Modifying the modifier: discovering mechanisms of SMCHD1 mediated chromatin repression

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Stellingen behorend bij het proefschrift getiteld

Modifying the modifier

Discovering mechanisms of SMCHD1 mediated chromatin repression

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1. The observation that muscle cells attempt to repress *DUX4* transcription from the D4Z4 repeat with multiple repressor mechanisms argues that DUX4 is deleterious to these cells (This thesis)
2. Even when SUMOylation is ubiquitously present on a protein, this does not mean that a strong phenotypic effect can be observed when this SUMOylation is lost (this thesis)
3. The surface has barely been scratched on the post-translational regulation of SMCHD1 (this thesis)
4. The DNA methylation-independent repression of *DUX4* by SMCHD1 shows that there are still repressive mechanisms acting on the D4Z4 repeat to be uncovered (this thesis)
5. While reduced SMCHD1 levels can cause FSHD, restoration of SMCHD1 protein levels can silence DUX4, indicating clinical opportunities (this thesis)
6. While SUMOylation of individual proteins in a complex might be dispensable, SUMO acts as a 'chromatin glue' to stabilize repressor complexes and silence gene expression – Cossec et al. Cell Stem Cell (2018)
7. The clinically divergent phenotypes caused by SMCHD1 mutations, FSHD or BAMS, indicate that SMCHD1 plays a fundamental role in embryogenic development – Gordon et al. Nat Genet (2017)
8. Concerning the D4Z4 repeat: size definitely matters (Adapted from P.E. Thijssen, thesis, Leiden University 2016)
9. Treating the root cause of FSHD by genetic editing would grant greater clinical benefits, but is significantly more challenging and risky than intervention using pharmaceuticals – Lim et al. Front. Pharmacol. (2021)
10. The increasing anti-scientific movement of a minority of dominant voices resulting in self-censorship of scientists is a threat to the entire scientific community – Inspired by Nature 598, 236 (2021)
11. The poor reproducibility of many published experiments hinders credibility and advancement of scientific knowledge – Inspired by Errington et al. eLife (2021)
12. The inflating requirements for publishing fundamental research in established peer-reviewed journals is at odds with current standards for a PhD degree.