Obstacles to Translation Conference

II. OBSTACLES TO TRANSLATION OF PROMISING THERAPIES

Protein replacement and gene therapy for deficiency diseases are being tried throughout medicine for monogenic diseases and seem poised for clinical application in dermatology. Methods to regulate gene expression and to target mutant genes have progressed beyond the "proof of principle" stage. What prevents us from applying these technological advances to genetic skin disease?

a. Do we have adequate preclinical models? Are they necessary?

b. Do we have adequate clinical measures of efficacy to evaluate response? Do we have a cadre of trained clinicians who can negotiate the regulatory hurdles?

c. Are technical issues insurmountable or relative? Delivery? Large-scale production? Toxicity? Immunological reactions?

d. Regulatory requirements and cost of drug development are often tightly linked. Those considerations appear daunting for ultra rare, incurable (but usually not fatal) diseases. Is the risk benefit calculus the same for our diseases as for more common diseases and for drugs intended for much wider distribution? Are there ways of reducing development costs without increasing risk?

I. Problem/Analysis: Describe the Current Condition

- Lack of focus and structure - Too many novel approaches, too many therapies, too many diseases. Lack of completion of project
- Technical issues:
  - mechanism of delivery of therapeutics into skin
  - In vivo targeting
  - Defining endpoints in clinical trials
- Access of clinicians to novel therapy – sharing of resources
- Lack of incentives in academia for collaboration between academics
- Lack of funding

II. Approaches/Action

- Early gain of a positive outcome from a human trial
- How to choose what to focus on? Disease based vs. therapeutic based. We choose disease-based.
- Two pilot clinical trials, one for a recessive disorder and one for a dominant disorder. We favored siRNA for AR and protein therapy for AD. However, we recognize a need for animal models and industrial support for GMP and registries.

II. Approaches/Actions:

- How to choose which diseases? Start with either NIH planning grant or an FDA orphan disease grant to put together a consortium of experts to identify key questions for a clinical trial, including -
- Clinical trial experts
- Experts in animal models
- Clinicians
- Coordinator
- Expert in delivery technology
- Patient advocacy groups
- Communication strategy to groups whose disease entity is not focused on in the trial