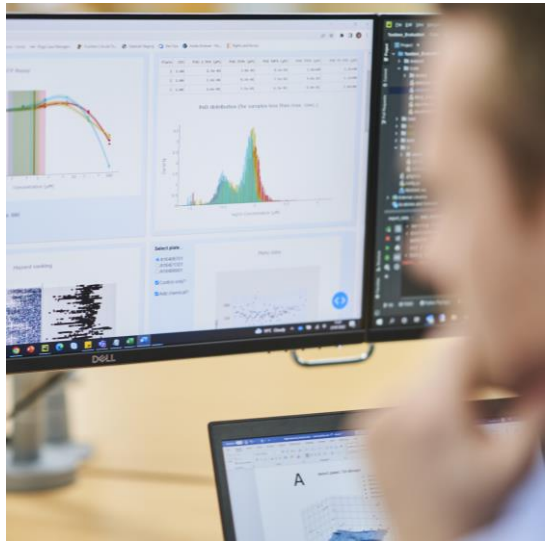
A tiered approach to risk assess microbiome perturbations induced by application of beauty and personal care products

Aline Métris, Safety and Environmental Assurance Centre (SEAC), Unilever

Introduction to SEAC and Risk Assessments

Unilever's Global Centre of Excellence in Safety & Sustainability Sciences



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Unilever's Safety & Environmental Assurance Centre (SEAC)

SEAC is Unilever's global centre of excellence in Safety & Sustainability Sciences, part of R&D's Safety, Environment & Regulatory Sciences Capability.

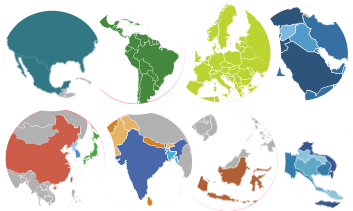
Diverse, multi-disciplinary team of ~150 scientists based at Colworth, UK; ~70 miles north of London

Highly collaborative, working with over 70 academic, industry, government & NGO partners worldwide

Business Group R&D

Global Teams

Business Units

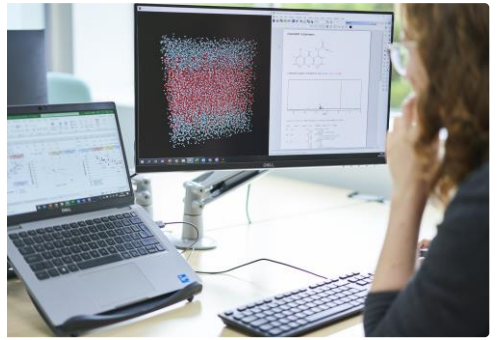


'One R&D' Centre

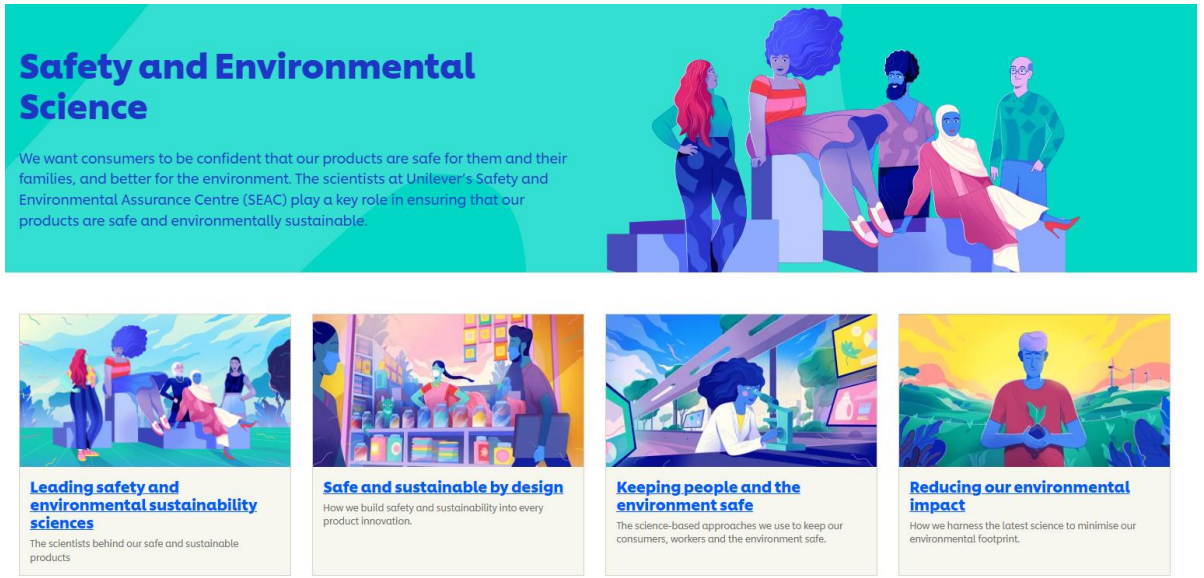
- Safety, Environment & Regulatory
- Digital & Partnerships
- Sustainable Packaging

