Cellular stress in vitro and longevity in vivo

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Stellingen behorend bij het proefschrift

Cellular stress *in vitro* and longevity *in vivo*

1. Offspring of very old siblings, belonging to families with exceptional longevity, show a lower mortality and a lower prevalence of age-related diseases when compared to their partners, representing the general population. *In vitro* cultured skin fibroblasts of these offspring and their partners also show different characteristics, reflecting the difference in biological age (this thesis).

2. Under adverse conditions, fibroblasts from offspring die more readily from apoptosis but are less inclined to become senescent, when compared to fibroblasts from partners (this thesis).

3. Pathways that control cell proliferation are differently regulated in fibroblasts from chronologically young subjects when compared to fibroblasts from chronologically old subjects (this thesis).

4. In addition to the *in vivo* differences in glucose metabolism found between offspring and partners (Rozing, J. Am. Geriatr. Soc. 2010, 58: 564-569) *in vitro* cultured skin fibroblasts from offspring and partners now also show a different metabolic profile *in vitro* (this thesis).

5. It is still unclear what the relative roles of apoptosis and senescence are in the ageing process.

6. Although there is a longstanding tradition of studying organisms' phenotypes and despite the fact that whole genome sequencing now also allows us to characterize complete genotypes of organisms, understanding the complexity of the relationship between genotype and phenotype should be addressed more extensively in modern biology.

7. The validity of *in vitro* cell models in the study of the corresponding human conditions is subject of debate (Horrobin, Nat. Rev. Drug Discov. 2003, 2:151-154). However, our ability to culture and even 'print' 3-dimensial cell models, resembling organs, allows for research that cannot possibly be done *in vivo*.

8. Brain cells help create ideas. Stress kills brain cells. Stress is not a good idea (Richard Saunders).

9. The greatest discoveries were not made by those scientists shouting 'Eureka!' (I found it!) but by those murmuring 'That's funny ...' (Isaac Asimov).

10. Do not regret growing older: it is a privilege denied to many.