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Boosting immunotherapy in non-small cell lung cancer

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Lung cancer is the leading cause of cancer-related deaths. Introduction of immunotherapy improved patient outcomes, but it often fails to provide long-term remission. Triggering inflammatory cell death in cancer cells, thereby altering the tumor immune microenvironment (TIM) may be a strategy to boost immunotherapy response.

Plasma membrane rupture (PMR) is the final event of lytic forms of cell death which are associated with damage-associated molecular patterns (DAMPs) release, propagating inflammation and subsequently influencing the TIM. Recent studies identified Ninjurin 1 (NINJ1) as a key mediator of PMR. NINJ1 de-regulation was implicated in different cancers, but its role in lung cancer is not well-understood.

Hence, this proposal aims to is to comprehensively characterize the role of NINJ1 in lung cancer and subsequently identify molecular mechanisms controlling immune cell evasion of lung cancer cells by using a state-of-the-art CRISPR-Cas9-based model system both *in vitro* and *in vivo*.

This allows us to elucidate the molecular processes controlling inflammatory cell death execution in lung adenocarcinoma *in vivo* with to-date unrivalled precision and speed. The data generated from this proposal will directly feed into understanding the relevance of inflammatory cell death in one of the most prevalent cancer entities and, in addition, aid in the urgently needed development of new treatment strategies to improve immune therapy in lung cancer patients.