Solarea Bio
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Managing inflammatory diseases and aging with edible plant microbes

Solarea Bio is harnessing the diversity of the edible plant microbiota to deliver medical food products that aid the dietary management of inflammatory disorders and support healthy aging.

Solarea Bio was founded on the insight that the microbes (bacteria and fungi) naturally residing within raw fruits and vegetables represent a diverse, untapped reservoir of novel functional potential for the dietary management of inflammation and to support healthy aging. The company has built the world's largest library of food-derived microbes and a formidable computational platform to unlock their genomic potential for functions that modulate inflammation. This platform has rapidly generated a robust pipeline of defined microbial assemblages (DMAs)—an innovative product concept consisting of synergistic combinations of food-derived microbes and prebiotic fibers functionally designed to reduce inflammation. Solarea's lead medical food DMA solution, SBD111, is currently in clinical trials for the dietary management of osteopenia and osteoporosis.

Harnessing an untapped source of beneficial functions, the edible plant microbiota

Fresh fruits and vegetables contain many beneficial components, including vitamins, phytosterols, and fiber, which can positively impact health. It is less well known that these healthy foods are also naturally colonized by a microbial community called the edible plant microbiota (EPM). When eaten raw, these foods carry bacteria and fungi through the gastrointestinal tract, where they can influence and modulate health.

Launched at the Illumina Accelerator, Solarea developed methods to isolate these food microbes from the plant matrix. The team performed deep metagenomic sequencing on over 200 fresh fruit and vegetable microbiomes to understand the extent of their genetic diversity and the functional potential encoded in these food-derived microbes. The company recently published a study describing the microbes that colonize tomatoes, spinach, brined olives, and dried figs[1] as examples of this rich and unexplored database. For the first time, these data revealed vast microbial genetic diversity, an abundance of previously uncultured and undescribed bacteria and fungi, and the presence of genes and biosynthetic gene clusters encoding powerful anti-inflammatory mediators important to human health—confirming that fruits and vegetables harbor novel, previously uncharacterized microbes with probiotic functional potential.

"Most people are unaware of the staggering microbial diversity in fresh fruits and vegetables. These microbes have not been well characterized, in part due to the technical challenges of purifying microbes from a plant matrix, but they are as diverse as those found in intestinal or freshwater habitats," said Gerardo V. Toledo, CEO and co-founder of Solarea. "Microbial communities have been studied in extreme habitats including the atmosphere and the depths of the oceans, but surprisingly we don't know the microbes we are consuming in our diet from fresh produce every day."

Solarea has also created an extensive collection of more than 5,000 fully sequenced individual bacterial and fungal strains, and assembled their genomes using scalable, cloud-based computational pipelines. The result is the richest fruit- and vegetable-derived microbial library and genomic catalogue in the world, containing over 14 million genes and over 1.6 million predicted biosynthetic gene clusters. This best-in-class database represents substantial potential for novel solutions to manage diseases and to promote human health through dietary interventions with DMAs as medical foods. In contrast to nutritional supplements, medical foods are required to show clinical benefit, must be administered under the supervision of a physician, and are allowed to make specific disease label claims based on validation in randomized controlled clinical food trials.

Function-based approach to product development

Solarea's product development platform begins with a function-forward approach (Fig. 1). Leveraging its expertise in host–microbe interactions, the team identifies specific microbial functionalities that can manage a desired immune response. The company then rapidly screens its extensive database of EPM genomes in silico to identify bacterial and fungal isolates harboring the genomic signatures of interest.

These organisms are then combined into DMA products, designed to work together and produce anti-inflammatory compounds and responses synergistically (i.e., greater than the sum of the individual members). Each DMA expresses functional properties that are most relevant to its target disease or application. For example, vitamin K2 and short-chain fatty-acid production are beneficial for bone health, while other indications may require different functional modalities, such as the production of molecules that signal through host receptors.

