Viome, Inc.
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VIOME

Decoding the human and microbial molecular mechanisms of chronic diseases, cancer, and aging

Viome has developed the world's largest metatranscriptomic platform for analyzing human and microbial functions at the molecular level to discover novel mechanisms underlying chronic diseases, cancer, and aging. The company is seeking partners to develop diagnostics, companion diagnostics, and therapeutics based on targets identified using the Viome platform.

Over the past five years, Bellevue-based systems biology company Viome has developed and commercialized a unique platform for identifying new therapeutic targets using metatranscriptomic profiling technology originally developed at Los Alamos National Laboratory, and exclusively licensed to Viome. The company's core mission is to prevent and reverse chronic diseases, cancer, and aging. In combination with a robust next-generation artificial intelligence platform, Viome is identifying actionable molecular signatures for cancer, metabolic, gastrointestinal (GI), autoimmune, neurological, and other chronic diseases, as well as aging. Viome is the only company able to integrate quantitative human gene (including mitochondrial) expression data, human microbiome gene expression data, strain-level taxonomy for all microorganisms, and exceptionally rich contextual metadata, and to be able to analyze them using cutting-edge machine learning techniques to discover the underlying molecular mechanisms for a range of diseases.

"Viome digitizes, decodes and deciphers human biology with a singular mission to develop novel therapeutic approaches towards prevention and reversal of chronic diseases," said Naveen Jain, founder and CEO of Viome.

The company has already translated these insights into at-home tests to deliver precise, actionable, and individualized dietary and supplement recommendations. Viome has collected longitudinal data and phenotype metadata from blood, stool, saliva, and vaginal samples from more than 200,000 individuals (Fig. 1), analyzing both human and microbial biochemical functions, and generating dietary (food and supplement) recommendations designed to modulate the microbiome and improve overall health and wellness.

Viome has also established partnerships with many leading pharma companies, universities and clinical centers such as GSK, the Mayo Clinic, UCLA, QUT, and AdventHealth to realize the potential of its systems biology platform towards personalized and preventative healthcare.

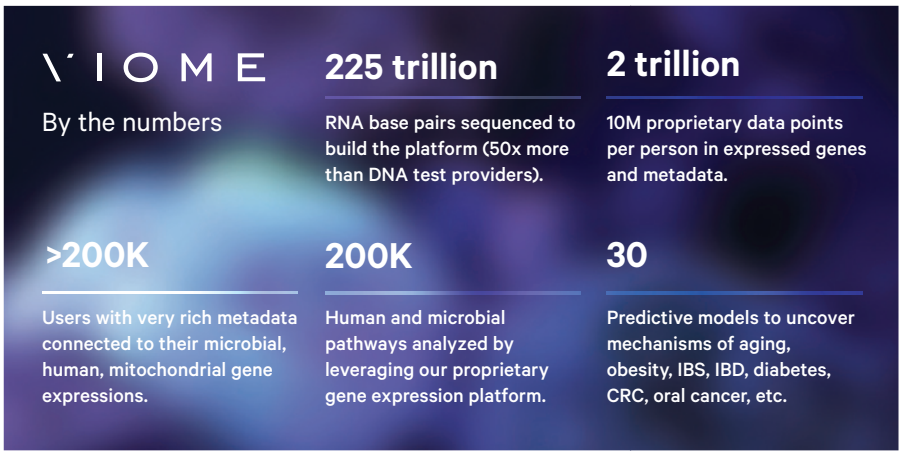

Fig. 1 | Viome has developed the world's largest metatranscriptomic platform for analyzing human and microbial functions at the molecular level. This platform integrates comprehensive metadata, pathway analysis, and advanced artificial intelligence tools. CRC, colorectal cancer; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

Unlocking health and disease using an integrative systems biology approach

Since the completion of the Human Genome Project almost 20 years ago, the understanding of the value of this blueprint of life has shifted to a realization that it is not the genes (DNA) but their expression (RNA) that truly determines health and disease. Viome uses gene expression as the basic unit of information that captures biological function. Gene expression is identified and quantified using the company's proprietary CLIA-certified metatranscriptomic platform.

To capture a complete picture of the interactions among the different biological components that make a human 'human'—from the activities in the gut microbiome to the circulating human gene expression in blood—Viome has adopted a multi-omics systems biology approach. Viome's therapeutics platform leverages three technologies: 'metatranscriptomic sequencing' to digitize the human body; 'pathway analysis' to decode molecular insights from the digitization step; and 'artificial intelligence' to decipher actionable targets from the decoding step. By adapting the platform to different types of cells, and combining it with comprehensive molecular analysis tools, Viome can construct one of the most complete functional pictures of health and disease on the market.

