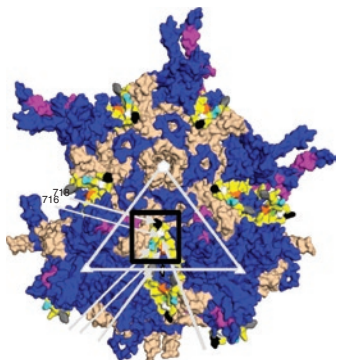


## Shuffled AAV genomes give rise to synthetic capsid variant



In this issue, Li *et al.* report a DNA shuffling-based approach for developing cell type-specific adeno-associated virus (AAV) vectors. Capsid genomes of AAV serotypes 1–9 were randomly fragmented and reassembled to generate a chimeric capsid library. An infectious clone (chimeric-1829) containing genome fragments from AAV1, 2, 8, and 9 was isolated from a melanoma cell line previously shown to have low permissiveness to AAV. Chimeric-1829 utilizes heparan sulfate as a primary receptor and transduces melanoma cells more efficiently than all serotypes. Further, chimeric-1829 demonstrates altered tropism in skeletal muscle, liver, and brain. The immunological profile based on neutralizing antibody titer and crossreactivity studies suggested that chimeric-1829 is a new synthetic laboratory-derived capsid variant. *See page 1252.*

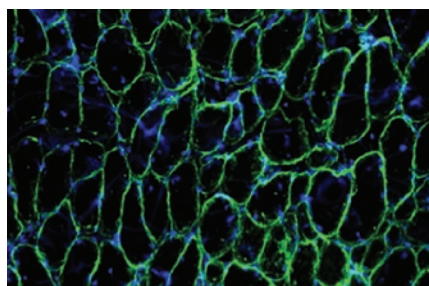
## MicroRNAs regulate ocular neovascularization

Shen *et al.* monitored changes in the expression of microRNAs during ischemia-induced retinal neovascularization (NV). They observed that the expression of three microRNAs (miR-31, -150, and -184) was substantially decreased in the ischemic retina. Intraocular injection of pre-miR-31, -150, or -184 significantly reduced ischemia-induced retinal NV, and injection of pre-miR-31 or -150 also significantly reduced choroidal NV. These data suggest that alteration of microRNA levels contributes to two types of ocular NV, and

that injection or enhanced expression of microRNAs is a potential therapeutic strategy. *See page 1208.*

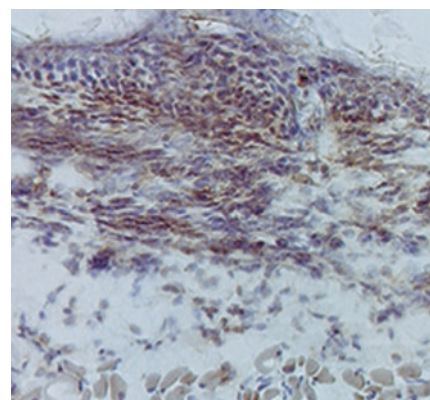
## Hematopoietic cell transplantation allows myoblast transplantation in dystrophic dogs

The goal of myogenic stem cell transplantation for Duchenne muscular dystrophy (DMD) is to increase dystrophin expression in existing muscle fibers and to provide a source of stem cells for muscle regeneration. Parker *et al.* induced immune tolerance in two DMD-affected (*cxmd*) dogs through hematopoietic cell transplantation (HCT) to determine whether allogeneic muscle progenitor cells can be successfully transplanted in an immune-tolerant recipient. Injection of muscle-derived cells from an HCT donor into either fully or partially chimeric *xmd* recipients restored dystrophin expression up to 6.48% of wild-type levels and improved muscle structure. *See page 1340.*



## Topical application of cream-emulsified siRNA treats skin disease

Induction of the co-stimulatory molecule CD86 on dendritic cells (DCs) in the peripheral tissues is a critical event in triggering antigen-specific immune responses. Ritprajak *et al.* propose a new small interfering RNA (siRNA)-based therapy using cream-emulsified CD86 siRNA, targeting DCs for murine contact hypersensitivity and atopic dermatitis-like disease. Topical application of CD86 siRNA efficiently inhibited contact hypersensitivity and markedly decreased the numbers of



infiltrating CD86<sup>+</sup> or major histocompatibility complex class II<sup>+</sup> cells in murine ear skin. These results suggest that the silencing of CD86 in local DCs inhibits the recruitment and migration of DCs into the skin, resulting in reduced antigen-specific local inflammation. *See page 1323.*

## Delivery of Dicer-substrate RNA for pain

Several ongoing clinical trials are using 21-mer small interfering RNA (siRNA) as an active pharmaceutical agent. Doré-Savard *et al.* report intrathecal delivery of 27-mer Dicer-substrate RNAs (DsiRNAs) targeting the G-coupled receptor NTS2 in rat spinal cord. Using a rat model of pain sensation, the authors demonstrate that low concentrations of two different DsiRNAs targeting NTS2 are effective in modifying the pain response when formulated with the cationic lipid i-Fect. Along with specific decrease in NTS2 mRNA and protein, the results show a significant alteration of the analgesic effect of a selective NTS2 agonist, reaching 93% inhibition up to 3–4 days following DsiRNA administration. *See page 1331.*

