

Session II Objectives

Considerations for gene-targeted therapies

- Targeting the RNA
 - Delivery approach
 - The safety of chronic expression vs. redosing or regulated expression
- Targeting the DNA
 - Does the delivery modality match the biodistribution goal
 - If not, can you redose?
 - Issues with sustained delivery
 - Editing machinery and immune responses
 - What happens at an editing site?

Considerations for CNS gene therapies

- Fitting the genetics to the therapy
 - Targets
 - Monogenic vs. modifier
- Considerations of delivery
 - The region, the cells, and cross correction
 - For RNAi, e.g., cell autonomous vs. secretion via exosomes
 - For loss of function disorders, taking advantage of cross-correction
 - Are all gene products secreted equally well
 - Are all secreted gene products well tolerated