First, Viome digitizes the human body using 'metatranscriptomic sequencing' technology developed at Los Alamos National Laboratory for biodefense purposes. This RNA and DNA sampling and processing platform is designed for scalable at-home collection of stool, blood, saliva, vaginal and other tissue samples, and shipment around the world at ambient temperature[1,2]. Low-cost and fully automated RNA extraction, rRNA depletion, molecular barcoding, and sequencing of the samples ensures accurate and reproducible readouts. Raw data are processed through a high-throughput bioinformatics platform to produce quantitative human and microbial gene expression data representing an individual's functional and taxonomic features at a high resolution and with high fidelity.

Second, Viome has built a 'translational science' platform consisting of proprietary algorithms for analyzing the transcriptomic data from the first step against an extensive in-house pathway and nutrient knowledge database. Processing and scoring the connections among pathway activities helps to identify what is actively happening on a mechanistic level and to suggest precise molecular points of intervention. These are further prioritized in the context of interventions via molecules in food, supplements or pharmaceutical agents to address each individual's unique biology. This is the only existing personalized yet scalable approach to interpreting and translating basic biological data—the metatranscriptome—into actionable information.

Third, Viome has built a next-generation 'artificial intelligence' engine using cloud-based computing infrastructure to analyze vast amounts of molecular and clinical data every day. Viome has already built machine-learnt models for many chronic diseases from large scale clinical studies with more than 10,000 participants, as well as symptoms and phenotypes from internal big-data analytics with

more than 200,000 samples. This has helped Viome identify signatures for various chronic diseases (Fig. 2), including obesity, diabetes, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), oral cancer, colorectal cancer, and for aging.

A universal platform for decoding disease

Through a global network of collaborations, Viome has already applied its therapeutics platform to advance new insights into a broad range of diseases and solutions for managing and treating chronic conditions that affect millions of people worldwide. The company is now looking to partner its groundbreaking technology with companies and academic and clinical institutions interested in advancing the understanding of health and disease on a systems biology level. Viome is applying this knowledge toward the advancement of new therapeutic and diagnostic solutions through:

- the identification of personalized supplements and next-generation prebiotics and probiotics that modulate human physiology either directly or via the microbiome for better clinical outcomes.
- the discovery of small molecule drugs that target specific microbial and/or human pathways involved in disease, by either inhibiting them or replacing them with novel immune and phage therapies that can lead to removal of specific microbial activities that trigger disease onset or relapse.

Viome is applying its technology to areas including oncology, aging, glycemic response, gut-brain connection and drug-microbiome interactions, described below.

Oncology

Viome is harnessing the power of its massive data platform to detect underlying mechanisms for early-stage oral, colorectal, pancreatic, and other GI and head and neck cancers.

From simple saliva samples, Viome's metatranscriptomic analysis can accurately detect the signature of oral cancer. Over the past four decades, the five-year mortality rate for oral cancer has remained unchanged at about 60% despite advances in treatment. With early diagnosis, the rate can be reduced to about 16%, but a lack of non-invasive, early diagnostics is the main reason the overall rate has remained unchanged. In a recent study, using metatranscriptomic data from saliva samples collected from about 500 patients with premalignant or malignant oral cancers, Viome researchers identified a metatranscriptomic signature incorporating both taxonomic and functional microbiome features that provided specificity of up to 97.9% and a sensitivity of up to 92.3% in stage 1 patients[3]. The discovery of such a highly reliable early biomarker could usher in a new era of early diagnosis and treatment in oral cancer. Viome is pursuing regulatory approvals for this test with the US Food and Drug Administration and CE marking in the EU.

With the focus of oncology increasingly turning toward individualized precision, Viome is co-developing novel and more reliable diagnostic and companion diagnostic tests based on combined human and microbiome data with a goal of turning non-responders to responders. In addition, the discovery of novel molecular mechanisms underlying cancer creates opportunities for the development of improved therapeutic interventions.

