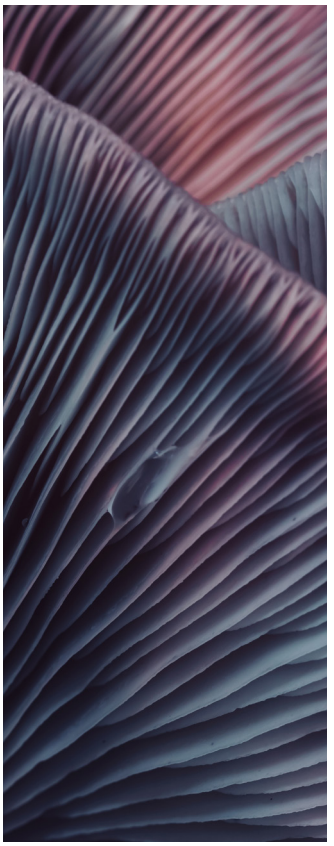

Immunity isn't about urgency anymore – it's about **resilience**

If there's one thing the last few years have taught us, it's that immune health is no longer something consumers think about only when they feel a tickle in their throat. The pandemic may have accelerated that shift, but the lasting outcome is that immune support has become part of daily wellness – something closer to a multivitamin mindset than seasonal support.

Yes, the category's whirlwind moment has passed. After experiencing record high growth in 2020, this market felt a sharp -15.6% growth correction in 2022. Immune health settled near flat in 2023 before returning to 3.2% growth in 2024.

That's not headline-grabbing double-digit expansion, but it represents something more meaningful: stability. Cold, flu and immunity supplements now represent a $5 billion market, one of the largest condition-specific segments that NBJ tracks. Even a modest mid-4% growth rate through 2028 adds nearly $900 million in incremental revenue. When a category is that large, steady beats dramatic.

Consumers have simply recalibrated. They're no longer chasing "quick fix" immunity spikes; they're investing in resilience. This is where probiotics have quietly won the long game. The pandemic didn't send them soaring the way elderberry surged – probiotics have maintained growth while elderberry saw steep declines in 2022 and 2023. Today, immune support is a core pillar of the broader probiotics and gut-axis movement, tied to gut health, stress recovery and whole-body wellness. What once felt like a leap is now intuitive.

We may not see another explosive surge in immune health unless the world sees another disruptive event (and here's hoping we don't). But we are seeing something more durable: immune support positioned as foundation, not reaction. It's in the morning routine, the "just in case" travel pouch, the wellness app reminder, the quiet habits that stack over time.

The era of immune health as a spike is over. The era of immune health as a baseline has just begun.

