

# **RNA PRIME—Harnessing tumor RNA for Immunotherapy against Osteosarcoma**

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# Disclosures

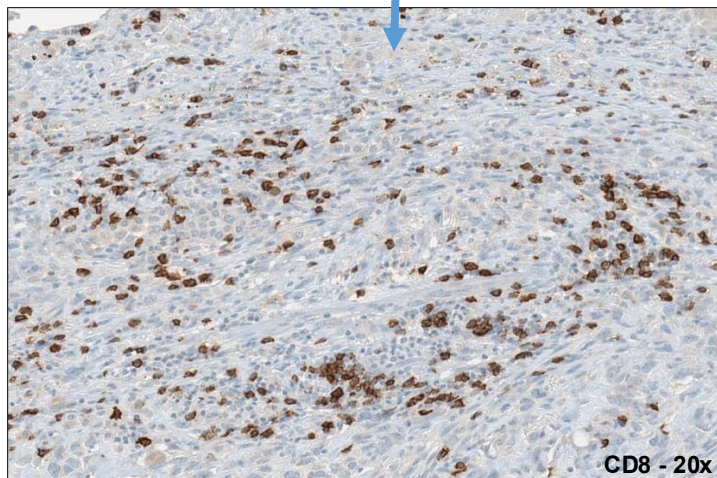
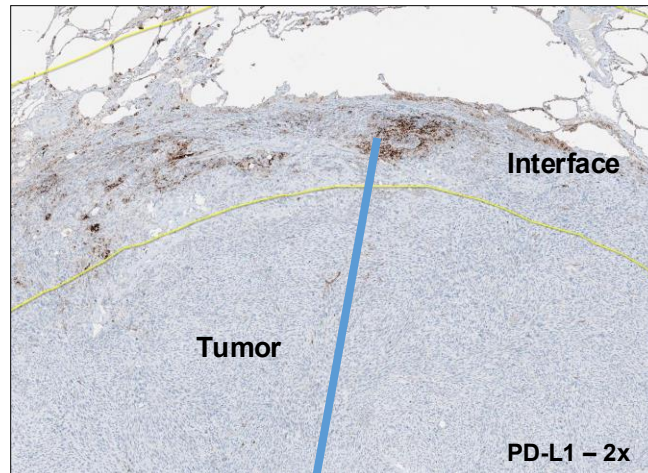
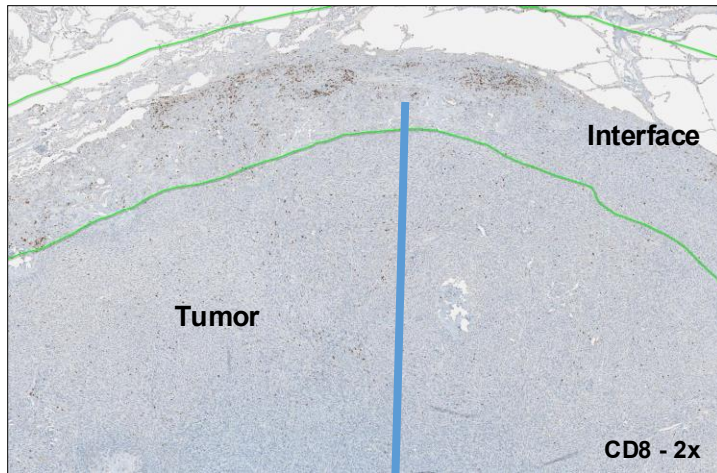
- I am discussing an investigational agent that is in phase I clinical trials.

# CHALLENGES IN PEDIATRIC CANCER IMMUNOTHERAPY

- Diversity of tumors
- Antigenic heterogeneity
- Low mutational burden
- Immunosuppressive TME

