

Targeting hope

DNA methylation markers to predict treatment success of biologicals in Crohn's disease, rheumatoid arthritis and psoriasis



Duration
4 years



Budget
10 Million



17 partners, 9 countries



General Information

The METHYLOMIC project aims to improve the selection of biologic treatment for patients with chronic immune-mediated diseases such as Crohn's Disease (CD), Rheumatoid Arthritis (RA), and Psoriasis (PsO). Biologics are advanced medications that target specific molecules implicated in the inflammatory pathways.

Predictive biomarkers

Such biologics have become a mainstay of therapy in common immune-mediated inflammatory diseases (IMID) including CD, RA, and PsO. Currently used biologics target inflammatory proteins such as Tumor Necrosis Factor (adalimumab), leukocyte trafficking (vedolizumab), or IL-12/IL-23 (ustekinumab). However, IMIDs are complex diseases with a multifactorial background, so the same drug does not work for all patients. At present we cannot predict which biological will be effective in an individual patient,

fewer than 40% of patients achieve sustained remission with any given treatment. Treatment failure is associated with lasting disease course and disease complications, and increased health care costs. Hence the overwhelming need for predictive biomarkers to guide personalised medicine in IMID is evident, but no such predictive biomarkers are validated in clinical practice to date.

Better treatment response

While most previous efforts have focused on genomic mutations or gene expression, METHYLOMIC takes a different approach. Building on several previous cohort studies, we identified and validated epigenetic biomarkers - specifically DNA methylation profiles in peripheral blood - as predictors of response to biological therapy, with a particular focus on Crohn's disease. These profiles were associated with treatment response and deep remission for three approved biologics in Crohn's disease. Using state-of-the-art machine-learning algorithms, treatment response could

be predicted with an accuracy of up to 93% for individual biologics in Crohn's disease and rheumatoid arthritis.

Validation studies

METHYLOMIC is now committed to bringing personalised treatment-selection in CD and other IMID to clinical practice. We have brought together clinical, epigenetic, and DNA diagnostics experts, patient organisations, and companies across 7 countries in Europe, for further validation studies. We will also develop a marketable rapid (2 weeks) targeted methylation assay that we then validate in a unique prospective randomised clinical trial for CD. Efficiency and cost-effectiveness are assessed in great detail and regulatory approval is guided by experts to assure delivery of the first epigenetic kit personalised treatment of CD.

Objectives

Our main objective is to develop and clinically validate a rapid machine learning powered epigenetic biomarker assay that predicts response to biologics for the treatment of Crohn's Disease. To achieve this, 5 specific aims have been put forward:

1. Validate the algorithms predicting response to biological treatment based on epigenetic markers in Crohn's Disease (CD), Rheumatoid Arthritis (RA) and Psoriasis (PsO).
2. Develop a rapid capture-based NGS assay for restricted methylome detection in CD patients.
3. Execution of a prospective clinical trial to clinically validate the predictive power of the rapid assay to

distinguish responders from non-responders to biological therapy in CD.

4. Confirm the potential of DNA methylation markers for the prediction of biological therapy success in RA and PsO.
5. Establish the biological relevance of the DNA methylome-based biomarkers in therapeutic response in CD.

"We will be satisfied if there is at least a 15% difference in favour of the AI group compared to the standard of care group. We believe it is achievable for at least half of the people in the AI group to reach remission after six months."

Prof. Geert D'Haens

Impact short term

METHYLOMIC is committed to bringing personalized treatment-selection in Crohn's disease and other immune-mediated inflammatory disease to clinical practice.

Impact long term

METHYLOMIC will potentially revolutionize the management of patients with these lifelong and impactful chronic diseases.



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