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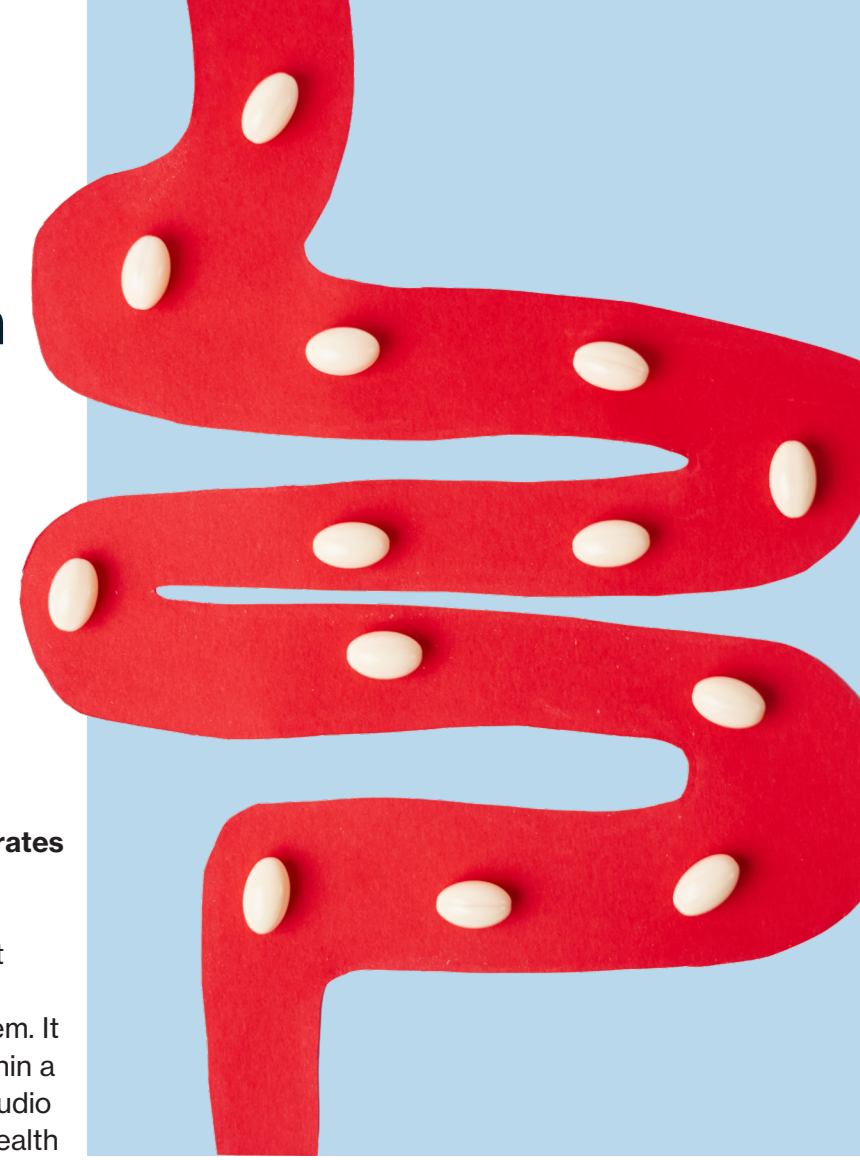
The next generation of gut-immune health solutions blurs the lines between biotics

by Peter Rejcek



The ancient Greek physician Hippocrates believed that "all disease begins in the gut." It took more than 2,000 years for modern science to recognize that the gastrointestinal (GI) tract is the central regulatory hub for the body's immune system. It houses the majority of its immune cells within a surface area the size of a New York City studio apartment. Today, the intersection of gut health and immune defense is arguably the most dynamic frontier in modern wellness research.

James Munro, N.D., medical director and senior director of innovation at Xymogen — a supplement brand with key distribution through health care practitioners — noted that the GI tract and the immune system share a "super complicated relationship" but emphasized the underlying simplicity: "The GI tract needs to be healthy for the immune system to work. The immune system has to work for the GI system to work."

In the last few years, new insights have emerged about this complicated relationship. For instance, one critical component of the gut-immune interaction likely involves microbial metabolites — the fermented byproducts of beneficial gut bacteria feasting on prebiotics.

Cassondra Saande, Ph.D., scientific adviser at biotics-focused ingredient supplier and developer Novonesis Human Health, explained that recent findings suggest microbial metabolites — such as short-chain fatty acids (SCFAs), already well-known metabolic powerhouse molecules, and compounds created by the essential amino acid (EAA) tryptophan — modulate immune signaling pathways and influence T-cell differentiation and function.

"These insights deepen our understanding of gut-immune crosstalk and pave the way for innovative strategies aimed at improving health outcomes," Saande noted.

Sandra Saville, director of education and communication with the International

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> Emerging research highlights the ability of human milk oligosaccharides to **modulate the gut microbiota** and **strengthen the gut barrier.**

Probiotics Association (IPA), added that recent "mechanistic and clinical studies have clarified how the gut communities tune vaccine responses, antiviral defenses and inflammatory tone, while practical formats" such as human milk oligosaccharides (HMOs), postbiotics and pasteurized next-generation probiotics, among other products, "make these insights manufacturable."

In other words, the convergence of new research discoveries and innovative product solutions is helping reshape the field of gut-immune health. Let's dive deeper into several of these bleeding-edge insights and solutions.

