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Combinatorial testing of viral vector and CRISPR systems for precision genome editing

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Stellingen behorende bij het proefschrift:

Combinatorial testing of viral vector and CRISPR systems for precision genome editing

1. CRISPR nickases are better choices when manufacturing safer products related with cell therapies, but the efficiencies of nickases-based gene editing need to be improved, while comparing with the counterparts nucleases. (this thesis)
2. The AAV-vectored base editor as a robust option can augment the dystrophin repair in Duchenne muscular dystrophy (DMD). (this thesis)
3. The combination of adenoviral and adeno-associated viral vectors serves as efficient delivery vehicles of CRISPR nuclease-mediated gene knock-in in different cell lines. But the ideal match of exact elements involved can result in presumably perfect gene editing. (this thesis)
4. Top on the platform of dual viral vector system, the mark-free selection system can get rid of imprecisely gene-edited cells. (this thesis)
5. The AAV-vectored Cas9 for gene editing has not only been demonstrated impressively high efficiencies on both HSCs and iPSCs, but is used for other therapeutically relevant cell types, including CAR-T cells. (Fabian P. Suchy *et al*, *Nature Biotechnology*. 2025, 43:204-213)
6. Further investigations into recombinant AAV-host interactions are crucial for instructing vector engineering and underscoring the detailed mechanism of transgene expression. (Jianghui Wang *et al*, *Signal Transduction and Targeted Therapy.* 2024*,* 9:78)
7. For applications of CRISPR-mediated gene therapies into humans, one should concern the potential influence of pre-existing immunity originated from exposure to *S. aureus* under inflammatory conditions on the host response to Cas9. (Rumya Raghavan *et al*, *Nature Communications.* 2025, 16:105)
8. Venture capitalists chase the profits while scientists realize their idealism along the road leading to a successful therapy but with substantial upfront capital, risks of high failure rates and long timeframes of persistence. (Melinda Kliegman *et al*, *Nature.* 2024, 634*:*307–314)
9. The devil is in the details, but before being "picky", it would be better to get a clear orientation.
10. Actions make the results, but only part of the mind can be transformed into actions.