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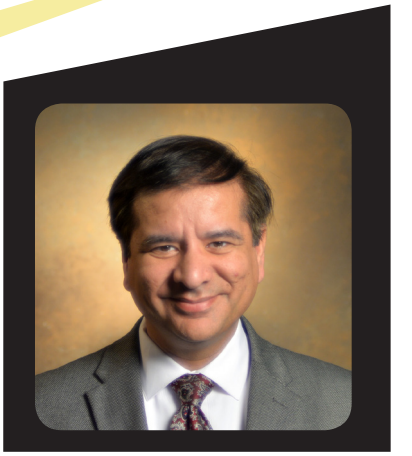

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IMAGING GENE EXPRESSION

Clinical trials of gene therapy have been hampered by a lack of clinically relevant methods for *in vivo* detection of gene transfer. Evaluating success of gene transfer in the clinic is currently confined primarily to biopsy sampling, which provides limited evaluation of *in vivo* gene delivery, is prone to sampling error, has associated morbidity and mortality and can have problems with patient compliance especially when repeated evaluation or monitoring of multiple sites is needed. Instead, monitoring of exogenous gene expression should be noninvasive and easily repeatable over time in the same patient to inform regarding the location, magnitude, and kinetics of gene expression. Moreover, this could prove instrumental towards the rational development of innovative formulations designed to selectively target particular tissues, organs, or disease sites. Reporter genes may be used to approach these needs. These often encode enzymes, transport proteins, and receptors that most frequently bind and/or entrap an imaging agent. These may be limited for percutaneous imaging of humans because of scatter, such as light based agents, size, immunogenicity, particularly if not of human origin, quantification and availability of clinically approved imaging agents. A desirable feature of such a reporter would be that it does not affect the intracellular milieu by signaling or pump action so that it does not cause untoward effects in expressing cells. We find that human somatostatin receptor type 2 gene-based reporters (SSTR2-based) reporters have such desirable features for imaging in animals and for translation to humans. The SSTR2-based systems enable *in vitro*, *in vivo* and ex vivo assessment of the reporter, can be imaged using clinically approved radiopharmaceuticals, and can be designed to be signaling deficient. Using small animal cognates of clinical machines as well as machines designed for patients, we have used a combination of functional and anatomic imaging to quantify *in vivo* expression of SSTR2-based reporters and have used these to evaluate methods for improving expression. Imaging and quantification of such reporters has been performed in small animals and, as a bridge to translation, in large animals.

Biography

Vikas Kundra is a Professor and Director of Molecular Imaging in the Department of Radiology, U T-M D Anderson Cancer Center with joint appointment in the Department of Cancer Systems Imaging. He received his MD and PhD from Harvard Medical School/University. His clinical and research Residency and Fellowship were at Harvard Medical School's Brigham and Women's Hospital. He practices as a Clinical Radiologist focused on body imaging. He is a Fellow of the Society of Body Computed Tomography-Magnetic Resonance Imaging and Distinguished Investigator of the Academy of Radiology Research. He has had multiple clinical and basic/translational science papers and grants. Basic/translational research focus is on imaging of gene expression, therapy response, imagable models of disease, and nanoparticles.

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