Regulation of p27 in the process of neuroblastoma N2A differentiation

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Neuronal differentiation implies morphological and biochemical changes to generate a specialized neuron. N2A neuroblastoma cells can be promoted to undergo differentiation associated to neurites outgrowth, a process linked to the arrest of cell division. Using N2A cells as a model, we investigated the detailed molecular aspects on the involvement of p27 in dibutyryl cAMP-induced neuronal differentiation. In the undifferentiated N2A phenotype, an unusually high level of accumulated p27 protein mass was evidenced. Data suggest that in proliferating cells, p27 could be sequestered by direct interaction with cyclin D1, thus preventing its inhibitory action on cell cycle Cdks. Studies also indicate that p27 is functionally active and that its loss of action on Cdks in proliferating cells is due to its strong association with cyclin D1. Therefore, when cell differentiation is triggered, the action of p27 on Cdks seems to depend on both p27 and cyclin D1 degradation during the early steps of