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Optimising antisense oligonucleotide-mediated exon skipping for Duchenne muscular dystrophy

1. When optimising a drug dosage regimen, balancing on-target effects (in muscle) and off- target effects (in other organs) is required (*this thesis, chapter 3*).
2. The dystrophin protein has a long half-life outliving AON and skipped transcript, which facilitates the use of intermittent (on/off) scheduling to reduce side effects (*this thesis, chapter 4*).
3. While searching for compounds that enhance exon skipping, the focus should not only be efficacy at the point of interest, because off-target skipping effects increase the chance of toxicity (*this thesis; chapter 5*).
4. The use of prednisone or prednisolone does not affect the efficacy of AONs, so it does not impede participation in clinical trials, but it does influence functional outcomes and should be taken into account as a covariate (*this thesis, chapter 6; Henricson EK (2013), Muscle Nerve; 48: 55-67*).
5. Lack of reproducibility of published results is often a problem (*this thesis, chapter 7*).
6. There should be more effort spent to publish and communicate negative results to prevent unnecessary repetition and waste of time and money.
7. For therapeutic approaches the feasibility of translation into humans should be taken into account.
8. It is unethical to post no results of clinical trials in case of unwanted findings.
9. At the moment all scientific research should have direct economic benefit to obtain research funding, which compromises fundamental science. This is harmful in the long run, since basic science is essential for translational science.
10. Instead of humanizing mouse models, we had better make humans more murine, since mice are a lot easier to cure than patients.
11. The work of science has nothing whatever to do with consensus. Consensus is the business of politics. (.....) In science consensus is irrelevant. What are relevant are reproducible results (*Michael Crichton, 2003*).
12. Even though the positive correlation between chocolate consumption and number of Nobel price laureates per country (*Messerli FH (2012) N Engl J Med; 367: 1562-1564*) might be a coincidence, it is worth trying.