Genome sequencing as a first-line test to diagnose intellectual disability

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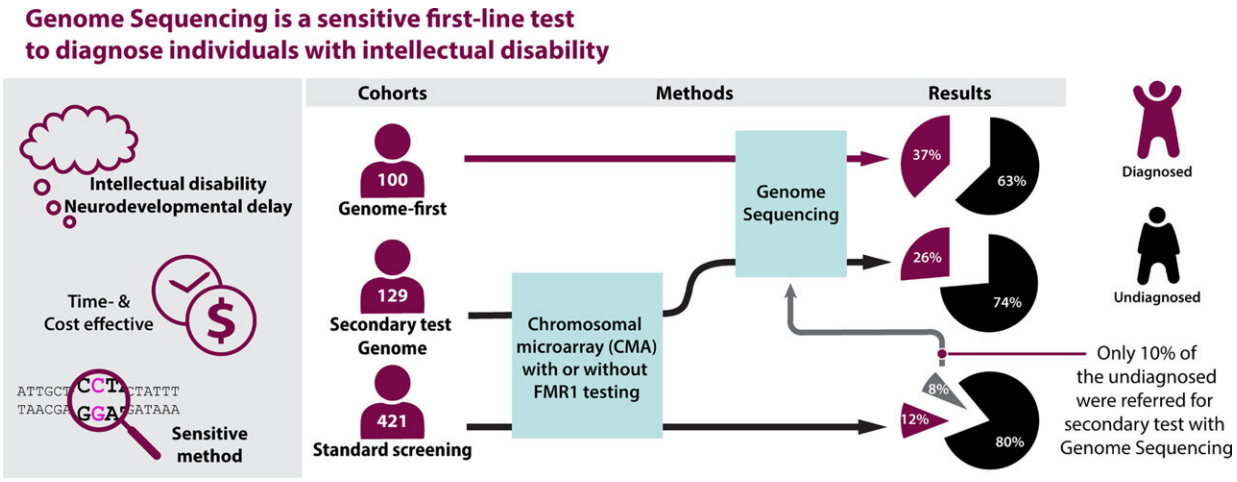

Graphical abstract. Credit: *Genetics in Medicine* (2022). DOI: 10.1016/j.gim.2022.07.022

Researchers at Karolinska Institutet have shown in a new study that genome sequencing is a sensitive first-line test to diagnose individuals with intellectual disability. These findings are published in *Genetics in Medicine*.

Individuals with intellectual disability (ID) and/or neurodevelopmental disorders (NDD) are currently investigated with several different approaches in clinical genetic diagnostics. In this study the scientists compared the results from three diagnostic pipelines in patients with

ID/NDD; genome-first (n=100), genome as a secondary test (n=129) or chromosomal microarray (CMA) with or without FMR1 analysis (n=421).

The diagnostic yield was 35% (genome-first), 26% (genome as a secondary test) and 11% (CMA/FMR1). Notably, the age of diagnosis was delayed by one year when genome was done as a secondary test and the cost per diagnosed individual was 36% lower with genome-first compared to CMA/FMR1. Furthermore, 91% of those with a negative result after CMA/FMR1 analysis (338 individuals) have not yet been referred for additional genetic testing and remain undiagnosed.

"Our findings strongly suggest that genome analysis outperforms other testing strategies and should replace traditional CMA and FMR1 analysis as a first-line genetic test in individuals with intellectual disability and/or neurodevelopmental disorders," says Professor Anna Lindstrand at the Department of Molecular Medicine and Surgery, Karolinska Institutet, who led the study. "Genome analysis is a sensitive, time- and cost-effective method that results in a confirmed molecular diagnosis in 35% of all referred patients," she adds.

More information: Anna Lindstrand et al, Genome sequencing is a sensitive first-line test to diagnose individuals with intellectual disability, *Genetics in Medicine* (2022). DOI: 10.1016/j.gim.2022.07.022

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