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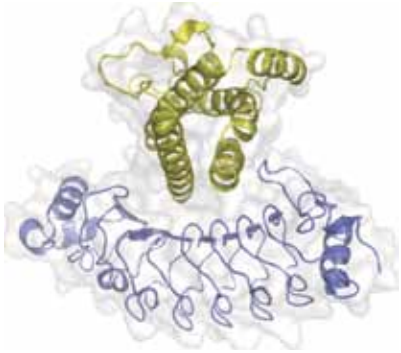
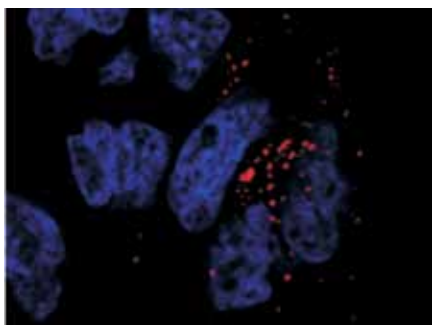
A high-affinity protein binder suppresses non–small cell lung cancer



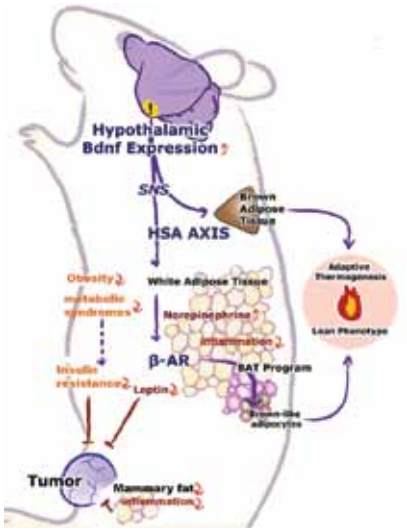
Tumors are sustained and promoted by inflammatory signals, such as interleukin-6 (IL-6), from the surrounding microenvironment. Increased expression of IL-6 leads to constitutive phosphorylation of signal transducer and activator of transcription 3 (STAT3), which activates multiple oncogenic pathways and drives an inflammatory cascade. In this issue, Lee *et al.* describe a high-affinity ligand—which they term a "repebody"—that they engineered to block IL-6/STAT3 signaling. The repebody was highly specific for IL-6 and interfered with binding to its receptor by causing steric hindrance. Intraperitoneal administration of repebody suppressed the growth of non–small cell lung cancer xenografts in mice. ***See page 1254.***

Aptamer-targeted antigen delivery

Conventional protein vaccines are usually unable to elicit robust T cell–mediated immunity. Targeting of antigen to dendritic cells (DCs)—a cell type that is pivotal for eliciting T-cell activation—can activate T-cell responses. Antigens are most commonly targeted to DCs by coupling to an antibody specific for a readily endocytosed cell-surface receptor. Owing to their unique chemical properties and low immunogenicity, RNA and DNA aptamers provide a promising alternative to antibody-based antigen delivery. Wengerter *et al.* show that the immune responses elicited by aptamer–ovalbumin conjugates were sufficient to inhibit the growth of established ovalbumin-expressing tumor cells in mice. ***See page 1375.***

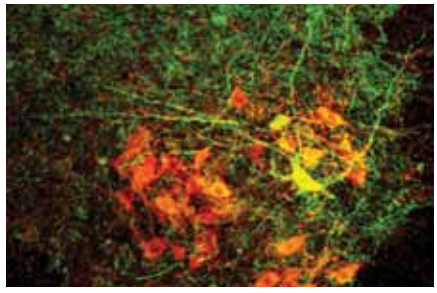


Hypothalamic gene transfer of BDNF inhibits breast cancer in middle-aged obese mice



Environmental factors and lifestyle have profound effects on the initiation, promotion, and progression of cancer. Environmental enrichment (EE), a housing environment designed to boost mental health, has been linked to robust reduction in adiposity, resistance to diet-induced obesity, enhanced immune functions, and inhibition of tumor growth. The effects of EE have in turn been linked to activation of the hypothalamic–sympathoneural–adipocyte axis. The physical, social, and cognitive stimulations provided in EE stimulate brain-derived neurotrophic factor (BDNF) expression in the hypothalamus. Liu and colleagues' study shows that hypothalamic gene transfer of BDNF inhibits its breast cancer progression and metastasis in middle-aged obese mice. ***See page 1275.***

Retrograde transduction of spinal motor neurons using lentiviral vectors



Eleftheriadou *et al.* describe lentiviral vectors engineered to exhibit tropism to motor neurons by coexpressing onto the lentiviral surface a fusogenic glycoprotein and an antibody against a cell-surface receptor on the presynaptic terminal of the neuromuscular junction. Targeting these receptors made it possible for the vectors to be transported retrogradely from the axonal tip, leading to transduction of motor neurons *in vitro* in compartmented microfluidic cultures. Delivery of the vectors to the leg muscles of mice resulted in motor neuron labeling in the lumbar spinal cord. These vectors should be useful for minimally invasive administration of central nervous system–targeted therapeutics in motor neuron diseases. ***See page 1285.***

Widespread CNS transduction of adult mice and nonhuman primates by rAAVs

Some recombinant adeno-associated viruses (rAAVs) can cross the neonatal blood–brain barrier (BBB) and efficiently transduce cells of the central nervous system (CNS). However, in the adult CNS, transduction levels by systemically delivered rAAVs are significantly reduced, limiting their potential for CNS gene therapy. Yang *et al.* report that the ability to cross the adult BBB and achieve widespread CNS transduction is a common characteristic of AAV serotypes following intravenous delivery. The results indicate that rAAVrh.8, along with rh.10 and 9, hold promise for the development of strategies to treat neurological diseases in adults. ***See page 1299.***