Synaptic synthesis, dephosphorylation and degradation: a novel paradigm for an activity dependent neuronal control of CDKL5.
Journal of Biological Chemistry 2015.

This is a laboratory study from Italy looking at mechanisms that regulate or control the levels of the CDKL5 protein in the neuron. Before reading this, it might be worth your while revising some of the basic neurophysiology that I have put on The CDKL5 Protein page, particularly in relation to the "structure of a neuron" and "dendrites and spines". Much of the research that the authors have produced in this study is in relation to the regulation of the CDKL5 protein in the dendrite.

In this study, the authors have examined how levels of the CDKL5 protein change in relation to stimulation of the neuron. From their results it would appear that CDKL5 is regulated in different ways depending on the maturity of the neuron. In both mature and immature neurons, stimulation produces a rapid rise in CDKL5 levels over about a 5 minute period. However, whereas CDKL5 levels in mature neurons return relatively quickly back to their base level over the next 10 to 30 minutes depending on the maturity of the neuron, levels in immature neurons remain elevated for over an hour or so.

In both cases, the initial rise in CDKL5 levels appears to be due to local production of the protein – by translation of localized mRNA (see Genetics Page). The subsequent fall in CDKL5 levels then occurs due to the protein first being dephosphorylated (removal of a phosphate group) and then broken down by protein splitting enzymes. The stimulus for the change in activity of the CDKL5 protein appears to be a localized depolarisation – where the electrical charge in the neuron flips from negative to positive. Various mechanisms are involved - again depending on the maturity of the neuron - but it appears that the same neuronal stimulation initiates both the initial increase in CDKL5 and its subsequent degradation

Note - This study isn't telling us what the CDKL5 protein does but rather is telling us something about the way in which it is regulated or controlled. What is apparent is that whatever it is that the CDKL5 protein does, in order for it to function properly its levels have to be tightly regulated. As I have mentioned before in other reviews this may well have implications for certain therapies – particularly protein replacement or even gene therapy. It may not be enough just to try and replace the CDKL5 protein – it may also be necessary to ensure that it is being regulated correctly.