Team SEAC's purpose is to protect people & the environment by ensuring:
Unilever's products & innovations are Safe & Sustainable by Design without animal testing

- Around the world, 3.4 billion people use a Unilever product every day.
- We use **scientific, evidence-based approaches** to ensure that our products and innovations are safe & sustainable without animal testing.



https://www.unilever.com/planet-and-society/responsible-business/product-safety-and-quality/



https://www.unilever.com/planet-and-society/safety-and-environment/

Introduction: Risk Assessments (RA) approaches

Microbiology & food

CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS
Food and Agriculture Organization of the United Nations
World Health Organization

C O D E X
A L I M E N T A R I U S
International Food Standards
World Health Organization
Food and Agriculture Organization of the United Nations

PRINCIPLES AND GUIDELINES FOR THE CONDUCT OF MICROBIOLOGICAL RISK ASSESSMENT
CAC/GL 30-1999

Adopted 1999. Amendments 2012, 2014.

Toxicology

Next Generation Risk Assessment (NGRA) is defined as an exposure-led, hypothesis-driven risk assessment approach that integrates New Approach Methodologies (NAMs) to assure safety without the use of animal testing

Exposure assessment

Frequency and level at the point of application

e.g. skin/oral microbiome

Hazard identification & characterisation

hazard=agent capable of causing adverse health effect

Hazard characterisation = Nature/intensity of adverse effect as a function of the dose

NOT AVAILABLE for product-induced changes to the microbiome

Risk characterisation

= likelihood X severity of the adverse effect

With uncertainty and variability

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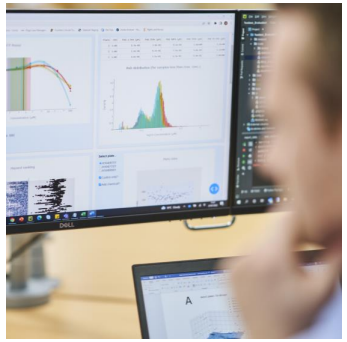
The microbiome and risk assessments



The microbiome composition has been correlated to health and disease states (e.g. psoriasis, acne, atopic dermatitis, caries, periodontitis…) however there is no definition nor characterisation of microbiome dysbiosis.

- Need an alternative approach to "traditional" CODEX-type risk assessments
- Experimental data need to be sought at the point of application rather than in products i.e. in clinicals
- Only relative risk assessments can be presently carried out

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A tiered approach to risk assess microbiome perturbations induced by application of beauty and personal care products

