SPEAKER INTERVIEW

INDUSTRY PARTNER

NIZO FOR BETTER FOOD & HEALTH

NIZO is world leading in contract research for better food and health. We believe food and health are closely connected. Moreover we are convinced that working closely with our customers, leading food and health companies, is the only road to success. For pharma, (functional) ingredient, nutraceutical and personal care companies we perform discovery, development programmes and clinical trials related to gut health, oral health and skin health with a specific focus on microbiome modulation. **www.nizo.com**

Wynand Alkema
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How did NIZO's journey with the skin microbiome begin?

NIZO has a long tradition in working with microbiomes. This started 70 years ago when NIZO started to study the 'microbiomes' involved in fermentation of milk to produce dairy products like cheese and yoghurt. For cheese making, these 'microbiomes' are essentially mixes of sometime hundreds of different strains that are essential for making good quality cheese, and of which the ratios vary throughout the process. Of course the techniques available at that time are not at all comparable to what we have available today, but nevertheless, charting the diversity of organisms and their biological functions was also then, as it is now, the basis of understanding and manipulating the microbiomes with the aim to get beneficial product characteristics. With a 20+ year track record in the gut, we entered the skin microbiome domain in 2012. Since then we have been servicing multinational companies and start-up companies in the skin microbiome field, more specifically in relation to: acne, skin ageing, dandruff, malodour and eczema. Activities include the whole pipeline: discovery, in vitro validation, clinical validation and upscaling of production of microbiome modulators.

What are top three challenges and risks when harnessing the skin microbiome for product development?

The challenges can be found at all stages of product development. Discovery of new leads have to deal with not only finding the right species or strains to target, but also to identify the right biological functions to interfere with. This can be an enzymatic function, the production of a specific metabolite, or a protein that is important for interaction with the host.

After lead discovery, validation in a clinical setting needs to be done. The challenges are to select the right target population, the right intervention and also to follow the correct biological markers to assess whether the product has been active and efficacious.

A pre-requisite for performing a successful trial is to formulate and produce the product in a safe and reproducible manner. Especially for live biological products this is a challenge, because survival of the organisms need to be ensured throughout the production process.

When conducting early discovery research, how do I select the right body site to find safe, specific compounds from skin microbial communities?

There are two main steps in the discovery process. First, it is very important to take the entire microbiome and the interaction with the host into account, rather than focussing on a single organisms or a single molecule. A lot of knowledge on the interaction between micro-organisms and the host in the skin environment, the metabolites and proteins that play a role in these interactions, is already available from the scientific literature and open access databases. With the increasing movement towards open data access, the wealth of open source data analysis algorithms and the reduction in costs of generating these data, these data sources are becoming more and more valuable.

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What steps can be taking to select and identify the correct organisms with predictable modes of action?

The second step in the discovery process is the validation of the predictions in reliable in-vitro models that have sufficient predictability towards an in-vivo setting. Key points in establishing reliable in-vitro models are not only the choice of a reference set of organism that represent as much as possible the metabolic and physiological processes that take place on the skin, but also the choice of growth media and culture conditions that should reflect the skin environment. In addition, these models should be run in a high-throughput manner combined with easy to measure read-outs, allowing for testing of hundreds of conditions in a single experimental set-up.

Microbial communities can be variable and hard to produce on a large scale, how do you foresee this improving?

Indeed, one of the strategies for modulating the skin microbiome is to formulate live bacteria on a large sale. Both for single strain and community productions, genome based prediction on essential (micro)nutrients and carbon sources to increase growth rate and yield become feasible with the abundance of publicly available sequences and low costs of sequence data generation. Other improvements can be expected in the area of large scale anaerobic production. Lastly, a better understanding of the parameters that influence downstream processing yield, such as harvesting and drying will prove to be essential in improving the overall production.

Clinical validation will prove to be vital for skin microbiome modulators, what steps should researchers take when entering the clinic? What are the challenges here?

There are a lot of challenges. Some of them are generic to all clinical trials, such as selecting the right human target population and the right intervention, so as to maximize the response rates. For skin microbiomes in particular, it is important to assess the influence of the intervention not only on the host but also with respect to the changes in the skin microbial community. For this, protocols that are able to isolate DNA and RNA from low biomass environments are extremely important.

How do NIZO overcome these challenges to de-risk variability and develop effective skin microbiome modulators?

With an integrated approach. We are in the unique position at NIZO to have all the relevant capacities for (skin) microbiome research under one roof: Bioinformaticians, fermentation specialists, preclinical and clinical experts and formulation experts. So the findings in the development and clinical trials on what works and what does not work are directly fed back into our knowledge database and predictive models as well as into our in vitro MicroSkin platform, to allow for a continuous improvement of the discovery and validation cycle.

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A huge thank you to Wynand Alkema for taking the time to share his insights with us.

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