Diseases of the nervous system associated with calcium channelopathies

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Propositions

1. The auxiliary subunits $\alpha_2\delta$-2, β_4, and γ_2 of $Ca_V2.1$ channels are dispensable for neurotransmitter release at the NMJ synapse.
   (*This thesis*)

2. *Cacna1a* conditional knockout mice will be instrumental in dissecting the cell-specific role of $Ca_V2.1$ channels in motor behaviour.
   (*This thesis*)

3. Dysfunction of Purkinje cells, rather than cerebellar granule cell neurons, is the cause of the abnormal cerebellar morphology and ataxia seen in $Ca_V2.1$ $\alpha1$ knockout mice.
   (*This thesis*)

4. Increased, not decreased, irregularity in Purkinje cell simple spiking results in motor deficits and cerebellar ataxia.
   (*This thesis*)

5. The fact that the FHM1 S218L gain-of-function mutation causes cerebellar ataxia compromises the hypothesis that only loss-of-function mutations in *CACNA1A* cause this phenotype.
   (*Hans M. et al., J Neurosci 1999; 19:1610-1619; Guida S. et al., Am J Hum Genet 2001; 68:759-764)*

6. Drugs such as aminopyridines and EBIO that restore normal Purkinje cell function in experimental animal models, deserve to be tested in prospective clinical trials of patients with cerebellar ataxia
   (*Strupp M. et al., Neurology 2004; 62:1623-1625; Walter JT. Et al., Nat Neurosci 2006; 9:389-397)*

7. Modulation of calcium channel function by G-proteins and auxiliary subunit interaction is perhaps more relevant to explain disease pathology than direct biophysical consequences of *CACNA1A* mutations on these channels.
   (Weiss N. et al., Pflugers Arch 2008; 457:315-326; Mullner C. et al., J Biol Chem 2004; 279:51844-51850)

8. "Neurological disorders are among the greatest threats to public health."
   (*Neurological Disorders: Public Health Challenges. World Health Organisation, 2006*)

9. "Translational research means different things to different people, but it seems important to almost everyone."
   (*Woolf SH, JAMA 2008; 299:211-213)*

10. "The real act of discovery consists not in finding new lands, but in seeing with new eyes."
    (*Mascel Proust*)