Background: Gene-fusion genetic aberrations present unique challenges in cancer diagnosis and management. Current treatment strategies often yield low efficiency due to their non-specific targets leading to adverse side effects. Personalized immunotherapies targeting these genetic aberrations can potentially improve therapeutic outcomes. We proposed to create messenger RNA nanoparticles designed to target fusion-driven malignancies, aiming to enhance treatment specificity and minimize classic immunotherapeutic adverse effects.

Methods: We are developing a pipeline to identify gene-fusions, design amplification primers, and classify fusions for treatment using messenger RNA nanoparticles cancer vaccine. The immunogenicity and safety of this approach are to be evaluated using murine models and spontaneous canine and feline tumors.

Results: We demonstrated the synthesis of fusion-specific mRNA and identified common fusion breakpoints in various tumor types, such as Ewing sarcoma, glioblastoma, ependymoma, non-small cell lung carcinoma, and clear cell sarcoma. Importantly, we established two primary approaches for our fusion-based messenger RNA nanoparticles: 1) off-the-shelf gene-fusion immunotherapy vaccines, and 2) personalized vaccines developed for rare fusions.

Conclusions: Preliminary findings suggest that our formulation can target gene fusions with potentially improved treatment.

REFERENCES:

Ethics Approval: All animal experiments were conducted following protocols approved by the Institutional Animal Care and Use Committee at the University of Florida (protocol number 202009685).

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