

Hot Topic Discussion

The rise of RNA Nanotherapeutics: Current Trends & Future Challenges

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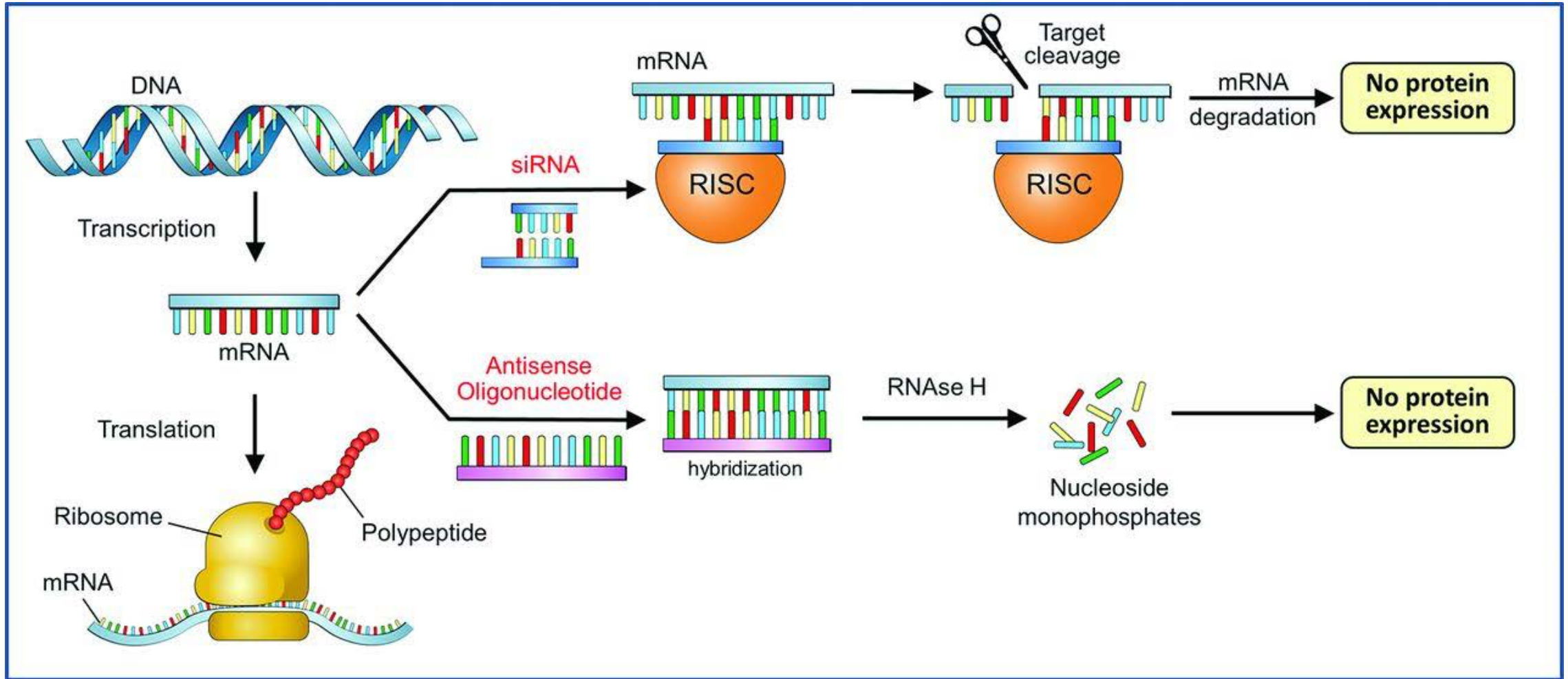
MARBLE
CENTER
FOR **CANCER
NANOMEDICINE**
Small technologies, **BIG** impact

