

The ENDOTARGET Project Advances Understanding of Rheumatic Diseases: Recent Progress and Milestones

ENDOTARGET, an EU-funded project aimed at investigating the relationship between gut microbiota, intestinal permeability, and systemic endotoxemia to unravel the triggering factors for health-to-disease transition in rheumatic diseases such as osteoarthritis (OA), rheumatoid arthritis (RA), and spondylarthritis (SpA), has achieved significant milestones since its start on January 1st, 2023.

Led by HUS Helsinki University Hospital, the ENDOTARGET consortium has been actively collaborating through nine interconnected work packages to drive forward research and innovation in the field. Following six months of intensive work, the consortium reconvened from April 11th to 12th in Naples, Italy, hosted by the project partner University of Campania.

During this gathering, partners engaged in comprehensive discussions regarding progress and challenges across different work packages.



Some glimpses into the current work of the ENDOTARGET project:

- **Scientific Endeavors:** The project involves 12 cohorts, with recent efforts focusing on extending in vitro measurements to explore biomarkers and lifestyle factors influencing the transition from health to disease. In particular, blood samples from the [Helsinki Businessmen Cohort](#) are being analysed to investigate biomarkers such as TLR4, Zonulin, LBP, I-FABP, sCD14 and S100A8/A9 by using reporter cell assays and Enzyme-linked Immunosorbent Assays (ELISA).
- **Mechanistic Studies:** Experiments on the inflammatory effects of different bacterial lipopolysaccharides on joint tissue (chondrocyte cell line), including proteomics and RNA-seq analyses, have been conducted. Additionally, the first rat model study with systemic LPS delivery to elucidate the role of LPS in OA progression is ongoing.
- **Intervention Studies:** Three intervention studies are ongoing, including a Fecal Microbiota Transplantation (**FMT**) study in Finland with SpA patients, a diet intervention study (**TASTY**) in Portugal to analyse the effects of the Mediterranean diet in RA patients, and the **LARA** study in Portugal, Finland and Italy investigating the effect of larazotide in untreated RA patients. The first results are expected at the end of 2024.
- **Data Integration and Analysis:** The consortium is working towards developing a machine learning (ML) and AI-informed Rheumatic Disease Prediction Tool for clinicians. Efforts are focused currently on extracting, standardising, and harmonising data, which are collected from all the different studies.
- **Collaborative Efforts:** Partners are actively engaged in work packages focusing on “Ethics, Regulations & GDPR”, “Dissemination, Communication, and Exploitation”, and “Project Management”. The recent in-person exploitation workshop held in Naples facilitated discussions on the anticipated project results and their potential exploitation.

Scientific Publications:

Pazos-Pérez, A.; et al. **The Hepatokine RBP4 Links Metabolic Diseases to Articular Inflammation**. Antioxidants. 2024. [doi: 10.3390/antiox13010124](https://doi.org/10.3390/antiox13010124)

Guillán-Fresco, M.; et al. **Formononetin, a Beer Polyphenol with Catabolic Effects on Chondrocytes**. Nutrients. 2023. [doi: 10.3390/nu15132959](https://doi.org/10.3390/nu15132959)

Charneca, S.; et al. **Beyond Seasoning—The Role of Herbs and Spices in Rheumatic Diseases**. Nutrients. 2023. [doi: 10.3390/nu15122812](https://doi.org/10.3390/nu15122812)

Franco-Trepat, E.; et al. **β Boswellic Acid Blocks Articular Innate Immune Responses: An In Silico and In Vitro Approach to Traditional Medicine**. Antioxidants. 2023. [doi: 10.3390/antiox12020371](https://doi.org/10.3390/antiox12020371)

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