Abstract

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"Potential for Non-Invasive Imaging in Anti-Doping Efforts"

Imaging technologies have improved significantly in recent years and permit anatomical, functional, and molecular studies in living subjects at high resolution and sensitivity. The purpose of this presentation is to review the imaging modalities that offer the potential for direct or indirect detection of gene transfer, particularly to identify doping. The goal is to describe the technologies that are immediately applicable and to summarize the molecular imaging approaches that await further research refinement prior to clinical translation. The potential for non-invasive imaging to speed the development of other testing strategies will also be discussed. Magnetic resonance spectroscopy (MRS) offers the capacity to detect metabolites during rest or after recovery from exercise. Changes in metabolites at rest or following exercise may reflect previous or current doping. Naturally, a normal range will need to be established. Positron emission tomography (PET) and single photon emission computed tomography (SPECT) are based on detection of localized but specific accumulation of radioactive tracers. These imaging modalities are ideally suited to detect changes in receptor expression during disease processes, or measure energy utilization. Gene doping may result in inflammation or other receptor perturbations that may be detected by imaging. One advantage of PET and SPECT is high sensitivity but a disadvantage is the requirement for administration of a radioactive tracer. Bioluminescence and fluorescence modalities are emerging optical imaging technologies to detect genetic reporters following gene transfer, and are widely used to evaluate gene therapy vectors. Advantages include the efficiency, high sensitivity, and accuracy to measure gene transfer in animal models. Examples of this approach will be presented, including adenoviral-mediated delivery to lungs and liver, and AAV-mediated delivery to skeletal muscle. Long-term and stable gene expression can be monitored over months to years. Our group has developed a genetic approach to reduce immune response to gene therapy vectors by display of complement-inhibitory peptides. Imaging of genetic reporters was necessary to evaluate the improved performance of these new gene therapy vectors. Recent advances by our group include a method to non-invasively monitor growth hormone receptor delivery to liver in live animals, and detect downstream pathway activation in response to exogenous growth hormone administration. This system can be expanded to repeatedly and non-invasively monitor the consequences of gene doping on liver signal transduction over time.

Keywords: imaging, gene transfer, doping