ISFG Peter M. Schneider short term fellowship 2024 Report

Recipient: Brando Poggiali, PhD student, Section of Forensic Genetics, Department of Forensic Medicine, University of Copenhagen, Denmark
Host: Department of Forensic Medicine, Seoul National University College of Medicine, South Korea
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The primary objective of my visit to Professor Hwan Young Lee's laboratory was to gain expertise in the discrimination of monozygotic (MZ) twins using DNA methylation (DNAm) and to validate previously reported twin-discriminating CpG markers on Danish MZ twins.

In the first phase of the work, we observed that the CpG sites identified across studies showed limited overlap. The discrepancies in outcomes originated from differences in DNAm platforms, array preprocessing pipelines, study populations, and marker selection strategies. We therefore decided to develop a new analytical pipeline aimed at identifying a robust set of CpG markers capable of discriminating MZ twins across populations, DNAm platforms, and longitudinal time points. During the analysis of several public and unpublished MZ twin datasets, we identified three principal challenges in defining reliable twin-discriminating CpG sites:

1. The biological variation in MZ twins is, in part, masked by technical variation inherent to DNAm methodology.
2. Certain CpG markers exhibit longitudinal variability, making them unstable for MZ twin discrimination.
3. Current approaches for assessing the discriminatory power of CpG markers often lack robustness, relying primarily on intra-pair β-value differences rather than simulating realistic forensic scenarios (e.g., assigning an evidence sample to one of two reference twin profiles).

To address these limitations, we applied multiple strategies: first, we implemented metrics to exclude CpG sites largely affected by technical noise; second, we tested candidate markers for longitudinal stability using time-series datasets; and third, we developed a statistical likelihood ratio–based framework to test the discriminatory capacity of CpG site sets on longitudinal MZ twin samples simulating a forensic scenario (twin evidence and reference samples).

This experience advanced our understanding of twin discrimination through epigenetics and laid the foundation for future collaboration between the two institutions and research teams. Ongoing analyses and meetings are planned, with the final aim of disseminating our findings to the forensic community.

Beyond the scientific work, my visit to Professor Hwan Young Lee's laboratory provided me with invaluable opportunities to exchange expertise, share perspectives, and experience a different laboratory culture. I learned new collaborative and methodological research approaches, enriching my scientific development.

Finally, I wish to express my gratitude to Professor Hwan Young Lee and her team for their kindness, professionalism, and hospitality, which made this experience both scientifically and personally rewarding. I am also deeply grateful to the Peter M. Schneider ISFG Fellowship for making this unique opportunity possible, as well as to my supervisors (Jeppe Dyberg Andersen, Athina Vidaki, and Jacob Tfelt-Hansen) for their continuous support and guidance.

Brando Poggiali