UNLOCKING THE GENETIC SECRETS OF MALE INFERTILITY BY EXOME SEQUENCING

In previous posts within this forum, we highlighted the potential of exome sequencing in understanding the genetic etiology of male infertility (“Male Infertility 07/03/2022" and "How to Select a Shortlist of Genetic Markers for Male Infertility? 15/01/2021"). In a new study published in *The American Journal of Human Genetics*[1], the authors delve into this question, analyzing 638 genes linked to male infertility in a group of 521 men with primary spermatogenic failure, including men with congenital hypogonadotropic hypogonadism (CHH).

Pathogenic and Likely pathogenic variants were uncovered in 12.3% of patients, regardless of their specific infertility conditions like azoospermia or oligozoospermia. This figure rose to 17% in the CHH group, a previously unreported result in this patient cohort. From the gene perspective, the study identifies disease-causing variants in 6% of the analyzed genes, including variants in genes not previously associated with male infertility. Some individuals even harbored multiple gene variants, adding more complexity to the puzzle. In another layer of the study, findings revealed that men with genetic infertility face a fourfold higher risk of early-onset cancer compared to the general population.

Overall, this study demonstrates, once again, the value of exome testing in male infertility diagnosis and management. With one in eight men receiving a molecular diagnosis, it's clear that genetic insights are pivotal in guiding personalized treatment strategies and early detection of potential health risks.

1. Lillepea et al., Toward clinical exomes in diagnostics and management of male infertility, The American Journal of Human Genetics (2024), https://doi.org/10.1016/j.ajhg.2024.03.013