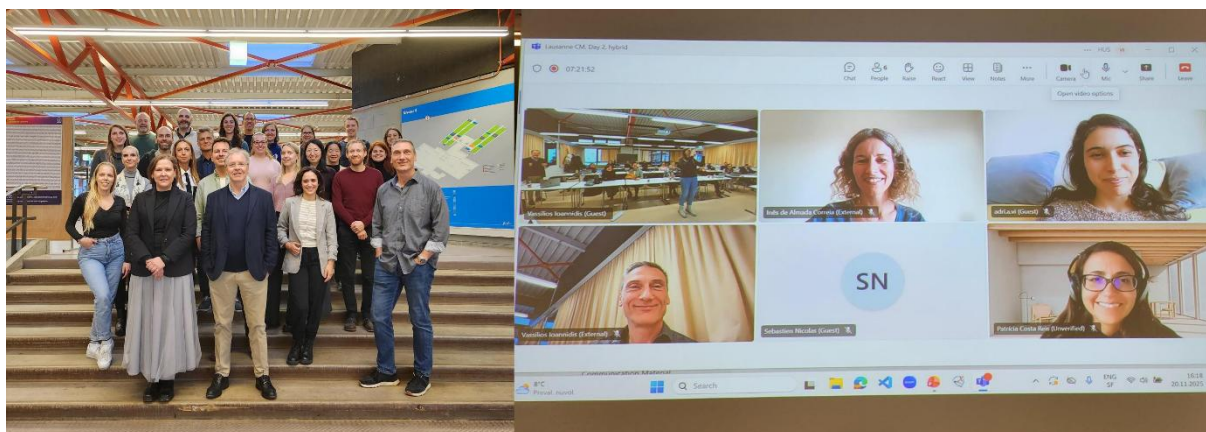


## ENDOTARGET EU Project: Entering the final year

The ENDOTARGET EU project, funded under the Horizon Europe Research and Innovation Actions, is now entering its final year. Since its launch on 1<sup>st</sup> of January 2023, the four-year initiative has pursued an ambitious goal: to improve the lives of people affected by rheumatic diseases (RDs). Through nine tightly connected work packages, the consortium investigates how gut microbiota, intestinal permeability, and systemic endotoxemia (SE) shape the onset and progression of rheumatic diseases such as osteoarthritis (OA), rheumatoid arthritis (RA), and spondylarthritis (SpA).

To reflect on the progress achieved during the past six months, the consortium met virtually on the 17<sup>th</sup> of November for updates on the non-scientific work packages, including “Ethics, Regulation and GDPR,” “Dissemination, Exploitation and Communication,” and “Project Management.” A hybrid meeting followed from 20<sup>th</sup> – 21<sup>st</sup> of November in Lausanne, Switzerland, hosted by SIB – Swiss Institute of Bioinformatics. Together, these meetings offered a valuable space to exchange knowledge, evaluate advancements, and address challenges across all work packages.



### Research updates across ENDOTARGET

**Population Cohort Analysis:** The consortium is carrying out large-scale cohort studies to reveal biomarkers and lifestyle-related risk factors across five of the project’s twelve cohorts. Biomarker assessment for the HBS, FINRISK, and EstBB cohorts is now complete, focusing on:

- Endotoxemia biomarkers: lipopolysaccharide binding protein (LBP), soluble CD14, and Lipopolysaccharide (LPS) bioactivity
- Intestinal permeability and inflammation biomarkers: zonulin, intestinal fatty acid binding protein (I-FABP), and calprotectin (S100A8/A9)

Preliminary analyses have provided first insights into biomarker distributions by sex, age, body mass index (BMI), and disease type (OA, RA, SpA) as well as differences between control

and disease groups. Early trends and correlation patterns are emerging, though deeper statistical modelling is still ongoing.

In parallel, partners are integrating microbiome and biomarker data from FINRISK and EstBB to identify microbial signatures associated with SE. To enable this, the team developed a novel diffusion-based statistical method to screen metagenomes, producing the first encouraging results.