Convergence 
Scholars Program

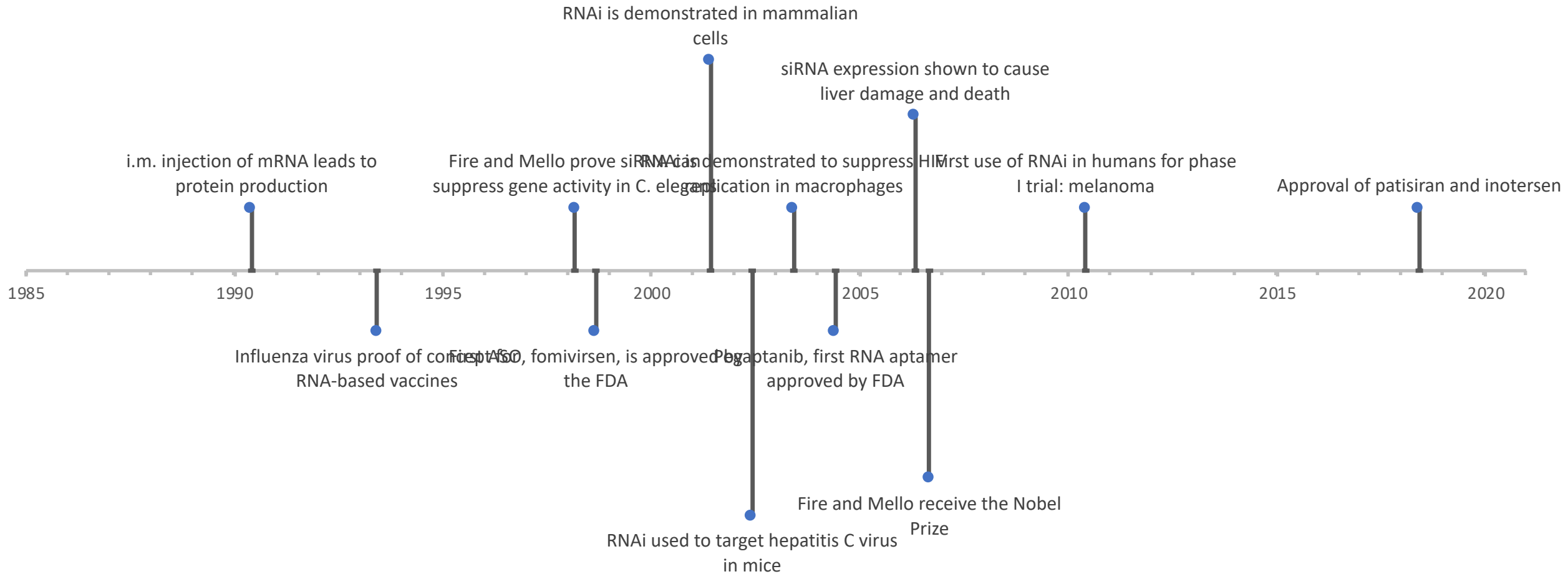


KOCH INSTITUTE
for Integrative Cancer Research at MIT

What are RNA therapeutics?