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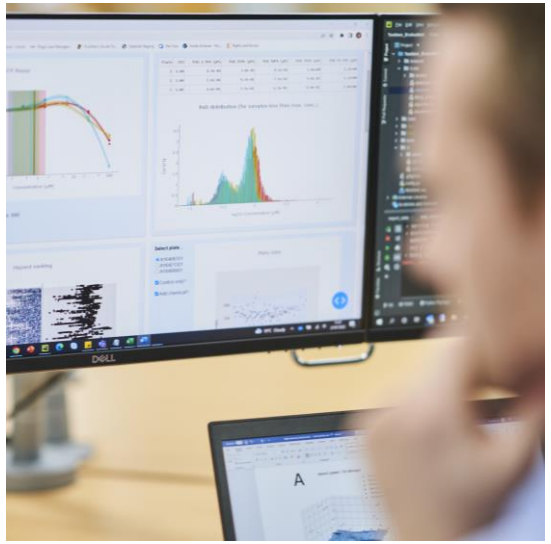
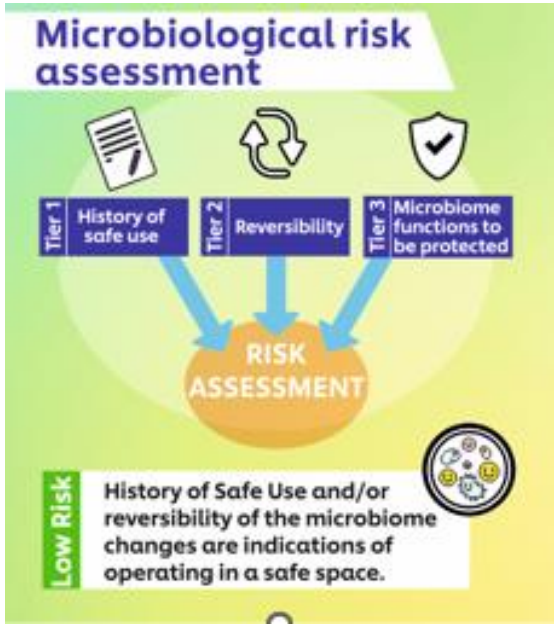
A tiered framework approach



A tiered framework to risk assess perturbations induced by the application of beauty and personal care products

Tier 1 History of Safe Use (HoSU)
Has the technology been on the market long enough without adverse effects at higher or similar levels or does it impact the microbiome less than marketed technologies with a HoSU?



Tier 2 Reversibility of change
Test with a clinical study whether the technology induces a permanent change in the microbiome

Tier 3 Microbiome functions to be protected – *Research using in silico-in vitro- clinical experiments to characterise endpoints*

- Protection against pathogen colonisation
- Environmental conditions still conducive to a functional community, e.g. resilience
- Host functions, such as immune response, barrier function or trans-epidermal water loss (TEWL)

Resilience is the capability of the microbiome to withstand perturbations without becoming dysbiotic. It has been identified as a key factor characterising health but is difficult to assess.