In addition, a genome-wide association study (GWAS) based on EstBB data is also underway to explore genetic factors linked to SE and RDs. The consortium is now defining the strategy for evaluating and interpreting these results

**Focused cohorts & *in vitro* studies:** This task examines the role of SE and gut permeability in RA, SpA and related inflammatory conditions. A major achievement has been the comprehensive collection and ongoing analysis of clinical samples. Key analyses include: (i) serum analysis of LPS, zonulin, calprotectin, and occludin, (ii) histological analysis of inflammation and expression of occludin and claudins in gut biopsies, and (iii) single-cell RNA sequencing of peripheral blood mononuclear cells and gut cells. So far, samples have been measured, and data analysis is ongoing.

In parallel, this task explores the impact of LPS derived from different bacterial species on intestinal epithelium to identify the most pathogenic forms. This *in vitro* LPS characterisation is almost completed, and two scientific publications describing the results are planned. Additionally, a gut-on-a-chip system has been successfully established and is currently used to study how LPS, outer membrane vesicles, and extracellular vesicles affect gut barrier function.

**Mechanistic and Proof-of-Concept Studies:** Current experiments investigate how joint cell types (chondrocytes, synoviocytes, osteoblasts, adipocytes, macrophages) respond to the most pathogenic LPS variants identified in the previous work. First results show a promising direction, but further experiments are required to draw meaningful conclusions. Furthermore, the selected LPS were also analysed regarding their effect on the metabolism of the different joint cell types, as well as their ability to modulate the inflammatory response. Parallel to this, developed animal models are used to evaluate the systemic and local effects of LPS on OA progression. Data has been collected and is now being analysed.

**Intervention Studies:** ENDOTARGET is carrying out two intervention studies as part of its translational research approach. These studies aim to investigate how targeted strategies can affect gut microbiota, the intestinal barrier integrity, and SE in the context of RDs.

**SpA-FMT Trial:** Recruitment for the Fecal Microbiota Transplantation (FMT) study in SpA patients has been successfully completed. The study focuses on evaluating the impact of FMT on gut and systemic inflammation. Data and biological material collected include (i) disease activity, (ii) gastrointestinal symptoms, (iii) quality of life assessment, (iv) blood samples for inflammatory markers analysis, (v) fecal samples for calprotectin and microbiome analysis, and (vi) ileum and colon biopsies for immunohistochemistry, RNA sequencing, and 16S rDNA analysis. Data pre-processing and analysis are ongoing with results expected for mid-2026.

**TASTY study:** This study investigates whether a Mediterranean diet enriched with fermented foods can improve intestinal microbiota, disease activity, and quality of life in individuals with RA. Recruitment is actively ongoing and will be concluded by the end of 2025. The initial data collection and analysis are already underway. Collected data includes (i) biological samples: feces, saliva, blood, urine, (ii) anthropometric and nutritional data: height, weight, BMI, waist circumference, body composition, adherence to the Mediterranean diet, and (iii) clinical measurements: 32-joint ultrasound, count of painful and swollen joints, disease activity (DAS28-ESR score), functional disability, and quality of life assessments.

In addition, *in vitro* experiments are ongoing to identify drugs and/or food-derived compounds that block the innate immune responses elicited by LPS, aiming to identify new preventive strategies for arthritis.

**Data management, multiomics modelling and AI:** This task aims to integrate the results of the different studies and to use them for disease prediction modelling. The consortium has concentrated on data extraction, standardisation, and harmonisation, which are essential steps to ensure the consistency and comparability of datasets across cohorts and study types. Next steps focus on the multilevel data integration analysis, the development of the Rheumatic Disease Prediction Tool and the development of risk prediction scores.