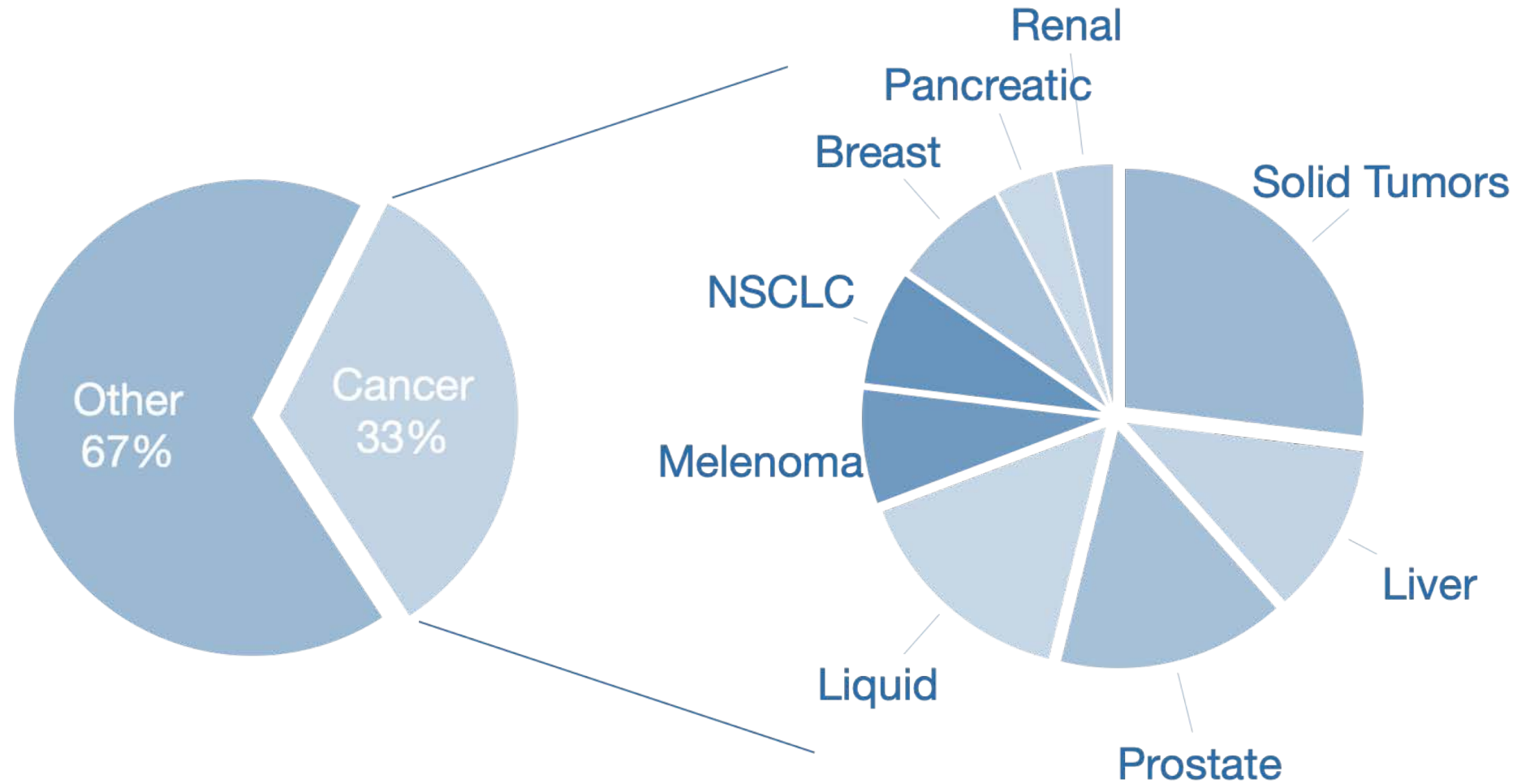
RNA therapeutics: a brief history



Commercial Landscape for RNA therapies for Cancer - \$41B in capita



Cancer RNA therapeutics are on the rise



Current Technologies used for RNA delivery

Delivery vehicle	Type of RNA in clinical trials	Advantages	Disadvantages
Naked RNA	siRNA, ASO, mRNA	No additional materials or synthesis required	Prone to degradation Immunogenic Difficulty entering cell Poor circulation half-life
Nanoparticle	siRNA, ASO, mRNA	Increased half life Protection from nucleases Aids in endocytosis and endosomal escape	Elevated risk of toxicity with introducing excipient materials
Conjugate	siRNA, ASO	Defined chemical structure Ability to target specific receptors Limited toxicity due to lack of excipient materials	High doses required Dependent on chemical modifications for RNA stability

