



Cluster of Excellence

- "From Regenerative Biology to Reconstructive Therapy"



Guest:

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„In vivo genome manipulation using nuclease
encoded chemically modified mRNA“

Freitag, 25. April 2014

Hörsaal N, 14:30 Uhr s.t.

Terminabsprachen für Gespräche mit dem Gast

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Abstract:

The use of Zinc-finger or Transcription activator like effector nucleases (ZFNs/TALENs) to facilitate homologous recombination offers a promising approach to repairing genomic mutations. Importantly, since transient expression of the nuclease is sufficient for the stable modification of the genome, alternative short term delivery approaches become attractive. Here, we describe nuclease-encoding chemically modified messenger RNA (nec-mRNA) as a novel delivery paradigm, which achieves short-bursts of nuclease expression and efficient genome editing *in vivo* when combined with an AAV-encoded repair template. Nec-mRNA/AAV-template delivery generated constitutive production of SP-B protein from the endogenous transgenic locus in a mouse model of SP-B deficiency, with significant improvement in survival. We demonstrate nec-mRNA as a new vector supporting transient delivery of genome-editing nucleases *in vivo*, providing the first report of therapeutic genome editing using ZFNs in the murine lung. These data raise the possibility of utilizing nec-mRNA/AAV combinations for the treatment of other severe inherited lung diseases.