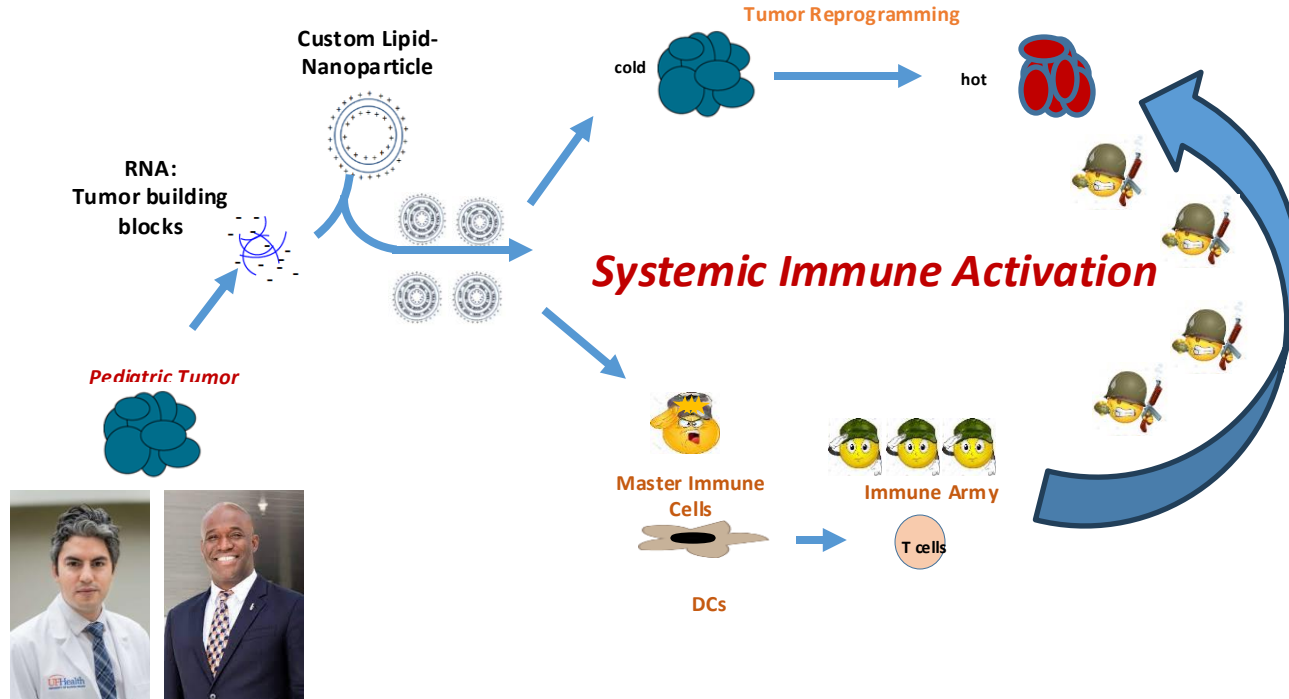


# Osteosarcoma PM—immune-excluded, tumor-normal lung interface



Focal PD-L1 expression,  
“**shield**” against immune  
attack

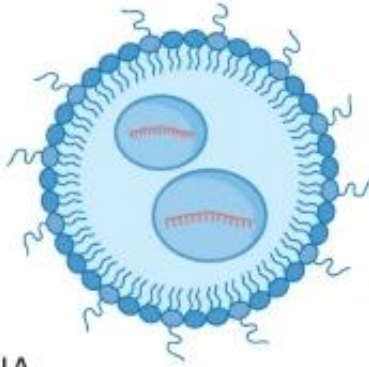
# RNA Lipid nanoparticle aggregate (RNA-LPA): Training the body to recognize cancer



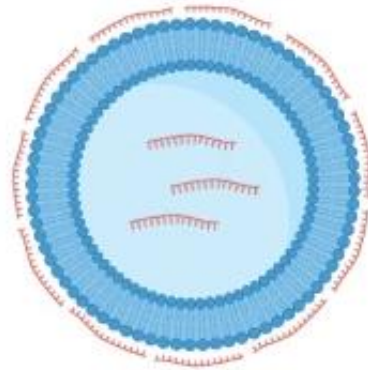
# RNA lipid nanoparticle aggregates (RNA-LPA)