Inorganic

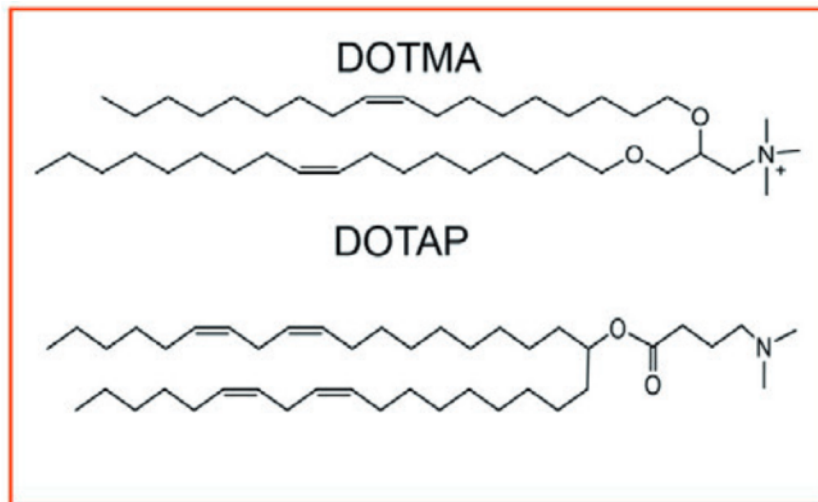
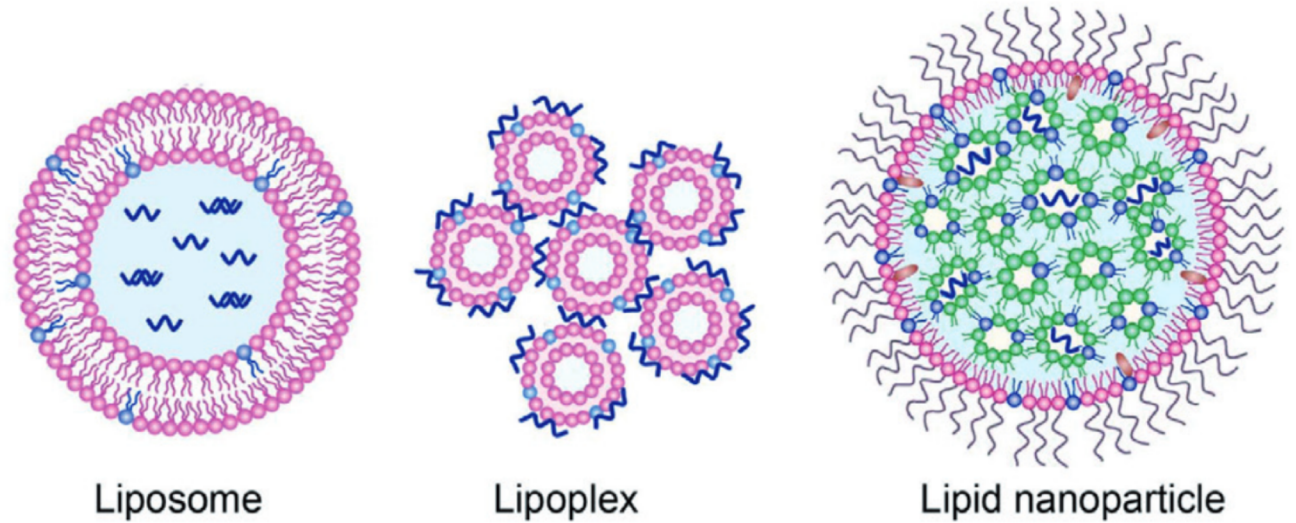
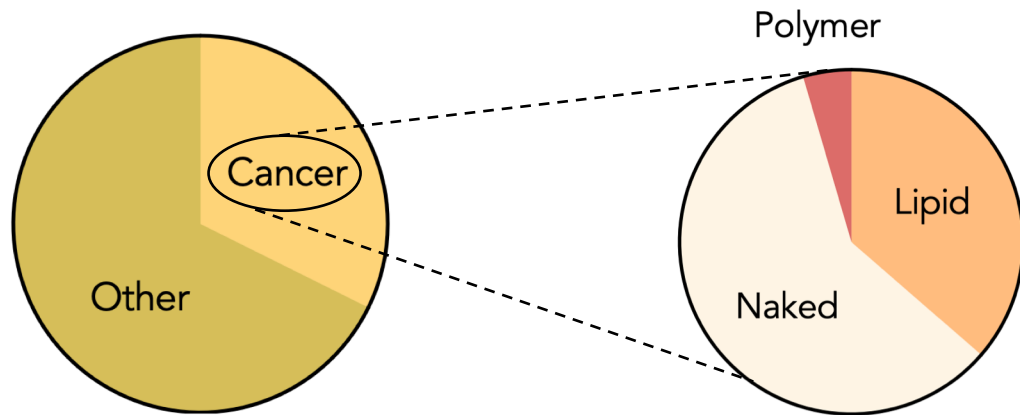


