Stellingen behorende bij het proefschrift

Tuning transcription from the HIV promoter: modulation of HIV-1 latency

1. Addition of histone affinity purification as the last step in Catchet-MS enabled specific enrichment and identification of the chromatin-bound fraction of the dCas9 bait proteins (this thesis)

2. Thalidomide class drugs represent a promising class of latency reversal agents that reverse latency via degradation of HIV-1-bound IKZF1 and consequent removal of polycomb complexes from the HIV-1 promoter (this thesis)

3. Gliotoxin, a molecule that targets the HIV-1 transcriptional elongation step, strongly synergizes with latency reversal agents such as BAF inhibitors and HDAC inhibitors that derepress the chromatin configuration of the HIV-1 5' LTR (this thesis)

4. Our data point to the GRIK5 inhibitor Topiramate as a potentially promising compound for latency reversal (this thesis)

5. A significant number of factors identified by Catchet-MS are likely recruited co-transcriptionally, through association with the nascent viral RNA, and may represent an important resource of putative post transcriptional regulators of vRNA processing (this thesis)

6. Studies on HIV-1 have provided groundbreaking insight into fundamental aspects of transcriptional regulation in general

7. To date, clinical trials with latency reversal agents have demonstrated that activation of viral gene expression is possible in vivo, but there is limited or no clearance of the reactivated cells (Archin et al, 2017; Archin et al, 2012; Elliott et al, 2015; Elliott et al, 2014; Gutierrez et al, 2016; Rasmussen et al, 2014; Sogaard et al, 2015). (reviewed in Kim et al., Cell Host & microbe, 2018)

8. Identifying factors bound to specific genomic loci in an unbiased manner is the holy grail of chromatin research because it would provide an ultimate description of locus function. (Vermeulen and Dejardin, Nature reviews molecular cell biology, 2020).

9. The enrichment of intact proviruses in repressive chromatin functional domains, as recently shown by Jiang et al in elite controllers, supports the notion that for a functional cure we may not require complete elimination of the reservoir; shock and kill strategies may be sufficient to effectively eliminate the reactivatable part of the reservoir (Jiang et al., Nature, 2020)

10. HIV diagnoses and treatment initiations have been disrupted by the COVID-19 pandemic in many countries. Modelling indicates that the impact of the COVID-19 pandemic on the HIV response could result in 123,000 to 293,000 additional HIV infections and 69,000 to 148,000 additional AIDS-related deaths globally. (Addressing inequalities and getting back on track to end AIDS by 2030, Report of the UN Secretary General, António Guterres)

11. "Science grows by its mu answers more than by its yes or no answers." - Robert M. Pirsig

Enrico Ne, June 23rd, 2021