

Propositions (stellingen) for thesis

1. The observation that a founder mutation affecting the expression of the short isoform of the essential gene UGP2 can cause a severe form of developmental and epileptic encephalopathy, emphasizes that variants affecting the start codon of tissue-specific isoforms of essential genes potentially cause rare genetic disorders and should not be overlooked in routine genetic diagnostics. *This thesis*
2. Although the chromatin architecture of the UGP2 locus does not dramatically differ between embryonic stem cells (ESCs) and neural stem cells (NSCs), this observation provides preliminary insights into the tissue-specific regulatory mechanism of UGP2 pointing both to distal regulatory elements and differential promotor activity that is regulating the isoform switch of UGP2 expression. *This thesis*
3. The more additional enhancers a differentially active enhancer (DAE) identified during human brain development is interacting with, the more likely the target gene of this DAE is disease-associated. *This thesis*
4. Integration of existing high-throughput data can improve the prediction of likely functional enhancers relevant during brain development. Data integration can be cost-effective, produce scientific discoveries, and provide insights into biological mechanisms. *This thesis*
5. A genome-wide activity map of functional enhancers in neural stem cells using massively parallel reporter assay shows that enhancers with different activity levels are enriched for distinct characteristics, including different levels of sequence constraint, level of conservation and CG content. *This thesis*
6. Humans make sense of the world around them by a process of observation, trial and error, and then learn to predict what might happen next. This is like building a sufficiently accurate and useful prediction model. *Greener et al., Nature Reviews Molecular Cell Biology 23, 40–55 (2022)*
7. The human brain's habit of finding what it wants to find is a key problem for research. Crowdsourcing research can balance discussions, validate findings and make results more reproducible. *Silberzahn et al., Nature 526, 189-191 (2015) and Nature 526, 163 (2015)*
8. The complexity and sheer amount of information contained in DNA remain roadblocks to complete understanding of all functions and interactions of the genome. New and innovative approaches are needed in genome science to enrich our understanding of biology. *Zou et al., Nature Genetics 51 (2019)*
9. Modern science isn't simply about publishing one set of results and hoping other researchers read it. It is about linking everything that is out there to provide new insights. Bioinformatics lets us bring together the data from lots of experiments in one place. *James Blackshaw, EMBL-EBI.*
10. Open data and data sharing allows us to use the potential of growing global scientific output to improve science worldwide, although some in the scientific community see data sharing as a threat, even labeling those who use others' data as research parasites. *Longo et al., N Engl J Med (2016) and Farnham et al., Genome biology (2017)*
11. It is not true that people stop pursuing dreams because they grow old, they grow old because they stop pursuing dreams. *Nobel winner: Gabriel Garcia Márquez*

Soheil Yousefi
11th April 2023