ligand for fms-like tyrosine kinase. However, the cells are able to differentiate *ex vivo* and *in vivo*, becoming myeloid cells in the presence of the cytokine granulocyte–monocyte colony-stimulating factor and lymphoid cells in the presence of stem cell factor, IL-3 and IL-7.

Although these Notch1 IC lines should be useful for determining the molecular mechanisms of hematopoietic differentiation mediated by Notch1 signaling, it is not yet apparent whether they will have any therapeutic potential. Stem cell activation of Notch1 not only increases their resistance to differentiation signals, but also is pivotal at many subsequent 'decision points' in maturation. In lymphoid development, for example . Notch1 activation induces a precursor cell to become a T lymphocyte rather than a B lymphocyte (Fig. 1). Once a cell has committed to the T lineage, Notch1 activation induces expression of αβ versus γδ T-cell receptors and differentiation toward a $CD8^+$ cytotoxic T cell rather than a $CD4^+$ T-helper cell phenotype[8]. In $CD4^+$ T cells, Notch1 activation induces a regulatory rather than a helper phenotype[9]. As a result, stem cells constitutively expressing Notch IC produce few B cells or $CD4^+$ T cells *in vivo*. The functionality of the T cells derived in this way is not known.

As Notch-influenced 'decision points' affect all stem cell-derived lineages, it may turn out that constitutive expression of Notch IC severely limits the developmental potential of progenitor cells. Constitutive expression of Notch can also be oncogenic: Transplantation of bone marrow stem cells expressing Notch IC may lead to T-cell leukemia[10]. The development of a Notch IC expression system that can be regulated may help assuage concerns about inducing tumor development, but for now we still lack immortalized bone marrow stem cell lines that can safely be used in a clinical setting. Nonetheless, continued study of Notch and other regulatory and 'decision-point' pathways[1] is required to determine the full potential of immortalized pluripotent stem cells and to advance the development of stem cell therapies.

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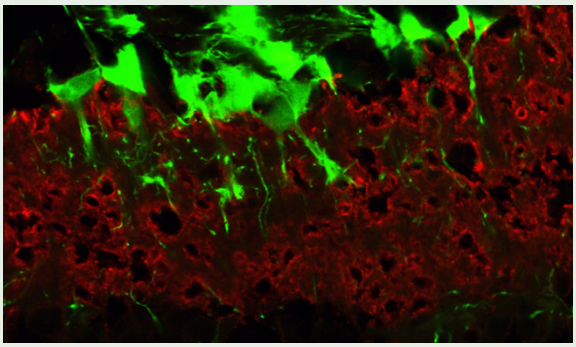
Seeing is believing

Neurons have been successfully grafted into several sites in the central nervous system (CNS), including the striatum, hippocampus and olfactory system, making this a promising approach for treatment of neural diseases or injury. However, attempts to repopulate damaged retina with grafted neurons have been unsuccessful. In the September issue of *Molecular and Cellular Neuroscience*, Young *et al.* demonstrate that neuronal progenitor cells, derived from adult rat hippocampus, are capable of integrating into retinas in a rat model of retinal dystrophy.

Neuronal progenitor cells exist in the adult hippocampus of rodents, monkeys, and humans. Adult hippocampal progenitor cells (AHPC) have been isolated from rats and shown to differentiate into neurons when grafted into the CNS. Young *et al.* isolated AHPC, labeled them with green fluorescent protein (GFP), and injected them into the vitreous of immature and mature dystrophic rats. The grafted cells were able to migrate within the dystrophic retina and then differentiate into mature neurons in one-, four-, and ten-week-old rats. GFP-labeled cells were also observed to extend neurites into the host optic nerve. The image shows grafted GFP-expressing AHPC (green) integrating and sending processes into the plexiform (synaptic) layers of the retina, labeled with antibodies against synaptophysin (red).



The AHPC were only able to integrate in animals with retinal disease or injury, suggesting that the ability to integrate and differentiate is enhanced, rather than suppressed by injury. The AHPC also failed to enter the retina or survive when transplanted into the eyes of 38-week-old rats, suggesting that there is loss of trophic support late in the course of dystrophy. "We're testing whether the grafted stem cells establish functional connections with the host visual system, and whether these connections convey useful visual information," says Young. The authors also hope to investigate the immunological properties of AHPC and to determine whether they exhibit immune privilege after transplantation.

This approach may someday be used to treat human diseases of the optic nerve and retina such as glaucoma, macular degeneration, retinitis pigmentosa, retinal detachment, and diabetic retinopathy. However, neural progenitor stem cells must first be isolated from human CNS and determined to have the same qualities as the rat AHPC. "We also have to optimize transplantation techniques that would allow us to reconstruct the layers of the retina in patients," adds Young.

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