Stellingen

Navigating the Genetics of Movement Disorders from a Family-based Standpoint

1. Family-based genetic studies have revealed a very large number of genes involved in the pathogenesis of movement disorders, paving the way to a deeper understanding of their underlying mechanisms.
(this thesis)

2. We report clinical, genetic, and protein expression data of a novel rare *SNCA* variant identified in two families with dominantly transmitted, late-onset PD and concomitant cognitive decline.
(this thesis)

3. Bi-allelic missense *PTPA* variants associated with impaired activation of the PP2A phosphatase cause autosomal recessive early-onset parkinsonism with intellectual disability.
(this thesis)

4. Future clinical studies will contribute to better delineating the phenotypic spectrum of *AOPEP*-related dystonia, while functional work is warranted to provide insights into the mechanisms by which *AOPEP* loss-of-function leads to dystonia.
(this thesis)

5. Our work expands the phenotype associated with *PDHB* variants and suggests that *PDHB* should be added to the genes implicated in paroxysmal dystonia.
(this thesis)

6. The next-generation sequencing technology has made it possible to accelerate the diagnosis of Mendelian movement disorders, but the number of unsolved cases is still too high.
(Martínez-Rubio Dolores et al., *Int J Mol Sci*., 2022)

7. Identification of variants that are unequivocally causal for movement disorders remains a difficult challenge because of the genetic heterogeneity and clinical variability associated with these conditions.
(Michael Zech & Juliane Winkelmann, *Nat Rev Neurol*., 2024)

8. The search beyond the obvious truly opens windows to the wonders of genomics, and while it untangles some complexity, it informs us of another complexity of human genetic conditions that we did not even consider.
(Tatiana Maroilley & Maja Tarailo-Graovac, *Genes (Basel)*., 2019)

9. As genetic diagnosis becomes more relevant in the landscape of movement disorders, diagnostic, and therapeutic approaches need to be reshaped to include new discoveries in clinical practice and maximize implementation of integrative resources from the clinical and research settings.
(Giulietta M. Riboldi *et al*., *Front Neurol*., 2023)

10. Efficient identification of the remaining rare-disease-causing genes will require an unprecedented level of cooperation and collaboration, as well as the infrastructure and informatic tools to share deep phenotypic data and genetic variation data on a large scale.
(Kym M. Boycott KM *et al.*, *Nat Rev Genet.*, 2013)

11. There are in fact two things, science and opinion; the former begets knowledge, the latter ignorance.
(Hippocrates)

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