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Monitoring of gene therapy

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Gene therapy is a therapeutic modality which is based on the transfer and expression of a specific gene into a target cell in order to achieve therapeutic benefit. As such, one of the main goals of gene therapy monitoring is to detect functional changes in a target tissue which in principle translates to detection of clinical effects. A large number of diseases including cancer, AIDS, diabetes and others are being been targeted with this therapeutic approach. In general, gene therapy of diseases requires are high expression of the therapeutic gene in the target cells and a carrier molecule, vector, is used to deliver the therapeutic gene. The most common vector is a genetically modified virus, however, non-viral gene delivery vectors such as naked DNA, oligonucleotides and liposomes are also in use. Viruses are the preferred mean of carrier due to their ability to encapsulate and deliver their genes to human cells. Examples of types of viruses use as gene therapy vectors include modified retroviruses, adenoviruses, lentiviruses and herpes simplex viruses.

An important feature of gene therapy is the verification that the gene of interest is expressed after its delivery. This is accomplished via techniques such as tissue biopsy, blood sampling or immuno-histochemical staining, however, these techniques do not provide information on location, magnitude and extent of gene expression in living animals or subjects1. There are several in vivo imaging modalities currently being used in different experimental settings to monitor gene expression. Examples include positron emission tomography (PET), single photon emission tomography (SPECT), magnetic resonance imaging (MRI) and optical imaging. The choice of an imaging modality, however, depends on the gene product under study. For example, PET- or SPECT-based imaging modality employs herpes simplex virus type 1 thymindine kinase reporter gene and optical bioluminescence-based imaging on the other hand uses luciferase reporter genes2-4. Radionuclide-based imaging modalities are highly more sensitive than for example MRI and therefore may be more suitable for imaging the relative low levels of gene product expression in a specific tissue.

In this overview talk, focus will be placed on progress made so far in evaluating and monitoring gene expression in experimental and clinical settings with emphasis on anti-cancer gene therapy and using radionuclide-based imaging modalities. During the last years, much progress has been made in this important biomedical discipline but some hurdles and practical challenges still remain to be tackled.

References

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