

A Drosophila model for Duchenne muscular dystrophy

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Propositions

Accompanying the dissertation

A Drosophila Model for Duchenne Muscular Dystrophy

- 1. *Drosophila* Dystrophin is involved in retrograde signaling at both the NMJ and at CNS synapses (Chapters 3 and 4 of this thesis).
- 2. Dystrophin and Dystrobrevin are required for muscle integrity and survival in *Drosophila* (Chapters 5 and 6 of this thesis).
- 3. Dystrophin and Dystrobrevin are shown to associate in some tissues in *Drosophila*, suggesting that the different DGC members cluster together in a complex in a similar manner as in vertebrates (Chapters 6 and 7 of this thesis).
- 4. Dp186 performs a similar function at interneuronal synapses as DLP2 at the NMJ, suggesting that the actin-binding domain of the *Drosophila* DLP2 Dystrophin isoform is not involved in this role (Chapter 7 of this thesis).
- 5. The importance of the DGC for normal brain function may be related to a role of the DGC in the formation and maintenance of synapses, as is shown for the NMJ. *Albrecht & Froehner, 2002, Neurosignals 11, 123-129.*
- 6. The muscle degeneration in DMD patients may not be primarily caused by the absence of Dystrophin, but by the absence of other DGC proteins, normally stabilized at the sarcolemma by Dystrophin, such as Dystrobrevin.

 Blake & Martin-Rendon, 2002, Trends in Cardiovascular Medicine 12, 224-228.
- 7. The absence of sarcolemmal damage does not preclude a mechanical defect residing elsewhere in the myofiber cytoskeleton as the cause of muscular dystrophy. *Ervasti, 2003, J Biol Chem 278, 13591-13594.*
- 8. Since ion channels are thought to be involved in the primary onset of muscle degeneration, electrophysiological exploration will contribute to the identification of molecular targets for pharmacological treatment of DMD.

 *Allard, 2006, J Muscle Res Cell Motil 27, 367-373.
- 9. The value of 'simple' animal models, like *Drosophila*, lies primarily in the discovery of novel insights into cellular and disease processes and not in duplicating results from vertebrate models.

Muqit & Feany, 2002, Nature Rev Neurosci 3, 237-243. Celotto & Palladino, 2005, Molecular interventions 5, 292-303.

- 10. Unraveling the human genome has not had the expected effect on the understanding of cellular processes, because new discoveries in the field of RNA regulation and modification have shown that gene expression is not only regulated at the DNA level.
- 11. Although competition (for instance in science) should lead to improved quality, it is also possible that quantity becomes more important than quality.
- 12. Policies to preferentially hire women for higher positions will increase the number of women versus men in such jobs, but will not solve the underlying problems, which caused the disproportionate low number of women in the first place.
- 13. The biggest error in the current debate about climate is that it is implied that climate is naturally stabile and that therefore all change is the result of human industry.
- 14. The fact that scientific presentations often exceed the allocated time, suggests that scientists forget they are the only ones who think their own research is the most significant.