HMOs are not just for kids anymore

HMOs are a unique and powerful class of prebiotics — complex, indigestible sugars that are naturally abundant in human milk. Historically, HMOs have been studied primarily in infants, where their primary role is to selectively nourish the developing infant microbiome and support immunity. However, advances in HMO production have greatly increased their availability, enabling broader applications beyond infant nutrition, according to Saande.

"More recently, their use has expanded into adult health, where they are being incorporated into dietary supplements and functional foods," she said. "While randomized controlled trials on HMOs — particularly in adults — remain limited, emerging research highlights their ability to modulate the gut microbiota and strengthen the gut barrier, positioning HMOs as a promising ingredient for products targeting digestive health and immune support across all age groups."

More broadly, HMOs belong to what Zac Lewis referred to as a "new class" of highly selective prebiotics that enrich very specific desirable microbes, rather than simply providing generic bulk fiber that can feed a wide range of microbes. "IFF [Health Sciences] is exploring more selective prebiotics and how to formulate potentially synergistic synbiotics that — through thoughtful product design choices — could deliver stronger benefits than what is currently on the market," explained Lewis, microbiome and biotics product innovation lead at the company, an ingredient supplier focused on microbiome bioscience.

Probiotics go postmodern with postbiotics

No longer an esoteric ingredient known to only a few well-read intellectual scholars,

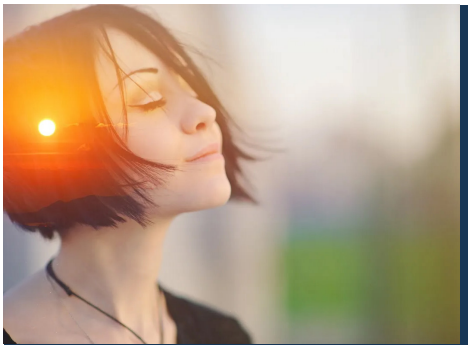
Precision platforms can deliver and release **higher cell counts** with more **reliable dosing**.

postbiotics are increasingly the subject of new clinical research and innovative formulations for immune health. In 2021, the International Scientific Association of Probiotics and Prebiotics (ISAPP) officially defined postbiotics as "a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host."

Postbiotics confer their benefits through various means, including inanimate microbial cells, cell wall fragments, secreted proteins and the rich matrix of metabolites produced during fermentation, all of which directly interact with host immune and epithelial cells. The benefits are also more commercially practical; they solve one of the major hurdles for traditional probiotics — stability — because postbiotics do not require the same careful handling during manufacturing and storage.

Justin Green is scientific affairs lead at ingredient supplier Cargill for the postbiotic EpiCor, which is derived from the fermentation of *Saccharomyces cerevisiae* (baker's yeast). He noted, "Postbiotics are particularly exciting because they don't rely on being alive to deliver benefits, which gives formulators much greater flexibility." A recent randomized double-blind placebo-controlled clinical trial, for instance, demonstrated the efficacy of EpiCor in a gummy format on immune health in children. The study was the first to assess the health benefits of postbiotics in a pediatric population and one of the few to use gummies, according to Green.

New research also indicated that pairing yeast- and bacterial-derived postbiotics may provide synergistic benefits, opening a promising path for further research and product innovation, noted Katie Oleksak, director of clinical education at Biohm Technologies — a microbiome-focused research and ingredient development company.



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Review sheds light on selenium's brain benefits

A new review has gathered the recent highlights of selenium's role in brain health. This adds to already proven benefits in immune health.

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Precision platforms can deliver and release **higher cell counts** with more **reliable dosing**.

Meet the next generation of probiotics

Despite the potential of postbiotics, no one is ready to do a postmortem on probiotics just yet. Indeed, recent advancements in gut microbiome sequencing and strain isolation technology have identified so-called next-generation probiotics. These novel microorganisms are often native inhabitants of the human gut, such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*. For instance, *A. muciniphila*, which accounts for up to 5% of the human microbiome, is critical for protecting intestinal barrier integrity and regulating immune response.

However, many next-generation probiotics, such as *F. prausnitzii*, are extremely sensitive to oxygen, which makes manufacturing and delivering them as viable, live organisms in a supplement format incredibly difficult. One seemingly counterintuitive solution is pasteurization. Studies have shown that pasteurized bacteria can not only retain their beneficial effects but, in the case of *A. muciniphila*, may even enhance them by preserving outer-membrane bioactives, including key proteins and lipids.

