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Electroporation-based Gene Transfer to Heifers

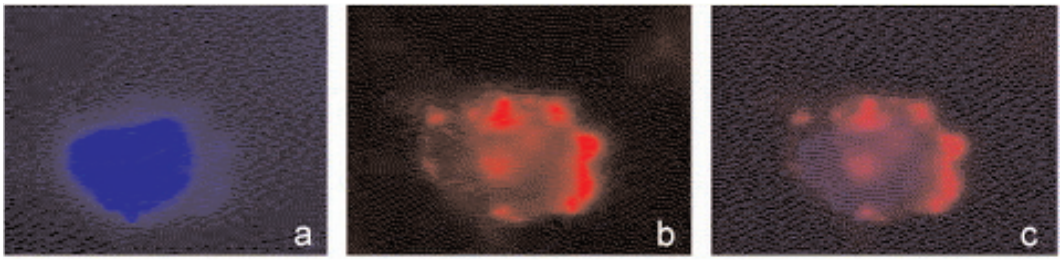
There have been relatively few studies of electroporation-mediated gene delivery in large animals. In this issue, Brown *et al.* examine the effects of a plasmid expressing the hypothalamic hormone, growth hormone-releasing hormone (GHRH), on immune function and general health of Holstein heifers. Administration of the plasmid by electroporation into muscle altered specific T-cell subsets, numbers of Natural Killer lymphocytes, and improved overall health and decreased mortality of the recipients. The animals expressed physiologically relevant levels of GHRH for nearly a year, suggesting that electroporation could prove to be an efficient method for the systemic production of therapeutic proteins.

Using PNAs to Develop New Antibacterials

The emergence of multidrug-resistant bacterial pathogens is an increasing health concern, and there is a strong demand for methods that speed the development of new antibacterials. In this issue, Nekhotiaeva *et al.* show that peptide nucleic acids (PNAs) attached to short cationic carrier peptides can be used to probe gene function in *Staphylococcus aureus*, an important drug-resistant pathogen. The method had previously been shown to work in *Escherichia coli*, but the extension of the approach to Gram$^+$ bacteria opens up new avenues to study these bugs. Peptide-linked PNAs might also be developed as antibacterial agents themselves one day. A related commentary appears on page 614.

Facilitation of Transfection by a DNA-intercalating Dye

In this issue, Fong *et al.* describe the transfection of plasmid DNA complexed to Hoechst dye, which intercalates into the minor groove of DNA. The incorporation of Hoechst into complexes of cationic liposomes and DNA significantly increased expression of a reporter gene. These complexes transfected cells as efficiently as a DOTAP-DNA complex, and a DOTAP-Hoechst-DNA ternary complex transfected cells with even greater efficiency. The authors suggest that modified intracellular trafficking of the plasmid DNA facilitated its delivery into the nucleus. While the results may lead to the identification of new DNA transfection reagents, it is not clear whether such agents would be clinically useful, since DNA intercalating agents are highly mutagenic.



Fluorescence microscopy of a cell transfected with rhodamine-labeled plasmid DNA complexed with Hoechst dye. (a) Staining of the nucleus. (b) Rhodamine fluorescence. (c) Overlapping images of (a) and (b) demonstrating colocalization.

Ad-AAV Hybrid for Vector Integration

There is strong interest in the development of methods to achieve site-specific integration of a transgene. In this issue, Recchia *et al.* explore the ability to integrate recombinant adeno-associated virus (AAV) genomes using a gutted adenoviral (Ad) vector construct. The vector uses tetracycline-regulated expression of the *rep* gene and an internal AAV genome to integrate AAV-ITR-flanked genomes into the AAVS1-specific integration site on chromosome 19. The authors describes technical advances that make the technique relatively efficient. They show that some AAV-based genomes integrate at the AAVS1 site in primary human cells and in mice transgenic for human AAVS1, based on sequencing of junction fragments.

Efficient Transduction of Muscle by rAAV

Vectors based on recombinant AAV have emerged as tools of choice for gene transfer to skeletal muscle. Multiple serotypes of AAV exist, but serotype 2-based vectors have been the most thoroughly characterized. In this issue, Blankinship *et al.* describe the production of recombinant AAV pseudotyped with serotype 6 capsid proteins. The authors demonstrate that the pseudotyped vectors can transduce the skeletal musculature of mice at levels 500 times more efficient than what has been observed with AAV2 vectors following direct injection. The vectors transduced the diaphragm and intercostal muscles of mice after injection into the thoracic cavity and transduced the musculature of mouse pups that were injected in the intraperitoneal space.