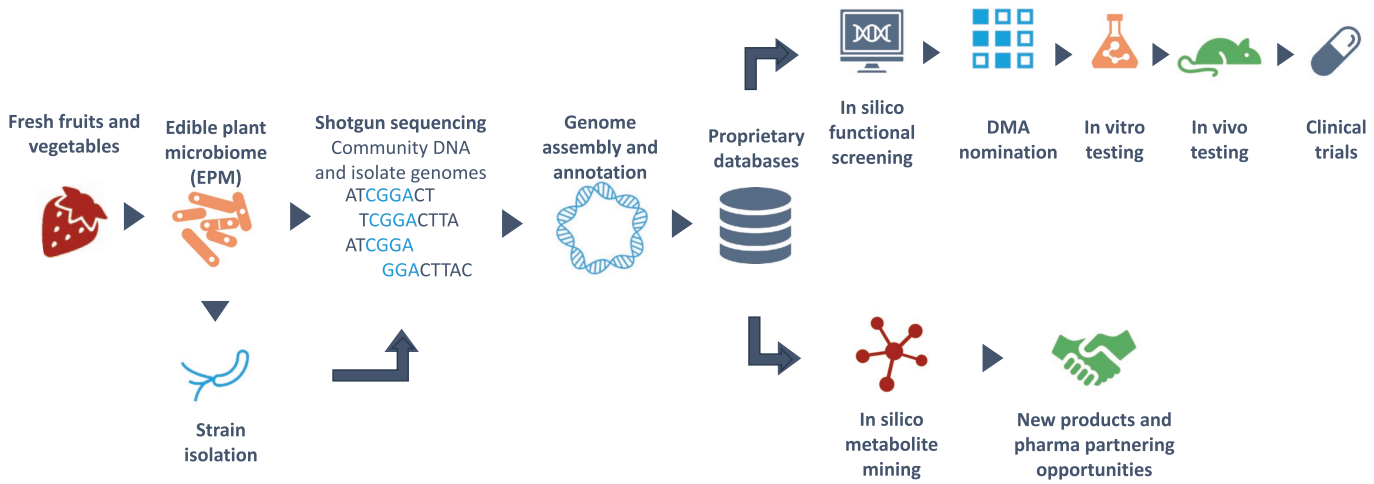

Fig. 1 | Solarea's transformation of food into medicine.

While over 10^{11} possible three-member DMA combinations are conceivable from Solarea's library, the company's function-specific computational pipelines enable selection of a feasible number of isolates for experimental validation. After confirming isolate functions in vitro, leading strains are strategically combined into consortia to assess their additive and synergistic properties using cell-based assays and analytical chemistry. Top-performing DMA candidates are then evaluated using in vivo preclinical models to advance a single lead candidate to the development of a medical food through rigorous double-blind, placebo-controlled clinical food trials.

DMA products are consumed in a user-friendly, enteric-coated capsule format that amplifies the probiotic potential of the EPM by delivering beneficial microbes at a much higher concentration than that observed in food. They pass safely through the intestine where their anti-inflammatory metabolites are delivered locally to host tissues before the microbes are excreted in stool.

Solarea's powerful discovery engine has rapidly and repeatedly enabled the design of a pipeline of products to deliver 'food as medicine' solutions to people in need. The biological effects of a DMA product can be summarized by a localized, transient, and time-released delivery of specific anti-inflammatory mediators to the intestine, where they can elicit beneficial effects, such as modifying immune-cell profiles and reducing inflammatory signaling. Solarea has rapidly established a robust pipeline of DMA products across various disease areas.

Lead DMA for the dietary management of osteopenia and osteoporosis

SBD111 is under development as a medical food for the dietary maintenance of bone mass post-menopause. Osteoporosis, a prevalent disease linked to low-grade, chronic inflammation and characterized by the progressive loss of bone-mineral density, is associated with high rates of mortality and low quality of life. One in three women entering menopause will experience an osteoporosis-related fracture, with hip fractures carrying a 30% mortality rate in the first-year post fracture. Thus, there are potentially devastating consequences associated with osteoporosis.

Although there are approved drugs to treat osteoporosis, options are lacking for peri-menopausal and post-menopausal women to maintain healthy levels of bone. Current recommendations for bone maintenance are diet, vitamins, and exercise, none of which have demonstrated clinical effect. Therefore, there is a large unmet need for natural, safe, and efficacious dietary solutions for women entering menopause to maintain healthy bone mass throughout their lives.

Gut microbes are thought to regulate skeletal homeostasis by signaling through the immune system. SBD111 consists of four beneficial microbes (three bacterial strains and one fungus) and prebiotic plant fibers delivered orally in capsules. SBD111 is designed to maintain healthy bone mass based on its capacity to modulate regulatory T cells and inhibit the inflammation that, in part, drives bone loss.

Preclinical studies demonstrate that administration of SBD111 maintains 60% more bone compared to untreated ovariectomized osteoporotic control mice[2] and is safe and well tolerated (Fig. 2). A food clinical trial in 300 post-menopausal women has been initiated to assess the effect of SBD111 on bone-mineral density over a 12-month period. The product is ready to manufacture at scale, exhibits favorable key performance indicators and shelf life, and has shown excellent safety in acute-toxicity studies in rats[3]. "There are currently very few options for maintaining perimenopausal and postmenopausal bone mass that people will accept," said Susan Bukata, chair of the Department of Orthopedic Surgery at University of California San Diego. "SBD111 would provide a safe, natural, and effective nutritional solution for millions of women entering menopause."