Whether such a product is considered a probiotic or a postbiotic (or a post-postbiotic?) would need to be revisited, according to Stacey C. Smith, Ph.D., senior medical science liaison at ingredient supplier Gnosis by Lesaffre. "As immune-related probiotic and postbiotic claims proliferate, alignment among definitions, postbiotic guidelines and regional authorities will be critical," she noted. "Such harmonization can accelerate innovation while maintaining scientific and consumer trust."

The future points to targeted immune support

Another emerging field of study is dedicated to improving probiotic delivery system efficacy, from hydrogels and nanocoatings to emulsions and core-shell microgels. In theory, these precision platforms can deliver and release higher cell counts with more reliable dosing.

The ultimate goal is to move from generalized gut and immune support to precise, personalized nutrition — products tailored to an individual's microbial profile. Smith asserted that advances in computational biology, artificial intelligence (AI)-guided discovery and metabolomic mapping are making it possible to identify microbial signatures linked to immune responses. This opens the door to personalized formulations based on specific immune phenotypes or microbiome "fingerprints."

"Companies are beginning to pair multiomics datasets with targeted formulation platforms — an evolution that could define the next decade

of gut-immune innovation," she said. "We are entering a phase where the microbiome is becoming a design variable in immunity."

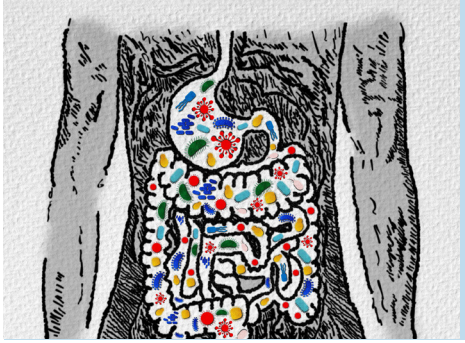
Munro, the naturopathic physician, said the techniques will only become more refined over time. "It's going to get so much more nuanced, and then we'll be able to actually impact very small little areas of the microbiome that can have profound impacts," he predicted.

To Munro's point: A 2025 study revealed that certain prebiotics, like gluconic acid-containing oligosaccharides, selectively promote the growth of beneficial next-generation probiotic bacteria such as *F. prausnitzii*. The authors concluded that the study underscores the "importance of microbial interactions in prebiotic research, offering new avenues for personalized microbiome modulation strategies."

Green nicely summed up this tidal wave of emerging research between gut health and immunity, stating, "These discoveries point to a future where categorizing microbiomes and harnessing both live and nonliving microbes open new pathways for personalized nutrition and targeted immune support." ■

We are entering a phase where the microbiome is becoming a **design variable in immunity.**

Formerly the world's only full-time journalist in Antarctica, Peter Rejcek is a professional editor and writer with nearly 30 years of experience covering science, technology, business and health, including the natural products industry. He also previously served as a senior editor for the supplements and health section of the Natural Foods Merchandiser.



