

Propositions

1. Next-generation sequencing (NGS) technologies have unprecedented power to establish the genetic diagnosis, disclose new genes, and study genotype-phenotype correlations in complex disorders such as frontotemporal dementia. (*this thesis*)
2. The functional evaluation and classification of newly discovered genetic variants requires a tightened collaboration of clinicians and researchers, which will facilitate further development of integrated variant-phenotype databases. (*this thesis*)
3. Investigating the non-uniform genomic architecture of the brain, including somatic variants and complex rearrangements, holds promise to obtain a more inclusive understanding of the etiology of neurodegenerative disease. (*this thesis*)
4. Currently available polygenic risk scores capture only a small proportion of familial Alzheimer's disease risk, and further study is warranted to substantiate the potential prognostic value when combined with other genetic and environmental risk components. (*this thesis*)
5. Mass spectrometry-based proteomics offers the possibility to uncover disease-specific molecular changes with spatiotemporal resolution, essential to comprehend disease mechanisms and to pinpoint candidate targets for therapeutic intervention. (*this thesis*)
6. The value of NGS can only be optimally exploited if novel approaches to detailed phenotyping are integrated with NGS results. (*Hennekam & Biesecker, Human Mutation, 2012*)
7. Data are of course necessary for good science, but they are far from sufficient. It is increasingly clear that deeper theory and more powerful computational methods will soon become the limiting factors in the progress of neuroscience. (*Russel Poldrack, Neuron, 2019*)
8. Provided costs are sustainable, a more preventative perspective on health could emerge, managed through proactive genomic, clinical and lifestyle surveillance using risk scores, complex biomarkers, liquid biopsies and wearables. (*Claussnitzer et al., Nature, 2020*)
9. Upholding a patient's wishes, while also taking a family-centered approach, is reportedly one of the most challenging aspects of genetic consultations. (*Young et al., European Journal of Human Genetics, 2019*)
10. Everyday available portions of dark chocolate can confer benefits to the brain in healthy consumers. (*Lamport et al., Nutrients, 2020*)
11. If you want to go fast, go alone; if you want to reach far, go together. (*African proverb*)