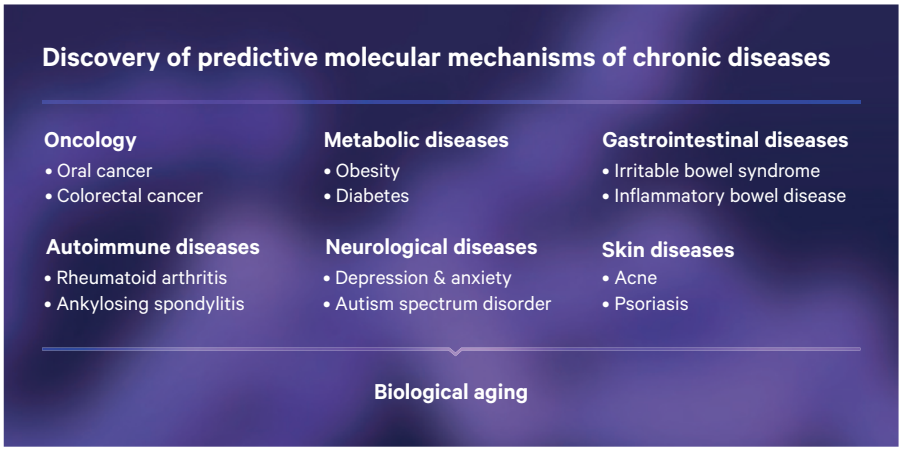

Fig. 2 | Viome's predictive signatures provide new actionable insights into chronic diseases. Viome uses metatranscriptomics and cutting-edge AI to discover underlying mechanisms for chronic diseases.

Aging

Viome has developed the most accurate aging clock to date based on biological markers and molecular mechanisms revealed by deep analysis of the largest dataset of microbial and human gene expression available. This aging clock can help assess longevity and quantify the contribution of specific lifestyle choices toward healthy aging. Pairing the largest existing metatranscriptomic dataset in the world with advanced machine learning techniques, Viome scientists have demonstrated that chronological age can be predicted accurately from the expression of human genes in capillary blood, and from the expression of microbial genes in stool samples[4]. The scientists have delineated the key pathways of systems-level biological decline based on the age-specific features of the model—targeting these mechanisms could aid in development of new anti-aging therapeutic strategies.

Glycemic response

Viome has discovered the underlying mechanism of what gut microbiome activities contribute to individual variation in glycemic response in adults. Controlling the postprandial glycemic response has been identified as an important factor in reducing the risk of chronic metabolic disease generally and in improving overall health condition in people with elevated blood sugar levels. Scientists at Viome analyzed the glycemic responses of 550 adults who consumed more than 30,000 meals from omnivore or vegetarian/gluten-free diets and for the first time showed that differential glycemic responses to the same foods among adults could be predicted and explained[5]. By using machine learning to integrate all variables including the human microbiome activity into the analysis, the scientists were able for the first time to predict an individual's response to a range of foods.

Gut-brain connection

The importance of the gut-brain axis is well established in IBS, depression, anxiety, autism, AD and Parkinson disease. There is a direct connection between the intestines and the brain via 100 million vagus nerve fibers. Together they regulate our satiety and hunger, intestinal motility and secretions, and via several neurotransmitters—dopamine, norepinephrine, serotonin, GABA—they affect our mental health. For example, IBS is a well-known GI condition strongly modulated by anxiety, making it truly a gut-brain disease. Viome has an unprecedented dataset containing both molecular and disease phenotype data, and a range of machine-learnt models that identify many of these neurological conditions accurately. These models have identified up-regulated and down-regulated molecular features for these conditions, enabling a targeted approach to therapeutic applications.

Drug/microbiome interactions

Viome's retrospective and prospective functional microbiome data can aid in drug development, dosing, personalization, and development of companion diagnostic tests. The role of the gut microbiome in determining drug pharmacokinetics and pharmacodynamics (PK/PD) of drugs is being increasingly recognized. Drugs can be activated or inactivated, their availability and uptake compromised, their toxicity elevated, and their detoxification in the liver inhibited by the gut microbiome. Since all of these effects on PK/PD are exerted by the activity of microorganisms, and not their mere presence, Viome's functional gut microbiome analysis is the most suitable for understanding these processes. Elucidation of drug–microbiome interactions to maximize drug efficacy and minimize toxicity based on an individual's microbiome will help improve the odds of successfully testing a new drug and obtaining regulatory approval.

According to Jain, "everything we do at Viome is in an effort to create a world where illness is optional, and to preventing and reverse chronic disease. We must do this together and we welcome partners to collaborate with us to move the health of humanity forward."

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