Summary: Exposure to changing synaptic excitation often leads to compensatory modifications of electrical excitability (i.e. the ability to fire action potentials) in mammalian neurons. Such a mechanism is ideally suited to allow neurons to fine-tune their electrical properties to match the precise requirements of the neural circuits to which they contribute and, importantly, to prevent seizure activity. The molecular bases of this fundamental mechanism are, however, unknown. We are using the genetic tractability of *Drosophila*, coupled with whole cell patch clamp recording, to characterise the underlying components. We have identified two mechanisms: 1) a cAMP and PKA-dependent reduction of sodium current and 2) activity-dependent regulation of sodium channel translation by the proteins Pumilio and Nanos. Intrinsic determinants also likely shape the electrical development of embryonic neurons. Using *Drosophila* genetics to over-express transcription factors, that form part of the combinatorial code of motoneuron axon-guidance determination. We have shown that these transcription factors (including even-skipped, islet and dHB9) are able to influence the electrical development of well-characterised motoneurons (aCC and RP’s 1-5). We are currently identifying downstream target genes of these transcription factors using a combination of real-time PCR and DNA methylation techniques (DAM-ID).

Recent publications.-