Protamine-mRNA  
complex



RNA-LNP

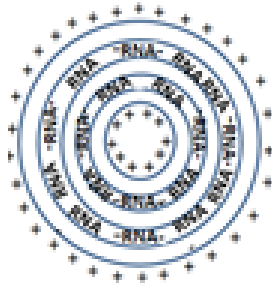


Anionic RNA-LPX



ML RNA-LPA

**By layering mRNA into multi-lamellar nanoparticles we can package more payload for enhanced immunity**



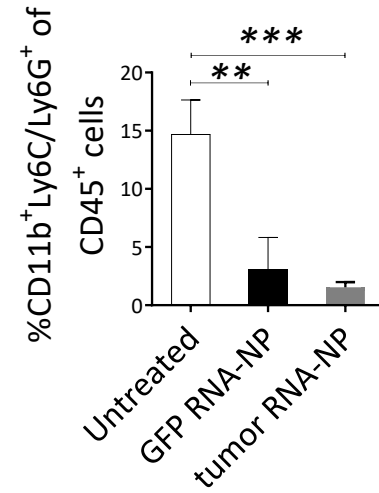
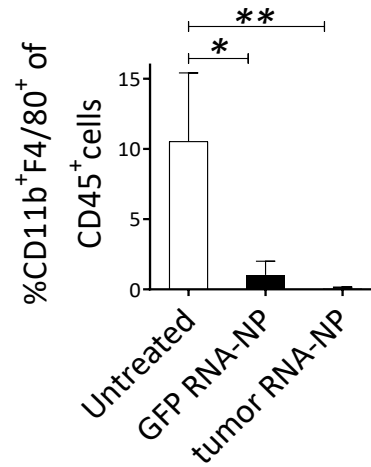
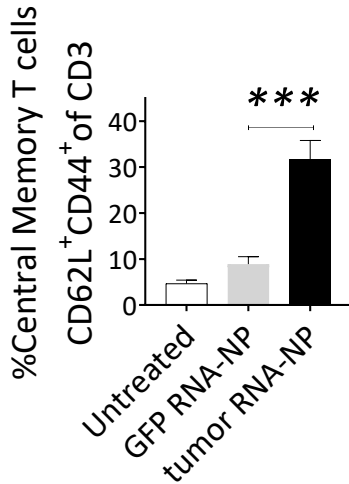
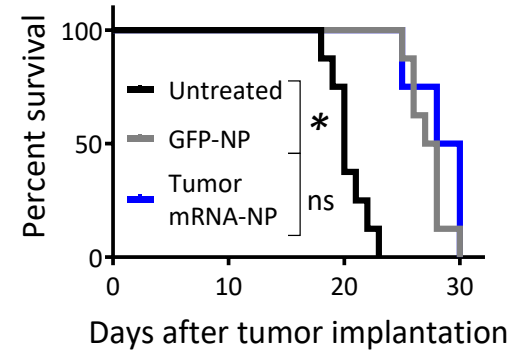
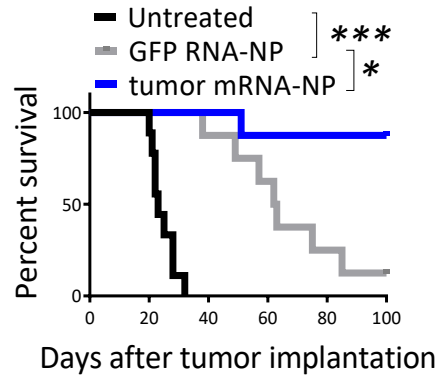
<https://sergiospizzafactory.com/product/onion/>



*PCT/US19/50850, PCT/US19/46618, PCT/US19/31385 and U.S. Patent Application No. 62/842,525, 62/877,598, and 62/970,646.*

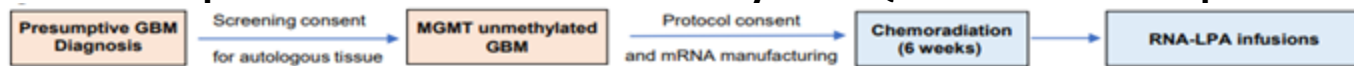


# RNA-NPs reprogram pulmonary OS microenvironment

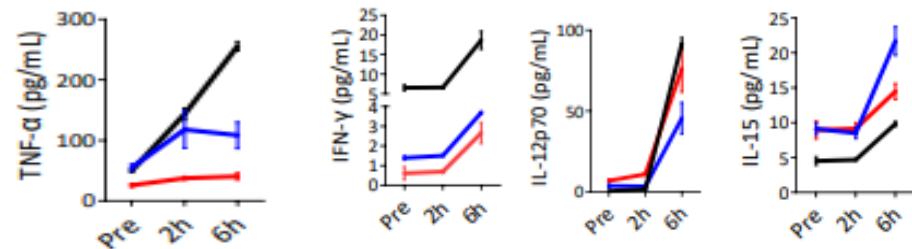




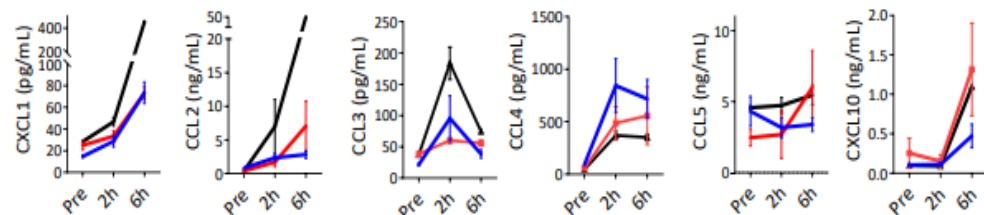
# RNA-nanoparticles activate the immune system QUICKLY in human patients



