



OrbiMed
Healthcare Fund Management

Session 1: State of the Art of RNA Technologies

Industry Perspective

Tal Zaks, MD, PhD

Partner, OrbiMed Advisors

Disclosures

- OrbiMed: Employee (equity)
- Teva Pharmaceuticals: Non-Executive Director (fees, equity)
- Adaptimmune: Non-Executive Director (fees, equity)
- PIC Therapeutics, Non-Executive Director
- ieCure, Non-Executive Director

People also ask :

What are the three steps of the Socratic method?

The Socratic Method is a way of thinking that involves three steps:

- Give an initial definition or opinion.
- Ask a question that raises an exception to that definition or opinion.
- Give a better definition or opinion.

Are “RNA medicines” a third pharmaceutical class distinct enough from NCEs and Biologics?

Regulatory Enablers of Translating Science into Medicine

- Science-based consistency in expectations

→ Predictability in what we do

How long should a patient be followed to define safety? What should be pre-approval and what can be later?

- Harmonization across geographies

→ Efficiency in what we do

Global trials are more efficient for everyone; but politics – and genetics – are local...

- Communication and language

→ Having our stakeholders understand what we do.

The layman's understanding of “gene” therapy ≠ regulatory use



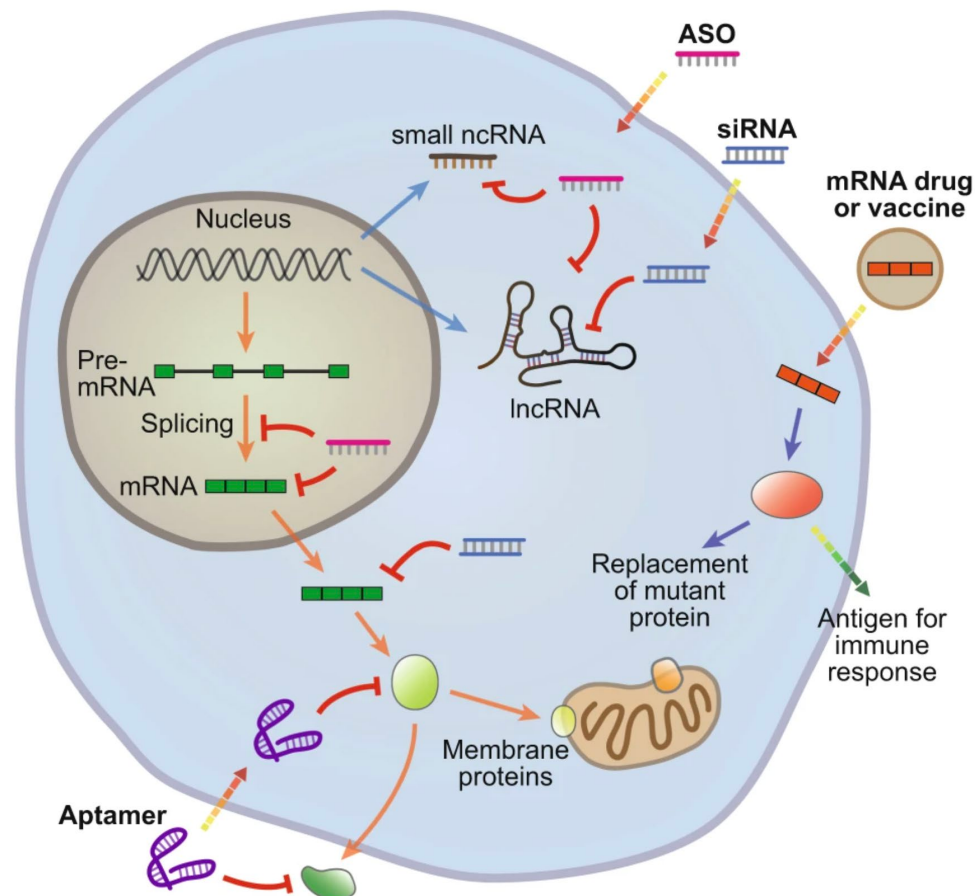
RNA therapy: rich history, various applications and unlimited future prospects

Young-Kook Kim 

Experimental & Molecular Medicine 54

Fig. 2: Diverse cellular molecules can be targeted by RNA therapy.

From: [RNA therapy: rich history, various applications and unlimited future prospects](#)



Is benefit / risk driven by:

- Sequence vs. composition?
- Payload vs. delivery vehicle?

RNA Medicines as a Class: Defining Risk vs. Benefit

- Emerging technologies do not fit neatly into categories
 - ▶ How would we think about a synthetically derived mRNA?
 - ▶ How would we think about a short guide-RNA that would “fix” a mutated RNA?
- Should the nucleic acid make-up (and its source) drive the definition or should the MOA?
 - ▶ Is there a scientific basis for a replicative effect that will be propagated over time (whether intended or unintended)? Implications for geographic inconsistencies?
- What and when would we consider a technology a platform?
 - ▶ How does benefit-risk translate from preclinical to clinical?
Should we better codify when and when not is the use of NHPs warranted?
 - ▶ How does benefit-risk translate from product to product? Does it alter the definition of a product?
 - ▶ How does benefit-risk translate from pre-approval to post-approval?
Do we need to be more consistent in expectations for RWE?

