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## Soft genome editing based on CRISPR nickases: it takes one break to tango

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# Stellingen

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## **Soft genome editing based on CRISPR nickases: it takes one break to tango**

1. Genome editing based on high-specificity CRISPR-Cas9 complexes and donor DNA constructs prone to defined HDR processes (i.e. HR, HMEJ or ITPN) constitute a complementary set of precision genetic engineering strategies with enhanced performances and heightened safety profiles. (This thesis)
2. The replication status of target cells influences prime editing activities and outcomes. (This thesis)
3. Combined delivery of full-length prime editing components in single high-capacity adenovector particles yields efficient and precise modification of *DMD* alleles in stem/progenitor cells with myogenic capacity. (This thesis)
4. The chromatin environment has a significant bearing not only on the activity but also on the precision and product purity attained by DSB-free genome engineering technologies based on prime editors and base editors. (This thesis)
5. The finding that, albeit at low levels, CRISPR-Cas9 nickases can trigger chromosomal translocations favors the implementation of high-specificity variants in therapeutic contexts. (This thesis)
6. Cell type-specific delivery within a particular tissue could offer advantages for certain therapeutic applications. (Raguram A., et al. 2022, Cell)
7. Maps of chromatin features are useful resources to choose the optimal target loci for genome editing. (Schep R., et al. 2021, Molecular Cell)
8. The rapid evolution of genome-editing technologies has led us into a new era—an era in which we can now edit our own genomes, as well as the genomes of many other organisms that affect our communities. (Anzalone A.V., et al. 2020, Nature Biotechnology)
9. When it is obvious that the goals cannot be reached, don't adjust the goals, adjust the action steps. (Inspired by Confucius)
10. Never stop questioning. Curiosity has its own reason for existing. (Inspired by Albert Einstein)
11. After endless mountains and rivers that leave doubt whether there is a path out, suddenly one encounters the shade of a willow, bright flowers and a lovely village. (Inspired by You Lu)