

Supporting CDKL5



Palmitoylation-dependent CDKL5-PSD-95 interaction regulates synaptic targeting of CDKL5 and dendritic spine development. PNAS 2013.

This is a nice laboratory-based study from China looking at how the CDKL5 protein localises to its target area within developing neurons. Post-synaptic density protein-95 (PSD-95) has an essential role in the development and function of synapses where it is seen to aggregate in little clusters. Palmitoylation is a process whereby a chain of fatty acids is reversibly linked to a protein, in this case the PSD-95 protein. This then facilitates the localisation of PSD-95 to the cell membrane - which is again essential to synapse development.

This study has brought all these factors together to show that the CDKL5 protein links with PSD-95 through an interaction that is dependent on palmitoylation. The distribution of CDKL5 is shown to correlate very closely with that of PSD-95 - suggesting a strong link between the two. It appears that the C-terminal of the CDKL5 protein interacts with the PSD-95-palmitoylated complex and this then allows the CDKL5 protein to get to the right place in the neuron where its kinase activity is required for dendritic and spine development. The authors also go on to show that interference with the CDKL5-PSD-95 interaction inhibits dendritic formation and growth - thereby establishing the importance of this interaction in delivering the CDKL5 protein to the right part of the neuron.

Note - This study is telling us that the PSD-95-palmitoylation complex is responsible for targeting the CDKL5 protein to the right place in the neuron - a very detailed study as you might expect so I have just tried to present the key points - ie the bits I understand!! These findings also suggests a way that mutations of that part of the CDKL5 gene coding for the C-terminal might consequently affect the function of the CDKL5 protein. Mutations affecting the C-terminal can interfere with the CDKL5-PSD-95-palmitoylated interaction, and therefore, even if the CDKL5 protein has normal kinase activity, its kinase action will be ineffective because it is just in the wrong place. Good study.