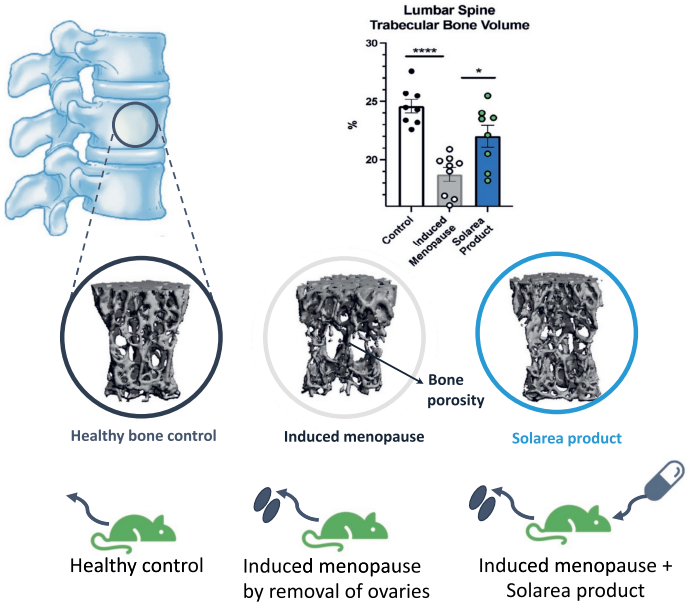

Fig. 2 | Solarea's medical food product, SBD111, maintains bone density in an osteoporosis mouse model.

The future of the Solarea platform

Bone health is the first of many programs with significant market opportunities for DMA technology. Using its powerful platform to harness the vast bacterial and fungal diversity of the EPM, Solarea is able to rapidly deliver novel and effective medical food products to aid in the management of many chronic inflammatory conditions. The company has established a robust preclinical pipeline of additional products, including DMAs designed for the dietary management of autoimmune disorders, including rheumatoid arthritis, and those that support healthy aging.

Beyond live microbial medical food products such as DMAs, Solarea's unique genomic database is being mined for natural product discovery and other metabolites of interest. With the diversity Solarea has observed in its strain collection and over 1.6 million predicted biosynthetic gene clusters, there is a treasure trove of potentially novel immunomodulatory therapeutics to be discovered. In particular, the library of fungal strains and genomes is an untapped source of novel biology with therapeutic potential. New programs in partnership with pharmaceutical companies could leverage both the rapid speed and the accurate hit rate of Solarea's platform combined with the knowledge, infrastructure, and breadth of a pharma company.

"Our vision is to create and lead a new way to rapidly discover, develop, and launch commercial products aiding the management of disorders where other products are not sufficient," said Eric Schott, Solarea's VP of Translational Research and Operations and company co-founder. "Beyond menopause, we are developing products in other markets that also have the potential to improve the quality of life for many people. Our technology has potential applications in pharmaceutical development, animal health, and agriculture in addition to medical foods."

The platform has already generated interest for licensing opportunities, and Solarea signed a technology licensing agreement in 2021 with global nutrition leader, Archer Daniels Midland. In addition, the company has teamed up with Hebrew SeniorLife investigators from Harvard Medical School's Marcus Institute for Aging Research on a 2021 US National Academy of Medicine (NAM) Catalyst Award grant to study the mycobiome as a novel class of probiotics to target inflammation associated with aging. Solarea was also recently selected as an awardee of the NAM Healthy Longevity 2022 QuickFire Challenge, launched by Johnson & Johnson Innovation together with the NAM for a project where they aim to develop DMAs to support healthy aging.

The company is currently raising $20 million in a Series B financing with commitment from all existing investors to deliver two commercial products and to expand its platform to additional targets. By leveraging its extensive capabilities in data science, microbial genomics, ecology, and product development, Solarea has developed a suite of innovative technologies to harness the rich functional diversity of fresh fruits and vegetables to improve health.

1. Soto-Giron, M. J. et al. *Sci. Rep.* **11**, 24017 (2021).
2. Lawenius, L. et al. *Am. J. Physiol. Endocrinol. Metab.* **322**, E344–E354 (2022).
3. Easson, D. D. et al. *Food Chem. Toxicol.* **168**, 113329 (2022).

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