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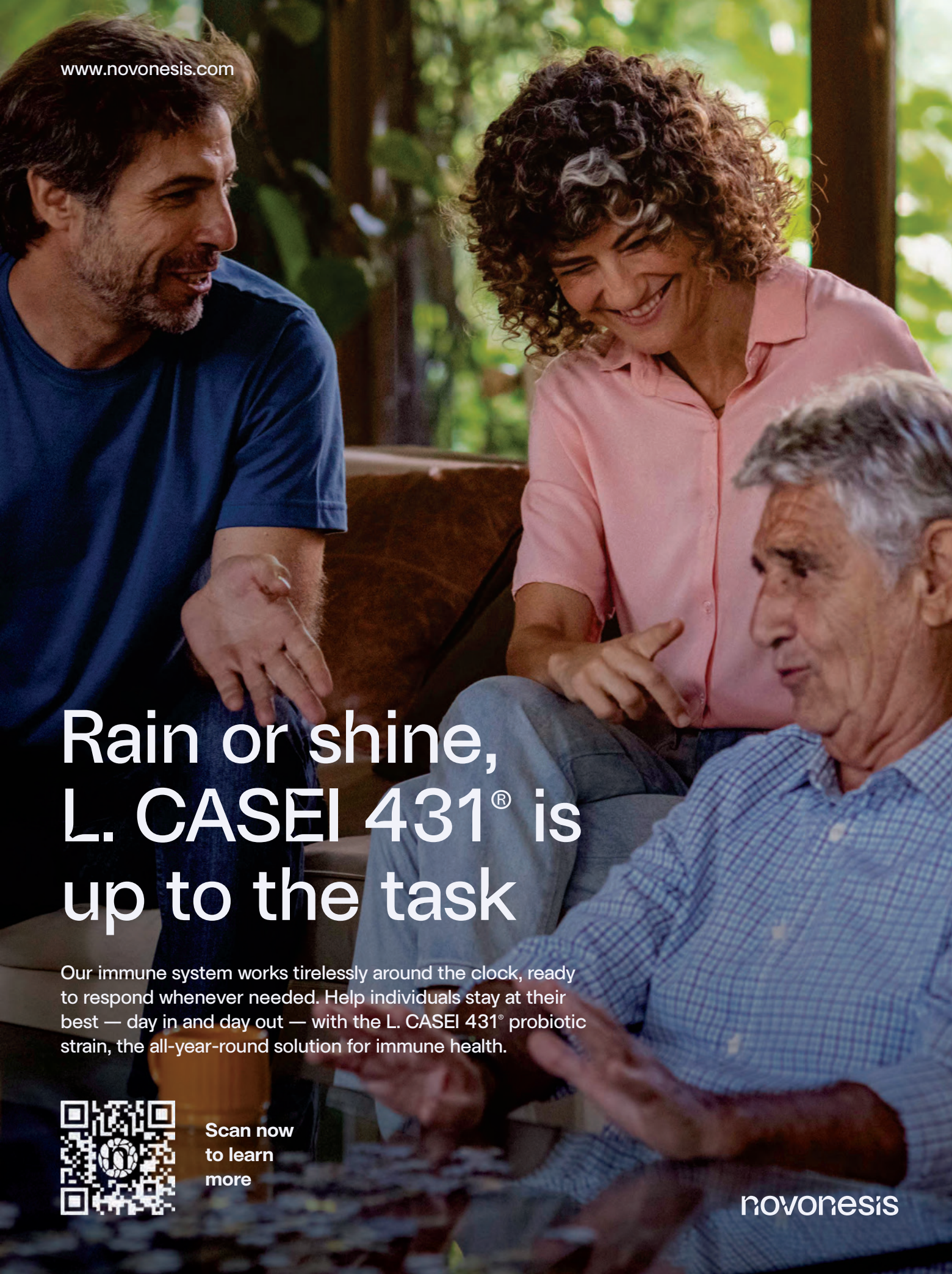
4 emerging postbiotic opportunities

Postbiotics are moving from niche to the nutrition mainstream, a development confirmed at the recent SupplySide Global show in Las Vegas. Here's what brands need to know before this trend explodes.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Immunity can be **herbalicious!**

by Devon Gholam

The cold and flu season has arrived, that time when many consumers play roulette with supplements and medication trying to keep a case of the sniffles from growing into a full-blown cold or bout of the flu. But immune health is no longer confined to the winter months — consumers are increasingly focusing on herbs and botanicals to support their immune systems.

Nutrition Business Journal ranks combination herbal formulas as the No. 2 top ingredient category by sales in 2025 for the cold, flu and immunity supplement market, generating $891.7 million in sales. Herbs lead the growth among the top six ingredients in this category, with their projected growth rate reaching 7.5% in 2025 and climbing to over 9% by 2028. This means herbs for immune health are on track to hit $1 billion in sales by 2027.

Elderberry (*Sambucus nigra*) and echinacea are two of the most commonly used herbs in immune supplements, yet nature's garden has many other solutions for support against viruses. Let's review the research on the traditional immunity-boosting herbs and dig into some other ingredients that may become key components in future formulations.

