

Final Report

6th Wael Almahmeed and IAS Research Training Fellowship

Project Title: Decoding PCSK9: New Perspectives on the Mature and Furin-Cleaved Forms

Fellow: Azin Kheirkhah, PhD

Host Institution: Institute of Genetic Epidemiology, Department of Genetics, Medical University of Innsbruck, Austria

Supervisor: Prof Florian Kronenberg, MD

Dear Members of the Wael Research Fellowship Review Committee,

I am writing to express my sincere gratitude for your support through the 6th Wael Almahmeed and IAS Research Training Fellowship, generously awarded by the International Atherosclerosis Society (IAS). From the outset, the primary aim was to establish the PCSK9 forms ELISA assay and make it compatible with our robotic platform. I am pleased to report that this goal has been fully achieved: the assay has been developed, validated in our laboratory, and successfully transferred to our Biomek i7 Hybrid instrument (Beckman Coulter).

This project began in mid-2025 and has met all objectives set for this funding period. I would also like to thank the committee for granting extensions while we managed delays related to our institute's relocation and materials procurement.

Preliminary outcomes, limitations, and next steps

- Using the newly established assay, we completed pilot measurements in a well-characterized European cohort. These initial analyses are encouraging and consistent with our expectations, suggesting potentially meaningful differences between PCSK9 forms that warrant further study.
- At this stage, we are intentionally cautious in interpretation: the preliminary dataset is modest in size and composed only of male participants, which limits generalizability. Additional validation and expanded analyses are needed before drawing firm conclusions.
- Building on the successful assay establishment and automation, our next phase will scale measurements to approximately 8,000 individuals of European ancestry. This expansion is designed to strengthen statistical power, enable sex-stratified analyses, and more rigorously evaluate reproducibility and clinical relevance.

Your support has been pivotal in establishing this methodological foundation and positioning the project for impactful follow-up work. Importantly, the progress achieved during this fellowship helped us secure two additional competitive grants (NOVARTIS: €10,000; MUI.START: €36,000), ensuring continuity and enabling the planned expansion.

Thank you for your invaluable support. Your investment has catalyzed key methodological advances and generated promising findings that will guide our larger-scale analyses. I look forward to sharing further results as the project progresses.

With sincere appreciation,

Azin Kheirkhah