CDKL5, a novel MYCN-repressed gene, blocks cell cycle and promotes differentiation of neuronal cells.
Biochimica et Biophysica Acta 2012.

This paper from Italy reports on cell culture studies looking at the role of CDKL5 in neuron development, and in relation to another gene called MYCN. The MYCN gene is known to have an important role in the embryonic development of various tissues, including the brain. The MYCN protein regulates the activity of other genes through a “transcriptional” action, where it binds to specific regions of DNA. This study suggests that the expression of the CDKL5 gene may also be regulated by MYCN.

Cell proliferation is defined as the increase in numbers of cells as a result of cell growth and division, while cell differentiation is the process whereby a cell develops into a more specialised type of cell such as a nerve cell. Cells will typically go through a period of proliferation and then differentiation. The authors observed that cells in which the CDKL5 protein was expressed, developed longer neuritic processes compared to control cells without CDKL5 - that is, showed better differentiation. Furthermore, the proportion of CDKL5 cells present in the resting phase of the cell cycle, when there is no proliferation, was significantly greater compared to control cells without CDKL5. These results therefore, not only support previous studies that have suggested an important role of CDKL5 in the differentiation of neurons, but also suggest a role for CDKL5in the control of neuron proliferation - possibly through blocking cells in the "rest phase" of the cell cycle. The authors then investigated the relation between the expression of CDKL5 and MYCN, and found an inverse relationship between the two. That is, an over expression of MYCN reduced the expression of CDKL5, while a decrease in MYCN expression led to an increase in CDKL5. It was noted that MYCN has a role in cell expansion through proliferation, a function that would fit with its inverse relation to CDKL5 levels. Furthermore, the authors suggest that the MYCN-CDKL5 axis might be particularly important in the development of the cerebellum in the early post-natal period through regulating a shift from proliferation to differentiation of cerebellar granule cell precursors - these are the small cells destined to make up large parts of the cerebellum. The cerebellum is that part of the brain involved in motor control, balance and co-ordination.

Note - This again is quite a technical paper, and took me a while before I felt I'd done it any sort of justice. One theme that seems to be emerging is the possible role of CDKL5 in the development of tubular structures. The neurites described in this study are long tubular structures as are axons, dendrites and even the spines of dendrites. I would refer you to the article above on the study of flagella to see how the CDKL5 protein might ultimately have a fundamental role in the development of tubular structures across species and hence throughout evolution.