Gene discovery and functional annotation in oncogenesis and cancer therapy: exploiting high-throughput forward and reverse genetics in mice.

Many fundamental processes in oncogenesis can only be studied at the organismal level, which is limited however by the low efficiency or long duration of forward and reverse genetics in mammals. I will describe our efforts to address such limitations by developing genetic tools, models and methodologies for gene discovery and functional genomics in mice.

I will first introduce transposon-platforms that we developed for genome-wide in vivo screening, and will show how we use these tools to systematically uncover molecular principles in various contexts, including tumor evolution, phenotypic diversification, metastatic spread or drug sensitivity.

I will also describe CRISPR-based approaches for somatic gene editing and chromosome engineering in various organs of living mice. Such somatic manipulation of mammalian genomes dramatically shapes our ability to interrogate gene function in organismal contexts and to model disease for preclinical research.

Finally, I will show examples how we combine genome-scale screening, large-scale pharmacogenomics, genome sequencing and systems biology approaches to functionalize cancer genomes.