Docket #: S07-252

Regulating Protein Stability in Gene Therapy and Biological Therapies

Stanford researchers have developed a highly specific, tunable system to improve the safety, efficacy and deliverability of gene therapy vectors and other biological therapies. This invention utilizes the Shield-1 technology (see Stanford Docket S06-024) to control the stability, and therefore the function, of proteins expressed from transgenes in vivo. The system allows therapeutic applications of genes that could not otherwise be used (e.g. too toxic, external regulation of gene function necessary).

This approach is ideally suited for gene therapy because it can be switched on and off, it can be applied to any protein, and it only requires a small amount of DNA to be incorporated into the vector. In addition, it could be applied to a variety of biological therapies. Initial studies in mouse models have shown excellent dose control, have reduced tumor burden when a therapeutic transgene product is stabilized within a tumor, and have demonstrated control over viral vector transgene product.

Stage of Research
In vivo studies have reduced tumor burden in mouse models of cancer with excellent dose control of the conditional stability of an immunomodulatory cytokine expressed from an oncolytic virus. The inventors have also applied the system to regulate the stability of over 30 proteins in cultured cells or in vivo.

Ongoing Research
Additional studies are presently underway involving the development and characterization of a second system for regulating protein stability using a different ligand. This new technology will allow the simultaneous regulation of two proteins or small groups of protein in cultured cells or in living animals. This technology is also useful for regulating proteins that are secreted from mammalian cells. These technologies will likely be useful for target validation/credentialing using animal

models of human disease.

Applications

- **Gene therapy** - to control function of protein expressed from transgenes
- **Biological therapy** - to control function of therapeutic proteins that require external regulation

Advantages

- **Dose control** - protein function can be switched on and off in a tunable fashion
- **Broadly applicable** - the system can be applied to any protein and has been demonstrated in over 30 proteins.
- **Highly specific**
- **Small insert** - the method only requires a small amount of extra DNA or peptide sequence to be incorporated into the therapy

Publications

- Banaszynski LA, Sellmyer MA, Contag CH, Wandless TJ and Thorne, SH. Chemical control of protein stability and function in living mice Nature Medicine, pp. 1-5 (Technical Reports), published online Sept. 28, 2008.
- Published US Patent Application (Publication No. 20100034777)

Patents

- Published Application: 20100034777
- Published Application: 20140010791

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