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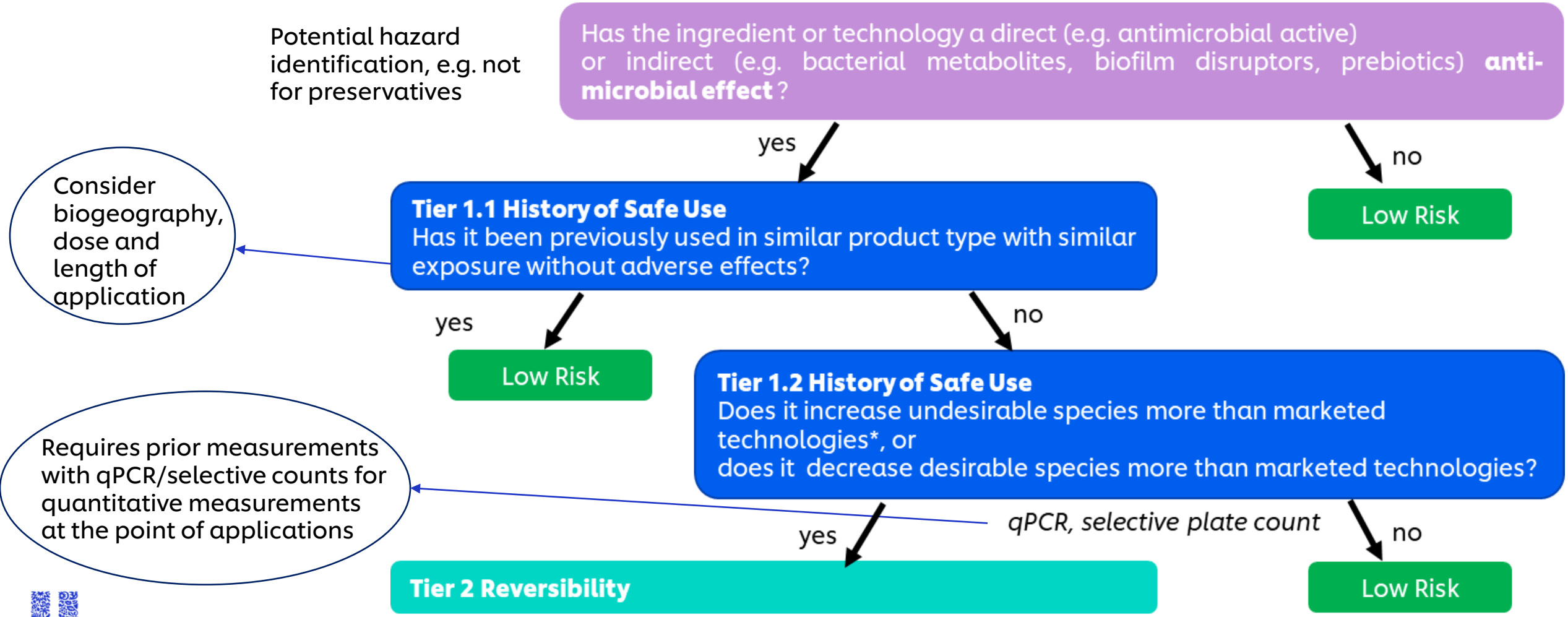
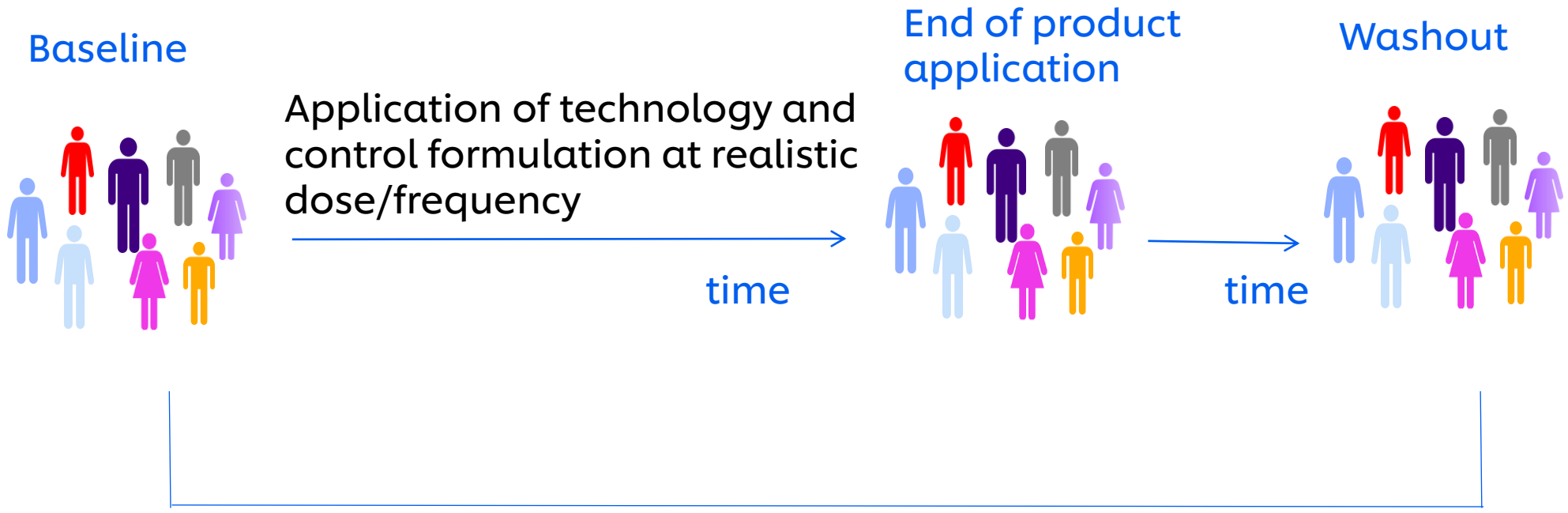
Tier 1: History of Safe Use
i.e. comparison to marketed formulations



Tier 2: Reversibility of change

i.e. the microbiome returning to its initial state after a period of application and washout is evidence of low risk – relative RA.



