Relevance of Notch pathway in addressing immature cells to a final differentiated phenotype

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New knowledge about the molecular mechanisms that regulate cell replication and differentiation are definitely needed to untangle the basic rules of cell life, to design innovative therapeutic approaches, and to improve the existing therapies.
In this scenario, Notch is emerging as new signalling pathway in cell differentiation. Notch pathway consists in a receptor family (Notch1-4) activated by ligands (Jagged and Delta) present on neighboring cells. Upon the ligand binding, Notch receptors are cleaved by the gamma secretase complex, resulting in the release of an active intracellular domain (NICD, Notch Intracellular Domain), that translocates to the nucleus and modulates gene expression.
In normal tissues, Notch regulates cell-lineage decisions during the embryogenesis and modulate differentiated state in mature cells. Considerable evidence suggest that Notch signalling plays a critical role also in the progression of several cancers through the regulation of the main cellular functions associated with tumorigenesis such as proliferation, angiogenesis and cell migration.
Notch pathway is also considered as one of the main factor in "cancer stem cells" regulation. γ-secretase inhibitors (GSI), that block Notch receptor cleavage and the consequent Notch pathway activation, were successfully proposed as cancer therapy. GSI were shown to inhibit cell proliferation and induce cell differentiation in several cancer models, both in vitro and in vivo and clinical trails are now in progress for some of these compounds.
Recently, Notch pathway has been found to be involved in neuroblast differentiation, addressing immature cells to a glial phenotype, and in neurite plasticity of mature neurons.
In summary, it is plausible that, independently from the cell phenotype, Notch is one of the most relevant regulators involved in addressing immature cells to a final differentiation state.