Blood and Biomarkers in Huntington's Disease

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Stellingen – Propositions

behorend bij het proefschrift

Blood and biomarkers in Huntington's Disease

Anastasios Mastrokolias, Leiden 2017

1. Even at very high sequencing depths of over 60 million reads, RNA samples from whole blood are not sequenced to saturation. *(this thesis)*
2. The inability of previous HD whole blood gene expression studies to identify and replicate significant and biologically appealing biomarkers can be attributed to tissue subpopulation overabundance and compositional variance. *(this thesis)*
3. The expression levels of robust, statistically significant genes can be combined with expression levels of modestly significant genes that provide complementary disease stage specific information in order to compile potential biomarker panels that best predict disease progression. *(this thesis)*
4. The integration of disparate biological classes of data can unmask disease specific biological connections and markers that would often be overlooked during the independent analysis of each set. *(this thesis)*
5. A battery of biomarkers comprised of a range of modalities will be required to best define HD disease progression and therapeutic efficacy. *(this thesis)*
6. While it is often said that changes in blood-based end points may not reflect pathology in central compartments (e.g. *Alzheimers Dement. 2014 Jan; 10(1): 115–131*) this drawback appears overcome by multilevel biomarker panel development. *(this thesis)*
7. The fact that a biomarker should be reliably measurable in HD patients at stages of the disease likely to be targeted in upcoming clinical trials (*CHDI Foundation - April 2015*) precludes the use of molecular biomarkers of central compartments.
8. The development of predictive tools for HD should consider that the progression in premanifest HD appears linear for imaging, cognitive, and psychiatric data, but non-linear for motor and functional data. *(Frontiers in Aging Neuroscience 2014, 6: 78)*
9. In a period of disruptive innovation scientists should adhere to Aristotle's position that "It is the mark of an educated mind to be able to entertain a thought without accepting it" - *Nicomachean Ethics 1094b24 - 340 B.C.*.
10. While preparing a thesis one learns the truth of Plato's Cratylus interpretations of Heraclitus: No man ever steps in the same river twice, for it's not the same river and he's not the same man - *Cratylus 402a - 360 B.C.*.