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Developmental Cell

Loss of PRMT5 promotes PDGFRα degradation during oligodendrocyte differentiation and myelination

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This paper identifies a protein arginine methyltransferase called PRMT5 as a regulator of growth signals emanating from platelet derived growth factor receptor alpha (PDGFRα). The implication of this discovery is that inhibitors of PRMT5 can be used therapeutically to attenuate cell growth of PDGFRα addicted cancer cells, such as glioblastoma and gastro-intestinal stromal tumors (GIST). It shows, for the first time, that genetically engineered mice display defects in diminishing PDGFRα signaling in OPCs and this results in mice that lack myelin. This work provides key observations about the process by which myelin in the central nervous system is produced and about the newly discovered relationship between PRMT5 and PDGFRα signaling.

PRMT5 is an interesting enzyme from a therapeutic point-of-view because it is overexpressed in many cancers. Specific inhibitors of PRMT5 have been developed and are currently undergoing clinical trials in patients with mantle cell lymphoma. This study suggests they hold promise for glioblastoma and GIST, as well. By dampening PRMT5 activity, the growth of cells dependent on PDGFRα signaling would be particularly vulnerable.

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