

Case study 1

- An epidemiologist has observed in a population cohort that consumption of green vegetables statistically associates with reduction of risk for cardiopathologies such as atherosclerosis. Therefore it is hypothesized that regular intake of green vegetables might help reducing atherosclerosis risk. At this stage the possible mechanism of action is unknown although it is accepted that increased risk of atherosclerosis correlates with increased low density lipoprotein cholesterol (LDL).
- How can you help testing the hypothesis with metabolomics? What analytical strategy and study design can you propose?

Case study 2

- The application of MS-based metabolomics (untargeted approach) to two different types of cell cultures reveals significant metabolic differences in the citric acid or Krebs cycle. More specifically the differences indicate a possible alteration of fumarate and succinate concentrations (increased succinate levels).
- What could you implement to:
 - a) Verify this hypothesis and quantify the alteration?
 - b) Determine the possible origin of the alteration and quantify the metabolic flux through succinate dehydrogenase ?

Case study 3

- You are requested to investigate the discovery of a biomarker of red meat consumption. You have access to a biobank of samples from 10'000 subjects including to an extensive repository of meta data (anthropometric, dietary intakes...).
- Briefly describe the key steps of your study design to discover and validate this biomarker.
- Describe the complementary analytical approaches you could deploy summarizing their respective advantages and limitations.

Case study 4

- You need to prove that dietary supplementation of medium chain triglycerides (MCT) increase brain energy metabolism in mice.
- What metabolomic approaches will you implement to:
 - a) Verify this hypothesis
 - b) Investigate how MCT diet affect systemic and brain-specific metabolism

Case study 5

- During the COVID-19 pandemic, higher vitamin D status is thought to improve patient condition by controlling cytokine storm.
- Propose a metabolomics-based investigation to build scientific evidence on the role of vitamin D either for prevention of infection complications or for acceleration of patient recovery.

Case study 6

- Consumption of nuts may play a significant role in prevention of non communicable chronic pathologies such as cardiovascular disease (CVD). You have access to a a biorepository of longitudinally collected blood samples and detailed dietary information. You want to demonstrate the relative contribution of nut intake in the prevention of CVD via the modulation of inflammatory status.
- Describe how metabolomics and lipidomics can complement with each other to understand global and lipid-specific metabolic effects of nut consumption.
- Propose a combination of observational and interventional studies.

Case study 7

- The pharmacometabolomic concept relies on the ability to exploit the latent metabolic information in metabolite profiles that is able to explain/predict the individual response to different pharmacological strategies. You are leading an innovation program in a large hospital that aims at improving therapeutic efficacies of its intensive care and oncology departments. The hospital laboratory has been recently upgraded with state-of-the-art NMR and mass spectrometry instruments and large-scale data mining capabilities.
- Define what could be success measures of therapeutic efficacy improvement
- Develop a metabolomic-driven strategy to achieve the goals of the innovation program

Case study 8

- You lead a Metabolomics facility in a state-of-the art hospital. Your laboratory is equipped with NMR spectroscopy with 2 spectrometers operating at 600 MHz and 1 GHz. Your 600 MHz spectrometer is equipped to perform both experiments at solid and liquid state. You don't have access to mass spectrometry facility.
- The head of the department of visceral surgery approaches you for a research on the discovery of a metabolomic biomarker of early onset of colon cancer and its progression in systemic biofluids. You have access to colon resection samples and histopathology endpoints.
- Propose a biomarker discovery and validation strategy.

Case study 9

- You develop clinical research program on lipids and cardiovascular risk factors with a particular interest for biomarkers indicative of early onsets of atherosclerosis. You suspect that the circulating level of large dense low-density lipoproteins and their related ceramides own predictive values of atherosclerosis events at 3-5 years distance. You have access to both NMR and MS facility as well as biological samples from atherosclerosis patient in a longitudinal cohort.
- How would you approach the discovery and validation of a simple lipoprotein-specific predictive biomarker of atherosclerosis?

Case study 10

- Inflammatory bowel disease is a complex and multifactorial pathology that is subdivided in Crohn's disease (CD) and ulcerative colitis (UC) that affect different parts of the small and large intestine. CD and UC require specific therapy and therapeutic monitoring. It is however important to predict the risk of relapse (inflammatory episode) following therapy in both CD and UC.
- You suspect that gut-microbiome associated metabolism carries information on the risk of relapse and you want to develop a rapid test to inform on possible relapse episode for both CD and UC. You have access to both NMR and MS facility as well as samples from well diagnosed patients including fecal, blood and urine.
- How would you design the discovery and validation of such relapse prediction biomarker?