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From signal transduction to targeted therapy : interference with TGF-_ and myostatin signaling for Duchenne muscular dystrophy

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PROPOSITIONS/STELLINGEN

From signal transduction to targeted therapy:

Interference with TGF-β and Myostatin signaling for Duchenne muscular dystrophy

1. Cripto delineates the function of different TGF-β family members in myoblasts (*This thesis*).
2. TGF-β/myostatin inhibition creates a more favourable milieu in the muscle so that more muscle fibers will become amenable to exon skipping (*This thesis*).
3. Differential activation of TGF-β signalling in dystrophic muscles explains their different responses to TGF-β inhibitors (*This thesis*).
4. Every therapeutic strategy should consider safety in addition to potency in an early stage of development (*This thesis*).
5. The current guidelines for antisense oligonucleotide design will not guarantee their efficacy and further optimization will still be necessary (*This thesis*; *Aartsma-Rus 2012*).
6. Myostatin is the long-sought molecular "chalone" that is produced by a specific tissue, circulates throughout the body and eventually inhibits the growth of the tissue of origin and has been postulated >40 years ago (*Bullough 1965*; *Lee 2004*).
7. An important consideration for TGF-β-directed treatment of fibroproliferative diseases is to select the right time point and cell type for targeted intervention (*Dooley 2012*).
8. Single-gene disorders are not simple in their clinical manifestation, and the value of clinical experiments to deepen our understanding of these conditions should not be underestimated (*Moore 2010*).
9. Drug development should be based on excellent biochemistry.
10. Young scientists must not only learn how to use a kit, but also how it works.
11. Scientists are stickers. They stick to solving their problems.
12. Being a graduate student is like becoming all of the Seven Dwarves. In the beginning you're Dopey and Bashful. In the middle, you are usually sick (Sneezy), tired (Sleepy), and irritable (Grumpy). But at the end, they call you Doc, and then you're Happy.