Development of mRNA Therapy to support TIL-therapy

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Background: Immunotherapies such as immune checkpoint inhibitors have revolutionized cancer treatment, however, for patients that do not respond to those therapies the options are still limited. Tumor Infiltrating Lymphocyte (TIL)-therapy has shown some promise in patients with melanoma. In this therapy TILs are isolated from the patient, expanded in the laboratory in presence of IL-2, resulting in high numbers of T-cells which are then given back to the patient. During treatment the patient is injected intravenously with high doses of IL-2, a cytokine that supports the survival and proliferation of the TILs but also is associated with systemic toxic side effects. Our goal is to use mRNA therapy to achieve local IL-2 production at the tumor site. We believe that this localized production of IL-2 will support the TILs at the tumor site leading to increased effectivity and reduced toxicity. Method: We synthesize IL-2 mRNA variants which are packaged into Lipid nanoparticles (LNPs). Those LNPs are then tested in vitro and in vivo on PDX mice models to study if they can support TIL-mediated tumor elimination. If shown successful in mice the treatment will be tested in companion dogs with cancer before entering human trials. Results: Our preliminary data shows that IL-2 protein can be expressed from our mRNA LNPs, that this IL-2 can support proliferation of TILs as well as TIL-mediated tumor killing in vitro. Further we show that by administrating our IL-2 mRNA LNPs in NOG-PDX mice models, we can achieve reduced tumor growth with TIL-therapy. Conclusion: In conclusion our goal is to use mRNA therapy to deliver tumor localized IL-2 for supporting TIL therapy. By supporting the TILs at the tumor site, we hope to achieve more durable responses and reduce side effects from TIL-therapy, thereby making this treatment more effective