Novel insights into cardiocutaneous syndromes

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Stellingen behorende bij het proefschrift

1) Continued dependency on mere algorithms without performing actual functional studies, is insufficient to provide substantial insight into the pathogenesis of cardiocutaneous syndromes (this thesis).
2) Guidelines for the interpretation of sequence variants by the American College of Medical Genetics and Genomics (ACMG) should include use of isogenic controls and therapeutic interventions as criteria to assess the strength of *in vitro* or *in vivo* functional studies supportive of a damaging effect on the gene or gene product (this thesis).
3) Isometric loading strategies are insufficient to recapitulate a clinically relevant cardiac phenotype in gene mutations causative for a cardiocutaneous syndrome (this thesis).
4) High loads and long loading periods are needed to provoke key characteristics of human DSP-cardiomyopathy in *in vitro* engineered heart tissues (this thesis).
5) KLHL24 is a regulator of desmin turnover in the heart (this thesis).
6) Pathogenic *KLHL24* variants cause early onset cardiomyopathy with fast progression (this thesis).
7) KLHL24-mediated K14 degradation is more pronounced in patient hiPSC-derived fetal-like keratinocytes than adult primary keratinocytes (this thesis).
8) “Were the various types of cells to lose their stickiness for one another and for the supporting extracellular matrix, our bodies would at once disintegrate and flow off into the ground in a mixed stream of cells.” *Warren Lewis* (1922)
9) “It’s a mystery to me. We have a greed with which we have agreed”, *Eddie Vedder*
10) “We zullen doorgaan, Telkens als we stilstaan, Om weer door te gaan”, *Ramses Shaffy*