The mainstays: Elderberry and echinacea

Although elderberry and echinacea are frequently the go-to immune herbs, Blake Ebersole, president of consulting and services company NaturPro Scientific, said they commonly are misused. He explained that many

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Elderberry and **echinacea** are two of the most commonly used herbs in immune supplements.

formulators throw these two ingredients into supplements without realizing echinacea is best used for treating acute illness, while elderberry provides long-term support for the immune system (study links follow).

Elderberries have a long history of use for their potential health benefits and healing properties. Jennifer Greer, N.D., consultant and scientific educator, said it isn't just about the berries, though — the flowers also have immune-supporting properties. Practitioners have used both flowers and fruit from European black elder to treat or prevent several diseases, including diabetes, arthritis and respiratory tract infections (RTIs). Greer added the berries are good for cold and flu prevention while the flowers may be helpful for seasonal allergies.

Elderberries contain several polyphenolic compounds, including quercetin, a flavonoid found in several fruits and vegetables known for its anti-inflammatory, antiviral and antioxidant properties. The Covid-19 pandemic sparked significant interest in elderberry. While there were initial concerns elderberry may cause a "cytokine storm," a review did not uncover any link between elderberry and inflammation.

Echinacea also received increased attention because of the Covid-19 pandemic. Researchers widely recognize Echinacea species — including *Echinacea purpurea*, *Echinacea angustifolia* and *Echinacea pallida* — for their antiviral and immunomodulatory activities. While this herb is most effective in treating acute conditions, Ebersole noted it can be challenging to conduct clinical trials on herbal solutions meant to provide acute symptom relief — for instance, because of timing issues when participants are ill or the efficacy of an ingredient not necessarily being equal against all viruses. Nevertheless, a recent study showed higher doses of echinacea accelerated viral clearance, and a review demonstrated reduced incidence of RTIs in children.

Product developers are exploring **olive leaf extract** for immune supplements.

Emerging herb solutions for immune health

When asked about other potential herbal supplements that support immune health, Ebersole and Greer had several options at the ready, including ivy leaf, white peony root and olive leaf extracts.

Ivy leaf extract (*Hedera helix*) is a well-studied ingredient that Greer said is gaining traction in Europe. This ingredient is established as a safe option for treating cough related to upper RTIs and bronchitis. Researchers have conducted several clinical trials on EA 575, a proprietary extract marketed as a syrup under the brand name Prospan, in cough products. Clinical trials showed EA 575 improved cough symptoms in both adults and children and reduced antibiotic use in children and adolescents.

Traditional Chinese medicine (TCM) practitioners have long used white peony root, known as *Paeoniae Radix Alba* or the root of the *Paeonia lactiflora* plant. The active components in *Paeonia* species are primarily monoterpene glycosides, with paeoniflorin being the most abundant. Peony glycosides provide immunomodulatory and anti-inflammatory properties, which may help treat autoimmune diseases.

While no clinical trials assessing white peony supplementation in healthy populations were readily located, the anti-inflammatory effects may be beneficial in shortening duration of illness. Greer noted compounds with antioxidant and anti-inflammatory properties may be beneficial during the middle to the end of cold and flu bouts, as they have shown to help combat oxidative stress and may otherwise support the body with repair and clean-up after battling viral illnesses.

Product developers are exploring olive leaf extract (*Olea europaea*) for immune supplements, which aligns with the health halo surrounding olive oil. Researchers have

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Prebiotics and probiotics have something to prove in menopause research

There's a bit of promise in a recent review that assessed the state of research for prebiotics and probiotics for ameliorating menopause symptoms.

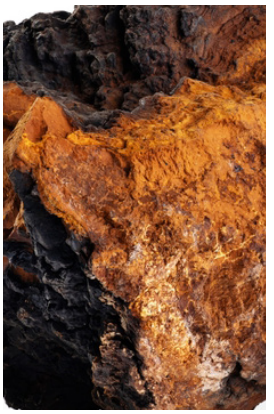
demonstrated that olive leaf extract offers various benefits, including reducing blood pressure and lipid profile, improving oxidative stress in obese women on restricted-calorie diets, and increasing bone mineral density in postmenopausal women.

