Non-invasive imaging of gene delivery and biodistribution using novel DNA-binding chelate

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Goal: The current study was designed to develop a technique allowing non-invasive imaging of biodistribution of non-viral gene delivery systems.

Results. There is currently no acceptable technique that would facilitate monitoring of biodistribution of viral or non-viral gene delivery vectors in vivo without the use of biopsies. We synthesized and characterized several novel low molecular weight molecules consisting of a chealte and DNA binding moieties. The DNA binding components of the molecule covalently associate with the double strand DNA upon short-term irradiation with near UV range light. The chelate moiety of the compound was designed for high-efficiency binding with a widely used imaging isotope (99mTc) and was comprised either of a protected meracptoacetyl triglycine or of dicysteinyl peptides covalently bound to a positively charged psoralen derivative. Binding of radioactivity to DNA was ca. 25% of total; electrophoresis revealed a single 99mTc-labeled plasmid band. Non-invasive imaging in vivo of biodistribution in experimental animals were performed for the first time. An excellent correlation between the biodistributions of control nick-translated and experimental DNAs was obtained. The utility of these psoralen derivatives for labeling plasmid expression vectors was thereby demonstrated.

Conclusion. The DNA-binding chelator can be utilized for non-invasive monitoring of DNA biodistribution during gene therapy.