

■ METABOLISM

Switching muscle to BAT

Boosting brown adipose tissue (BAT) development is of great interest because of its therapeutic potential for obesity and its related metabolic disorders. A new study identifies a key miRNA switch that controls the development of adult skeletal muscle precursor cells called satellite cells into brown fat (*Cell Metab.* **17**, 210–224).

Although brown adipocytes were known to originate from myogenic progenitor cells, satellite cells were thought to be committed toward muscle development. Hang Yin *et al.* now show that satellite cells from mice are multipotent and can differentiate into brown adipocytes or myogenic cells. The authors then identified miR-133 as a key determinant of the differentiation pathway adopted by satellite cells. They found that this miRNA targets and inhibits Prdm16, a transcription factor responsible for activating brown fat genes and repressing white adipose tissue- and muscle-specific transcriptional programs.

Using antisense oligonucleotides, the authors targeted miR-133 in activated satellite cells *in vivo* and showed that this stimulated the development of metabolically active brown adipocytes during muscle regeneration. In mice on a high-fat diet, similar treatment with anti-miR-133 oligonucleotides after muscle injury resulted in reduced weight gain and an improvement in metabolic symptoms. Although it remains to be determined whether miR-133 has targets other than BAT development in muscle, these results suggest that targeting this miRNA in satellite cells might hold therapeutic promise for reducing obesity.—MS

■ PARKINSON'S DISEASE

Parkinson gene partners

Common genetic variants at the *PARK16* locus and within the *LRRK2* gene modify an individual's risk of getting Parkinson's disease. Now, David MacLeod *et al.* demonstrate how variations at these loci interact to affect lysosomal function and neuronal health (*Neuron* **77**, 425–439).

The *PARK16* locus is composed of five separate genes. The researchers found that expression of only one of these genes, *RAB7L1*, can restore neurite outgrowth in cultured rat neurons that express mutant *LRRK2*. *RAB7L1* expression could also reduce lysosomal swelling caused by mutant *LRRK2*. When the authors expressed *LRRK2* and *RAB7L1* in cell lines, they observed that the proteins could bind each

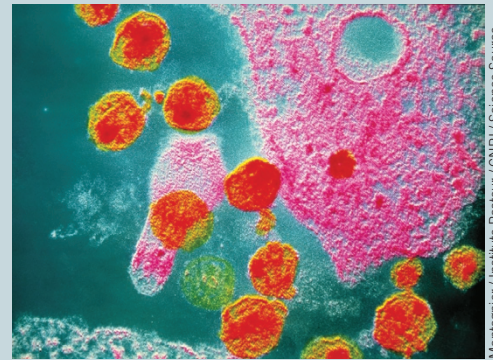
HIV INFECTIONS

HIV-1's access key

The cytokine interleukin-7 (IL-7) may facilitate transmission of HIV-1 to the female reproductive tract, according to new research published in *PLoS Pathogens* (**9**, e1003148).

Most HIV-1 infections in women occur after virus-containing semen contacts the vaginal mucosa. HIV-1-infected semen is rich in several molecules that may affect viral transmission, and IL-7 stands out as having one of the highest concentrations. Using human tissue, Andrea Introvini *et al.* found that IL-7 can facilitate HIV-1 infection of the cervico-vaginal mucosa *ex vivo*.

Mechanistically, the authors found that IL-7 directly acted on CD4⁺ T cells, preventing their apoptosis and promoting their entry into the cell cycle. These results are consistent with a model in which IL-7 promotes the survival of the founder pool of infected CD4⁺ T cells in the female reproductive tract early during HIV-1 transmission.—JCL



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other and that both localized within the same intracellular compartments.

The researchers showed that the *PARK16* variant that increased Parkinson's disease risk led to alternative splicing of *RAB7L1* and truncation of RAB7L1 protein. This version of RAB7L1 could not restore neurite outgrowth in cultured rat neurons expressing mutant *LRRK2*.

MacLeod *et al.* showed that expressing mutant *LRRK2* or reducing the expression of *RAB7L1* in a cell line led to loss of components of the retromer complex, which regulates protein sorting from the lysosome. Interestingly, overexpression of VPS35, a retromer component that had previously been linked to familial Parkinson's disease, could restore neurite outgrowth in rat neurons expressing mutant *LRRK2*. Although the mechanism by which *LRRK2* and *RAB7L1* affect retromer expression remains to be determined, these findings demonstrate a functional relationship between three loci that affect Parkinson's disease risk, which all impinge on cellular protein sorting.—EC

■ CANCER GENETICS

Telomere mutations boost melanoma

Mutations in the promoter of a gene that encodes a protein involved in maintaining telomere length have been found in human melanoma, according to two recent studies in *Science* (doi:10.1126/science.1229259 and doi:10.1126/science.1230062).

To identify previously unknown disease-segregating mutations, Susanne Horn and her colleagues studied members of a melanoma-

prone family who were not carriers of two common melanoma-associated mutations. In these individuals, they found mutations in the *TERT* (telomerase reverse transcriptase) promoter that resulted in a new binding motif for Ets/TCF transcription factors, leading to increased *TERT* transcription. The authors also found somatic ultraviolet (UV)-signature mutations, albeit different ones from those found in familial melanoma, in the *TERT* promoter in human cell lines derived from sporadic melanoma at a frequency of 85% in metastatic tissues and 33% in primary tumors. These mutations also created new binding motifs.

Using whole-genome sequencing, Franklin Huang and his colleagues identified two independent and exclusive mutations in the *TERT* promoter linked to UV damage in 71% of malignant melanomas that increased transcriptional activity. These mutations were much less abundant in human cell lines derived from other cancer types.

Although further investigation is warranted, these studies indicate that mutations in regulatory regions can act as cancer drivers and suggest a potential link between telomerase activity and other common activating mutations in melanoma pathogenesis.—CP

■ CANCER

Approaching GBM via EphA3

Currently, radiochemotherapy of glioblastoma multiforme (GBM), the most prevalent type of brain cancer, extends the mean survival of patients by merely 15 months. A recent study