CDKL5 Regulates Flagellar Length and Localises to the Base of the Flagella in Chlamydomonas.
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This is a study from the Department of Plant Biology at the University of Minnesota, on a type of green algae called Chlamydomonas - stick with me as it does get interesting.. honestly!! Chlamydomonas is a unicellular organism that is characterised by having flagella (hair-like structures) which have both a sensory role and a role in locomotion. The length of the flagella is controlled by a set of genes, and mutations in 4 particular genes (LF1-4) cause flagella to grow up to three times their normal length. In this study the authors describe a fifth gene (LF5) that encodes a protein kinase with a sequence that is very similar to CDKL5. The associated protein appears to localise towards the base of a growing flagella, and its localisation is affected by mutations in genes LF1-3. The authors suggest that the LF5 protein may regulate the entry of proteins into the growing flagella including proteins that control length. Based on studies of the distribution of flagella lengths that occur with mutations, they also suggest that the LF5 gene may be involved in setting the length of the flagella rather than enforcing length control.

Having set the scene with their basic research, the authors then go on to review the role of CDKL5 in humans. In particular, they discuss the interaction of CDKL5 with Rac1 (see The CDKL5 Protein) and point out that inhibition of Rac1 has been shown experimentally to alter the localisation of basal bodies, which are the foundations of structures called cilia, which in turn are structurally similar to flagella....are you still with me? So....given this, and the results of their study, the authors suggest the possibility of a link between cilia and CDKL5. There are indeed a group of conditions that are known as ciliopathies which are genetic disorders of cilia. It has been suggested that a particular form of epilepsy, juvenile myoclonic epilepsy (Janz syndrome) might also be a ciliopathy, although this remains unproven. The authors conclude, however, by suggesting that CDKL5 might be a ciliary protein and that what we now call a CDKL5 disorder might eventually also turn out to be a ciliopathy.

Note - when I started to read this, I thought I was going to be reading about plants.... botany...or perhaps even gardening! However, it actually turned out to be a fascinating read, with suggestions that, while a little speculative, nevertheless open up a whole new potential avenue of research which may ultimately influence our thought processes into the role of CDKL5. The one thing to bear in mind here is that the coding sequence of the CDKL5 gene is said to be highly preserved, appearing in many other species. The point about this, is that it implies that the functional part of the CDKL5 protein, the kinase domain at least, has survived through evolution and may therefore have a fundamentally important role necessary for basic normal function in life. Therefore, although the Chlamydomonas may seem a long way away from us humans in the evolutionary tree, the role of a "CDKL5-like" protein in this relatively primitive organism may actually have more relevance to us that we might otherwise give credit for.