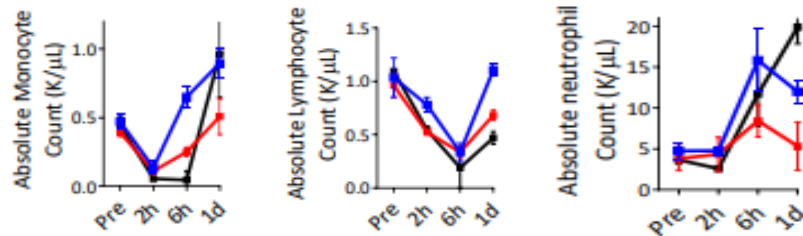
## Cytokines



## Chemokines



## Blood Counts



Mendez-Gomez\*, DeVries\*, Castillo\* ... Sayour. Cell. 2024

# RNA PRIME

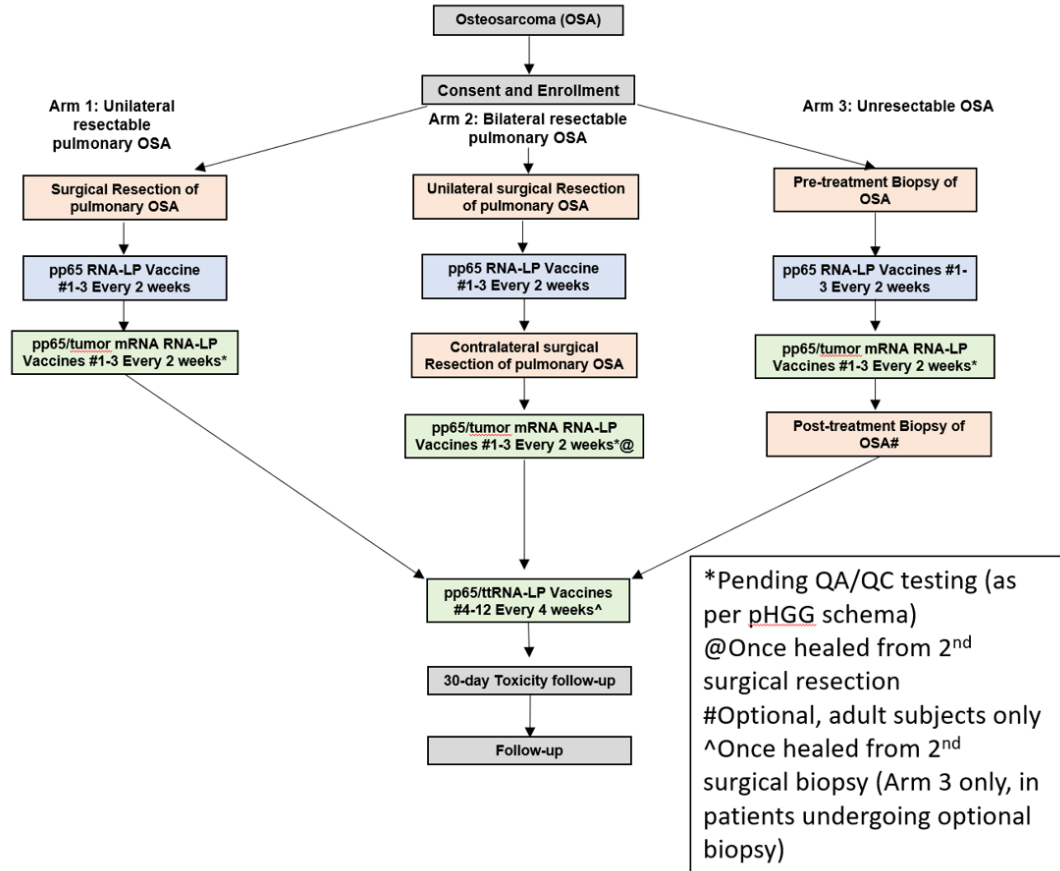


Title: RNA lipid particles targeting  
Pediatric Recurrent Intracranial  
Malignancies and other systEmic solid  
tumors

First two cohorts: Relapsed peds high grade glioma (pHGG) and  
osteosarcoma (OSA)



# RNA PRIME: Relapsed Osteosarcoma



### Key Inclusion (OSA):

- Age  $\leq$  39 years
- For OSA diagnosis of relapse must be histopathologically confirmed following resection/biopsy. Must be eligible for thoracotomy (Arms 1 and 2 only)
- Washout from prior treatments, in particular no greater than physiologic steroids within 14d of enrollment and stable neuro status.
- ANC > 1000, platelets > 100,000, Hb > 8 (no ALC), **and must return to these levels prior to surgery and prior to subsequent vaccines**
- Patients with pHGG must be willing to take an antiepileptic medication such as levetiracetam

# Translational Studies—Next iterations

**Between the UF College of Medicine and College of Veterinary Medicine**  
IACUC approved study evaluating toxicity, efficacy and immunologic responses of RNA-nanoparticle combinations targeting canine brain and osteosarcomas (UF IACUC Protocols: 201609430 and 201710053)—**Funded by MIB Agents**



Currently testing combination of RNA-LPA + radiation + canine anti-PD-1: 4 dogs living >4 months (median overall survival for canine OSA) **without surgical local control or new evidence of disease.**



## Ligon lab

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## UF RNA Engineering Lab Members

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