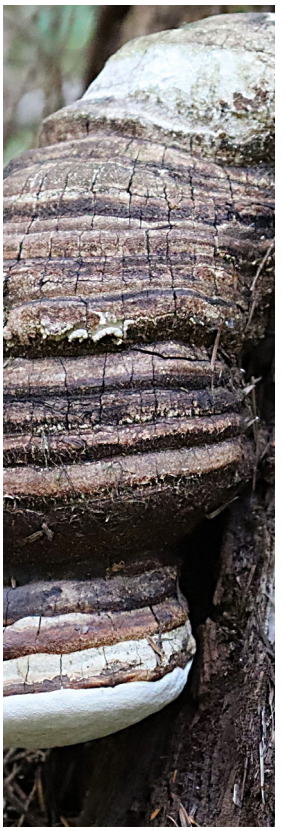
In addition to being cited as a potential therapeutic agent against Covid-19, researchers evaluated olive leaf extract in a clinical trial among high school athletes and found that supplementation significantly reduced sick days. While olive leaf extract reduces proinflammatory cytokines, likely due to the phenolic compound oleuropein, it also may impact immune health via interaction with the gut microbiome.

Polyphenols can also impact immunity by helping the body adapt to everyday stressors. VitAlign from Futureceuticals has been shown to maintain immune resilience by supporting a healthy immune system response and oxidative balance.

It is clear Mother Nature has much to offer in the way of immune health support. From leaves and roots to berries and flowers, product developers can use a wide variety of clinically validated ingredients in new formulations. Innovative formulators should evaluate clinical trials, provide guidance so that brands can make credible claims on packaging, and choose the full efficacious dose when selecting ingredients. Doing so can help make the world better — and a little less prone to viruses — one great product at a time. ■

Devon Gholam, Ph.D., is a SupplySide Supplement Journal editor.



Four **mushrooms**, dozens of studies, one clear message about **immune health**

by Julie Daoust

Comprised of mushroom growers, suppliers and brands, the Functional Mushroom Council is an organization that believes in the immense potential – and urgent need – for a unified voice in the rapidly expanding functional mushroom industry in North America.

The members of the Functional Mushroom Council have published dozens of studies that demonstrate the benefits of functional mushrooms, which includes human cell research that shows functional mushrooms – including mycelium – support immune function. Let's unpack the science behind four powerful functional mushroom varieties.

M2 Reishi 102

Reishi mushrooms (*Ganoderma lucidum*) – often called the "mushrooms of immortality" – are known for supporting immune balance, and new research confirms why. In a recent analysis by NIS Labs, M2 Reishi 102 was compared with another leading reishi extract to see how each affected immune activity under normal, bacterial and viral stress conditions.

Even without a threat present, M2 Reishi 102 helped "wake up" key immune cells like natural killer (NK) cells, monocytes and T-cells – essentially priming the immune system to be alert and ready. Under simulated bacterial stress, it helped calm excessive inflammation,

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> **Reishi** helps the immune system stay balanced, responsive and resilient.

reducing activation markers more effectively than a competitor. During simulated viral infection, M2 Reishi 102 showed a balanced immune response — boosting NK cell activity while preventing other cells from overreacting. This kind of moderation is important because an overactive immune response can do more harm than good.

The study also found that M2 Reishi 102 improved cytokine signaling — the chemical "messaging system" that immune cells use to coordinate their response. It was particularly strong at lowering inflammatory cytokines like interleukin (IL)-6 and tumor necrosis factor (TNF)-alpha, both linked to over-inflammation. The result: a steadier, more controlled immune defense.

In a separate clinical proof-of-concept study in healthy adults, M2 Reishi 102 again stood out. Within two hours of taking the supplement, participants showed a 30% increase in NK cells and nearly a 20% increase in NK T-cells, both critical for early immune defense. It also raised levels of granulocyte colony-stimulating factor (G-CSF), a natural protein tied to tissue repair and immune cell production.