### **Dissemination & Communication Highlights:**

- Partners from GIMM took part in the 47<sup>th</sup> ESPEN Congress held in September 2025 in Prague, Czech Republic.
- HUS, TU Wien and ETHZ attended the 18<sup>th</sup> ICRS congress in October 2025 in Boston, USA.
- Consortium partner GIMM presented the ENDOTARGET project at the 40<sup>th</sup> APTAC Congress in Lisbon, Portugal, in October 2025
- GIMM went to the 24<sup>th</sup> Congresso de Nutrição e Alimentação in Lisbon, Portugal.
- GIMM was invited to give a talk at the UM Global Symposium (05.-07.11.25) in Macau, China.
- Partners from HUS participated in the Stay Health Cluster Symposium in December 2025 in Berlin, Germany
- SERGAS/FIDIS attended the online conference VII Congresso Lire in November 2025

### **Upcoming Events:**

**Mark your calendars for our next webinar on the 2<sup>nd</sup> of April 2026 (10:00–12:00 CEST):**

“Modelling the Gut–Joint Axis: Organ-on-Chip Approaches for Chronic Inflammation”  
The webinar will feature expert talks from:

1. TU Wien: Organ-on-a-chip developments within ENDOTARGET
2. Nathalie Sauvonnnet (Institut Pasteur, Paris): Tissue microenvironments & intestinal pathologies
3. Alan Li Zhong (Chinese University of Hong Kong): Microbe–gut–cartilage axis-on-a-chip

Interactive virtual breakout sessions will allow participants to speak directly with the presenters. Registration details will be published early 2026.

## Scientific Publications:

E. Franco-Trepat, et al. 2023. Antioxidants.  **$\beta$  boswellic acid blocks articular innate immune responses: an in silico and in vitro approach to traditional medicine.** [doi: 10.3390/antiox12020371](https://doi.org/10.3390/antiox12020371)

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

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

A. Pazos-Pérez, et al. 2024. Antioxidants. **The hepatokine RBP4 links metabolic diseases to articular inflammation.** [doi: 10.3390/antiox13010124](https://doi.org/10.3390/antiox13010124)

P. Weber, et al. 2024. Osteoarthritis and Cartilage Open. **The collagenase-induced osteoarthritis (CIOA) model: Where mechanical damage meets inflammation.** [doi: 10.1016/j.jocarto.2024.100539](https://doi.org/10.1016/j.jocarto.2024.100539)

J. Parantainen, et al. 2025. Atherosclerosis. **Increased intestinal mucosal permeability and metabolic endotoxemia predict the risk of cardiovascular mortality.** [doi: 10.1016/j.atherosclerosis.2025.119220](https://doi.org/10.1016/j.atherosclerosis.2025.119220)

K. Brandauer, et al. 2025. Lab on a Chip. **Sensor-integrated gut-on-a-chip for monitoring senescence-mediated changes in the intestinal barrier.** [doi: 10.1039/d4lc00896k](https://doi.org/10.1039/d4lc00896k)

S. Charneca, et al. 2025. Nutrition Journal. **TASTY trial: protocol for a study on the triad of nutrition, intestinal microbiota and rheumatoid arthritis.** [doi: 10.1186/s12937-025-01089-6](https://doi.org/10.1186/s12937-025-01089-6)

K. Bevc, et al. 2025. RMD Open. **Evaluating the role of lipopolysaccharides in the joint: fibronectin as a novel protective mechanism.** [doi: 10.1136/rmdopen-2025-005622](https://doi.org/10.1136/rmdopen-2025-005622)

M. Tiemblo-Martin, et al. 2025. Chemical Science. **Odoribacter splanchnicus Lipooligosaccharide: an uncommon structure with weak immunostimulatory activity.** [doi:10.1039/D5SC08335D](https://doi.org/10.1039/D5SC08335D)

## For more information:

### Project Coordinator Team

Helsinki University Hospital (HUS), Helsinki, Finland

Project Coordinator

Kari Eklund ([Kari.eklund@hus.fi](mailto:Kari.eklund@hus.fi))

Deputy Project Coordinator

Gonçalo Barreto ([Goncalo.barreto@helsinki.fi](mailto:Goncalo.barreto@helsinki.fi))

Project Manager

Ana Valkama ([Ana.valkama@hus.fi](mailto:Ana.valkama@hus.fi))

### Stay updated!

 [www.endotargetproject.eu](http://www.endotargetproject.eu)

 [@ENDOTARGET EU Project](https://www.linkedin.com/company/endotarget-eu-project)

 [@ENDOTARGET\\_EU](https://twitter.com/ENDOTARGET_EU)

 [@ENDOTARGET](https://www.youtube.com/channel/UC...)