

Dear ESHG Education Committee,

I would like to express my sincere gratitude to the European Society of Human Genetics (ESHG) for the Observership Grant that allowed me to spend four weeks, from 30th June to 28th July 2026, at the Clinical Genetics Department of Erasmus MC, Rotterdam, the Netherlands, under the supervision of Prof. Tjitske Kleefstra.

I am a clinical genetics resident and PhD candidate at Rīga Stradiņš University (RSU), Riga, Latvia. My doctoral research focuses on the integrative analysis of the non-coding genome and transcriptome to improve the diagnosis of inborn errors of immunity (IEI). During my stay, I was embedded within the department's innovation team and had the opportunity to learn about their established diagnostic long-read genome sequencing workflow, with particular focus on ultrarapid sequencing and DNA methylation analysis. This observership was a wonderful opportunity to explore new horizons in methylation and episignature analysis, working with the team that developed MethaDory and seeing firsthand how it is built and how it works in practice.

During my stay, I deepened my understanding of episignature methodology, including principal component analysis, the calling of differentially methylated positions and regions, and SVM-based classifiers, through hands-on analysis and guided discussion of the relevant literature. I applied this pipeline to explore potential episignatures across several IEI genes, with the aim of helping resolve complicated or variant-of-uncertain-significance (VUS) cases, which arise frequently in inborn errors of immunity.

Beyond the technical and analytical work, I also had the opportunity to see how the department operates more broadly, attending routine clinical and laboratory activities, multidisciplinary meetings, and seminars that gave me valuable insight into the ongoing work and experiments of the wider team. This exposure will directly support my future research, and I intend to extend the pipeline developed during this stay to further IEI candidate genes and patient cohorts in my own work.

I would like to sincerely thank Prof. Tjitske Kleefstra and the team at Erasmus MC for their generous guidance, time, and hospitality throughout my stay, and the ESHG for making this enriching experience possible. This observership was a truly valuable step in my scientific development, and I would strongly encourage other young researchers to apply for the program.

Yours sincerely,

Marija Rozevska