Comparison of the microbiome composition between baseline and washout

- Including a **control/placebo** to define significant change
- Including qPCR for **quantitative** representation of the microbiome
- Considering **people variability** in the statistics (and control on the same person where possible)

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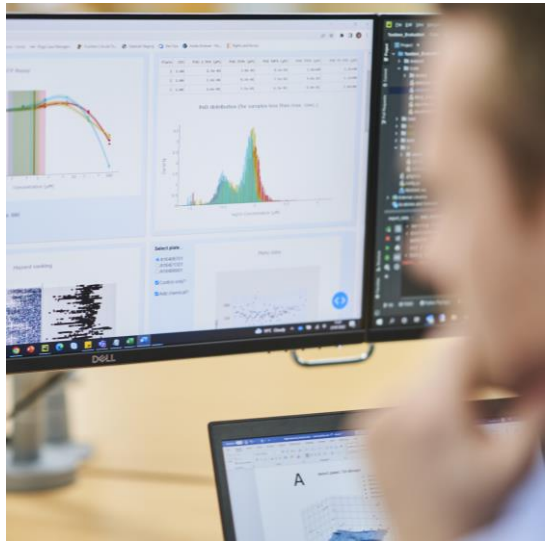
Tier 3: Some challenges with defining & characterising the functions to be protected for a healthy microbiome

Tier 3 Microbiome functions to be protected

- Protection against pathogen colonisation
- Environmental conditions still conducive to a functional community, e.g. resilience
- Host functions, such as immune response, barrier function or trans-epidermal water loss (TEWL)

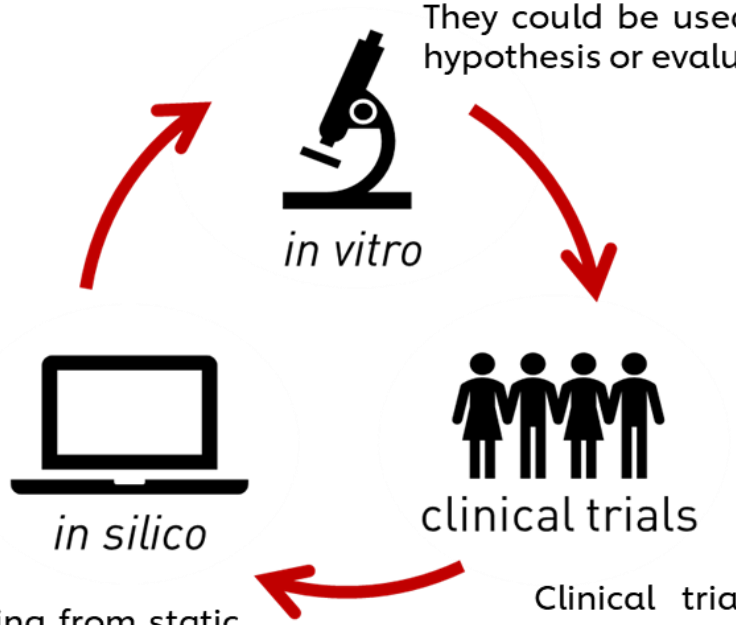
- Defining the factors influencing resistance to colonisation .
- Resilience is a “complex“ notion involving time evolution with no agreed definition.
- How host functions are affected by the microbiome such as barrier function/immune response is not fully established and is context dependant (e.g. in population at risk).
- Defining meaningful functions rather than taxa based on -omics data; e.g. which -omics, their integration, definitions of pathways/functions and their interpretation?
- Microbiome data bias (Western countries) and limited metadata in the public domain, no embedded “control” for batch effects, power needed because of people variability.

Towards mechanistic insights



Towards mechanistic insights: combining *in silico, in vitro* and clinical experimental approaches

In vitro model: The present challenge with 3D models is system longevity when different microbial species are used at the same time. They could be used to benchmark, validate a hypothesis or evaluate new ingredients.



In silico models: Progressing from static descriptive to dynamic mechanistic will aid understanding and prediction of microbiome states and will potentially allow the end points of concern to be quantitatively defined.

Clinical trials are costly but allow *in situ* measurements to be made and human-microbiome interactions (e.g. immunological markers) to be studied. Longitudinal studies contribute to the understanding the factors influencing the human microbiome.

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