《招待講演》

Multimodality Molecular Imaging in Living Subjects with Applications Towards Gene Therapy & Cancer Biology

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Technologies for small animal imaging are rapidly evolving and include micro positron emission tomography (microPET), micro computed tomography (microCAT), and charge coupled device (CCD) based optical cameras for imaging very low levels of light. We have developed reporter genes that can be imaged using PET and also married these approaches to optical reporter genes (e.g., firefly luciferase). The Herpes Simplex Type 1 Virus Thymidine Kinase (HSV1-tk) and Dopamine Type 2 Receptor (D2R) reporter genes have been extensively studied. These reporter genes when expressed allow for trapping of positron labeled tracers. Cells that do not express the reporter gene do not significantly trap these tracers. Methods to improve the sensitivity of these approaches have been developed. These approaches allow repetitive and quantitative study of basic cellular events in living subjects while utilizing multiple imaging modalities to provide synergistic information. The approaches are very generalizable because the reporter gene can be activated based on many different cellular events. This is accomplished through the use of any promoter/regulatory region of choice driving expression of the reporter gene. The developed reporter genes are being incorporated with various *in vivo* gene delivery approaches, cell trafficking models, and transgenic models to study specific biological processes *in vivo*. Multimodality approaches in which a mouse can be moved between the microPET, microCAT, and the optical CCD system are under active investigation. Applications of the developed approaches for optimizing gene therapy & studying cancer biology are now under active investigation. The PET reporter gene approaches have also been translated into clinical studies and are expected to have a direct impact on optimizing and making safer human gene therapy trials in the very near future.