Going with Your Gut Instinct

Sitting Down With… Paul Peter Tak,
President and CEO at Kintai Therapeutics

What inspired your interest in the microbiome?

I've been interested in this field since before the term "microbiome" was coined. In the 1990s, I conducted research at Leiden University Medical Center on the role of microorganisms in the pathogenesis of rheumatoid arthritis (RA). We were the first to take biopsies from the target tissues of inflamed joints of patients with RA and other forms of inflammatory joint disease, and analyze them using 16s PCR. We detected microbial DNA in different forms of arthritis and predicted that it would be derived from the gut.

There were a other things that I did after that, including working as a visiting scientist on sabbatical at the University of California, San Diego, being a Professor of Medicine and Head of a large academic department at the Academic Medical Center of the University of Amsterdam, and serving as Chief Immunology Officer and a Senior Vice President at GlaxoSmithKline. My move to industry was actually sparked when someone asked me about my impact on patients. Did I think I could have a bigger impact by treating hundreds or thousands of patients as a physician, or by developing medicines that may affect the lives of millions of patients?

I didn't work on the microbiome at GSK, but I've always remained interested in the field.

In your early career, did you have ambitions to become the CEO?

Absolutely not! Throughout my career, I was very much focused on the patients and the science. Even before joining the pharma industry, I had a reputation as a good physician – I received an award from the Minister of Health in the Netherlands for being the best rheumatologist, based on clinical work elected by my peers. But as well as being a professor and a physician-scientist, I also started my first biotech and enjoyed consulting for pharma companies.

How did you come to join Kintai Therapeutics?

During my seven years at GSK, I learned a lot about leadership and drug discovery and development. It was a very positive experience, but I liked the idea of joining a smaller, more entrepreneurial company and learning more about the business. I was particularly drawn to Boston, Massachusetts, which is currently the capital of the biotech world. I researched many companies and found Kintai Therapeutics. Kintai is applying gut microbiota knowledge to design small molecule-based therapeutics for various disease areas, including obesity, chronic kidney disease, oncology, and neurology.

How has research into the microbiome accelerated in recent years?

Each of us have about three pounds of microorganisms living in our gut. It can almost be considered as an organ but it has largely been ignored as a source of drug discovery. Moreover, when developing drugs, we don't just need to look at how the drug is cleared or metabolized by the kidneys and liver, but also how it may be altered by the gut microbiome. In recent years, the scientific community has realized that the microorganisms inside of us are important for many conditions and diseases, and can also affect how we respond to medicines; there have been a number of high impact publications in this field. However, translating microbiome science into therapies is a complex challenge because we harbor so many different microorganisms with variation in different parts of the gut

Kintai has a lead candidate that focuses on obesity – why?

Obesity is an area of enormous unmet need. Research published in the New England Journal of Medicine estimated that by the year 2030, 50 percent of the US population will be obese. Obesity leads to other health issues, such as type 2 diabetes and cardiovascular disease, and is also a strong risk factor for cancer and unfavorable outcomes in COVID19. However, it has proven highly develop safe anti-obesity medicines that induce distinct weight loss and have beneficial effects on other aspects of metabolic syndrome, such as glucose tolerance, hyperlipidemia, inflammation and liver health. Safety is also crucial – if a medicine is approved for treating obesity, it has the potential to be used in very large patient numbers. Many anti-obesity drugs fail because of safety.

KTX-0200 is a small molecule anti-obesity treatment. We can't reveal the mechanism of action here, but I am pleased to say that preclinical results have been consistently promising, showing that it can drive weight with improvement of all other features of metabolic syndrome.

Why focus on small molecules, as opposed to live biotherapeutics?

The growing research on the microbiome has opened, ultimately, it's important to turn this research into something that can be developed in a straightforward, safe and consistent way. The microbiome can almost be seen as a black box. There is still a lot that we don't know, and if we want to use actual microorganisms as treatments then there are many different complexities to consider, ranging from manufacturing, to CMC, to regulations.

At Kintai, we are inspired by the human microbiome. The microorganisms that dwell in our guts produce many small molecules that are critical to maintain health and fight disease. By studying the microbiome in relationship to the gut immune system and the enteric nervous system throughout the gut, we have developed a new class of medicines, called precision enteric medicines (PEM compounds), that are activated in a specific region of the body, under the influence of enzymes that are produced by microorganisms. Effectively, we are developing small molecules that can replicate the positive effects that microorganisms have on human biology. Small molecules, after all, are well understood by the industry and its regulators, and are more straightforward to develop.