Reishi continues to be one of the most respected functional mushrooms — helping the immune system stay balanced, responsive and resilient.

Chaga

Often called the "king of medicinal mushrooms," *Inonotus obliquus* (chaga) has a long history of traditional use for strengthening

resilience and vitality. Modern research confirms that these effects are rooted in the fungus's ability to modulate immune function and combat oxidative stress.

Polysaccharides from chaga — particularly beta-glucans — are among its most studied bioactive compounds. These complex carbohydrates have been shown to stimulate macrophage and NK cell activity, supporting both innate and adaptive immune responses. In parallel, chaga's sterols, melanin and phenolic compounds act as powerful antioxidants, helping regulate redox balance and reduce inflammation that can weaken immune defenses. Collectively, these mechanisms help the body respond more efficiently to stressors while maintaining immune homeostasis.

Importantly, recent studies have shown that the composition and potency of chaga extracts depend on the source material.

Functional mushrooms have been substantiated to promote **immunomodulatory** activity.

Traditional wild-crafted chaga conks are largely made up of birch tissue infused with only about 10% fungal biomass, meaning much of their chemistry originates from the host tree. In contrast, cultivated North American chaga mycelium represents pure fungal material rich in structurally diverse beta-glucans, polysaccharides and sterols. This cultivated approach ensures consistent, sustainable production of chaga's immune-supporting bioactives while avoiding the ecological and compositional variability of wild conks.

Turkey tail

In another study, a blend of turkey tail (*Trametes versicolor*) mushroom mycelium and fermented substrate was compared to each individual component and an unfermented substrate control. Interestingly, the fermented substrate was often found to provide the most robust immune-related impacts of these treatments, including a notable dose-dependent induction of the immune-engaging cytokines IL-2, IL-6 and IL-8 alongside strong activation of the immune-pacifying cytokines IL-10 and IL-1RA (receptor agonist), highlighting a balanced, whole-system immune modulation.

Fungi Perfecti's Turkey Tail mushroom mycelium also has been evaluated in a clinical study focused on immune health. The study found turkey tail mycelium to be well tolerated and supportive of natural immune cells including NK and CD8+ cytotoxic T-cells.

In another randomized, double-blind, placebo-controlled trial conducted by researchers at the University of California, San Diego, Fungi Perfecti's Agarikon and Turkey Tail capsules (FoTv) were studied for their effects on immune function in healthy adults. Participants who consumed FoTv showed consistent support for healthy immune response over a six-month period, while the placebo group — which received only an unfermented rice base — experienced a decline in key immune markers.

Agarikon

Compounds found in agarikon (*Fomitopsis officinalis*) have shown to safely affect multiple cancer-related pathways and help regulate the immune system, as outlined by this study.

The researchers tested two medicinal mushroom blends — Agarikon and Agarikon Plus — to see how they affect colorectal

(colon) cancer cells in the lab and in mice. They found that both mushroom preparations slowed the growth of colon cancer cells and triggered cancer cell death, but interestingly, they encouraged healthy cell growth, showing that they specifically target cancer cells.

When combined with a standard chemotherapy drug (5-fluorouracil), the mushroom blends also boosted immune response, reduced blood vessel formation that feeds tumors, shrank tumor size and helped mice live longer. These effects seem to come from how the mushrooms influence key immune cells — pushing them toward an anti-tumor mode (known as "M1" macrophages) and away from the types that help tumors grow. They also helped regulate important immune signals and reduced proteins (like VEGF, MMP-2 and MMP-9) that cancers use to spread and form new blood vessels.

Overall, this research provides strong early evidence that medicinal mushroom combinations could be a promising, low-toxicity addition to colorectal cancer therapy.

Functional mushrooms have been substantiated to promote immune-modulatory activity, aiding in the immune system's natural ability to both respond and return to equilibrium. The Functional Mushroom Council and its members are prioritizing and funding research to continue showcasing the wide-ranging benefits of mushrooms, including the undeniable effects on immunity. ■

Julie Daoust, Ph.D., is co-founder of the Functional Mushroom Council and chief science officer at M2 Ingredients.