

Stellingen

Behorende bij het proefschrift

From GWAS to Function:

Transcriptional regulation of pigmentation genes in humans

1. Human pigmentation is influenced by *HERC2* rs12913832; it regulates transcription of the neighboring pigmentation gene *OCA2* by attenuating a long-range chromatin loop between an enhancer and the *OCA2* promoter (*this thesis*).
2. *BNC2* transcription is regulated by an allele-dependent enhancer in combination with a constitutive enhancer that both act on an alternative *BNC2* promoter, resulting in a differentially expressed isoform that has a specific function in pigmentation pathways (*this thesis*).
3. The noncoding SNP rs12203592 controls expression of *IRF4* by modulating binding affinity of the transcription factors TFAP2 α , MITF and YY1, and by subsequently interacting with the *IRF4* promoter via chromatin-loop formation (*this thesis, and Praetorius, C. et al., Cell 2014*).
4. The MC1R-antagonist ASIP is not expressed in skin epidermal cells, in stead it exerts its role in pigmentation from within the skin dermis (*this thesis*).
5. The SNP rs12913832 is a strong genetic predictor for human pigmentation phenotypes. (*Liu, F., et al., Curr. Biol. 2009; Branicki, W., et al., Hum. Genet. 2011*).
6. The (strongest) associated SNP resulting from GWA studies is not necessarily the causal variant; identifying the actual causal variant(s) is crucial in order to explain the functional biology underlying the association signal (*this thesis and Edwards, S.L., Am. J. Hum. Gen. 2013*)
7. When studying the functional impact of genetics associations that are located in coding regions, one should not only focus on the protein code, but also on the regulatory potential of that region (*Stergachis, A. et al., Science 2013*).
8. The *BNC2* gene is present in regions of the human genome that show increased levels of Neanderthal ancestry, suggesting that Neanderthals provided modern humans with adaptive variation for skin pigmentation (*Sankararaman, S. et al., Nature 2014 and Vernot, B. and Akey, J.M., Science 2014*).
9. "Science never solves a problem without creating ten more." (*George Bernard Shaw*)
10. "Only two things are infinite; the universe and human stupidity, and I am not sure about the former." (*Einstein*)
11. "No act of kindness, no matter how small, is ever wasted." (*Aesop*)