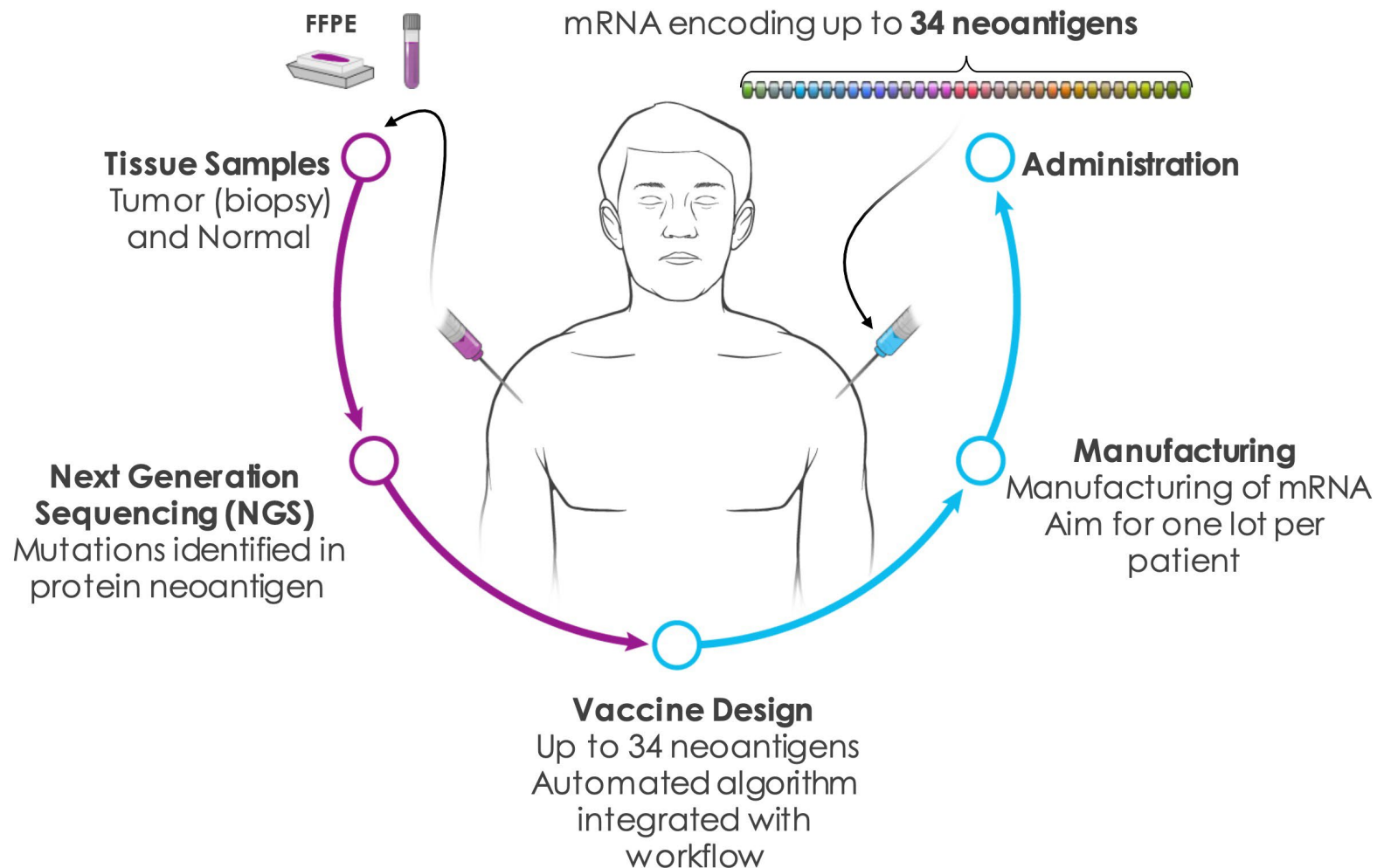
RNA Platforms

- What safety or benefit is inherent to the composition vs. the sequence-effect? If we can isolate them, can we be wiser about their clinical application?
 - ▶ Shared “platform” safety risks: infusion-related reactions of LNPs; ASOs and ↓PLTs
 - ▶ Shared “platform” safety benefits: lack of mRNA integration

Do we need QTc prolongation studies? What are the relevant “special populations”?
Approach to pediatrics?

- If we can consider some classes a “platform”, how can this be leveraged to benefit patients with the same (rare) disease but different mutations? Different HLAs?

The Case of a Therapeutic Personalized Cancer Vaccine



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Dictionary

Definition

Example Sentences

Word History

Phrases Containing

Entries Near

gene noun

'jēn 

plural genes

: a specific sequence of [nucleotides](#) in [DNA](#) or [RNA](#) that is located usually on a [chromosome](#) and that is the functional unit of inheritance controlling the transmission and expression of one or more traits by specifying the structure of a particular [polypeptide](#) and especially a protein or controlling the function of other genetic material

REUTERS FACT CHECK APRIL 8, 2021 / 5:10 AM / UPDATED 2 YEARS AGO

Fact Check-Moderna's chief medical officer did not say mRNA vaccines alter DNA

By Reuters Fact Check

7 MIN READ



Social media users have been sharing articles that claim Moderna's chief medical officer Tal Zaks has said mRNA vaccines – like the Moderna vaccine for COVID-19 – alter DNA. This claim is false. It is based on comments made by Zaks that have been misconstrued, and Reuters has found no evidence of him making any such comments elsewhere.

Thank you

Q&A