

Research profile for applicants

Name of DKFZ research division/group:	<i>Division of Molecular Thoracic Oncology (B220)</i>
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Group homepage: <i>Visit this website for further information on current research and recent publications.</i>	<i>https://www.dkfz.de/en/molecular-thoracic-oncology</i>

RESEARCH PROFILE AND PROJECT TOPICS

Non-small cell lung cancer (NSCLC) is one of the most common and deadly cancers worldwide. A significant driver of NSCLC is the fusion between the genes anaplastic lymphoma kinase (ALK) and echinoderm microtubule-associated protein-like 4 (EML4). To date, approximately 15 distinct EML4-ALK fusion variants have been identified, each with unique characteristics affecting their stability, genomic localization, responsiveness to targeted therapies, and implications for prognosis.

Our research is dedicated to unraveling the intricate mechanisms that drive development and progression of these fusion variants. We are particularly interested in how co-occurring genetic alterations, such as the loss of TP53, influence the behavior of these variants and identify new therapeutic targets. Beyond EML4-ALK fusions, our team is exploring other chromosomal rearrangements that contribute to NSCLC pathogenesis, including the effects of Y-chromosome loss, and the role of specific epigenetic regulators such as Kdm5d and Uty in the disease.

To probe these genetic intricacies, we leverage CRISPR/Cas9 gene editing to generate somatically engineered mouse models, enabling the inducible expression of specific gene fusions and the targeted inactivation of genes associated with NSCLC. Our approach integrates cutting-edge techniques, including tailored in vivo tumor models that mimic human disease, organoids derived from mice and patients, and sequential gene perturbation assays conducted in vivo. This comprehensive methodology not only replicates the histopathological and molecular characteristics observed in human lung cancer but also provides a powerful platform for dissecting NSCLC's molecular drivers and developing groundbreaking treatment options.



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