Organic

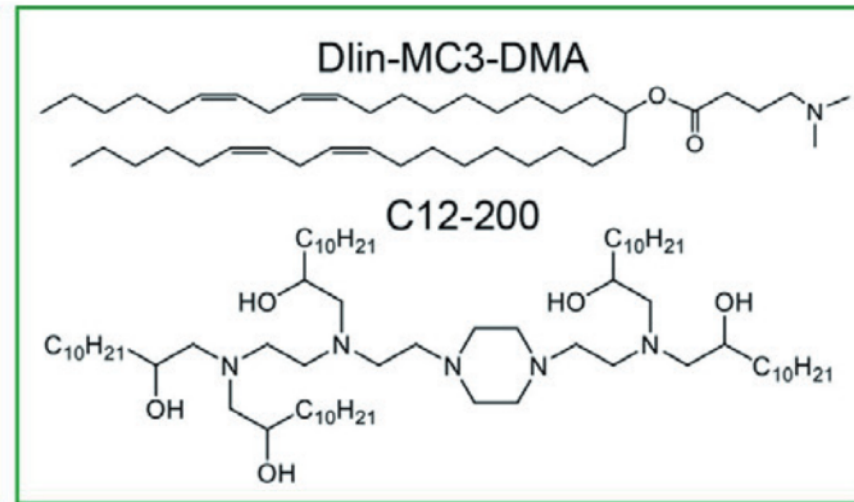


Current Technologies used for RNA delivery

Clinical Trials

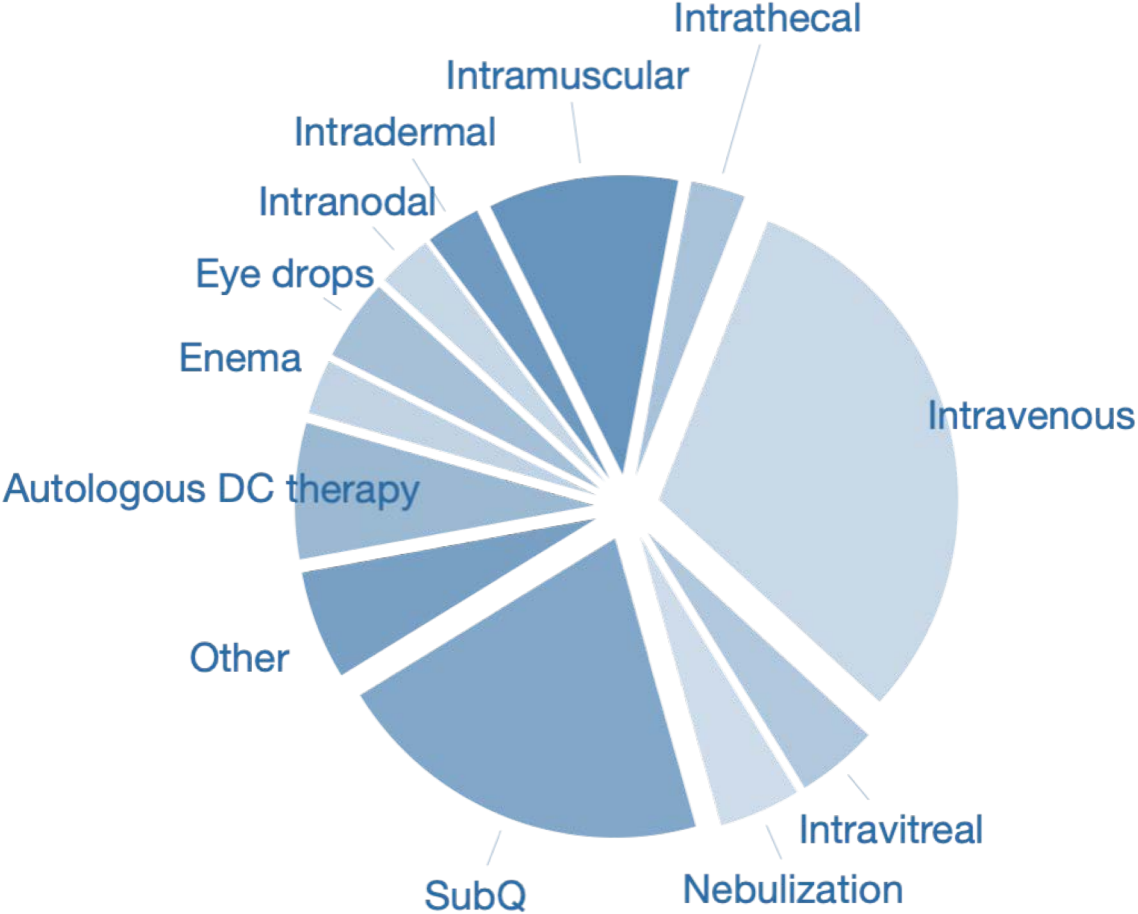


Cationic lipids

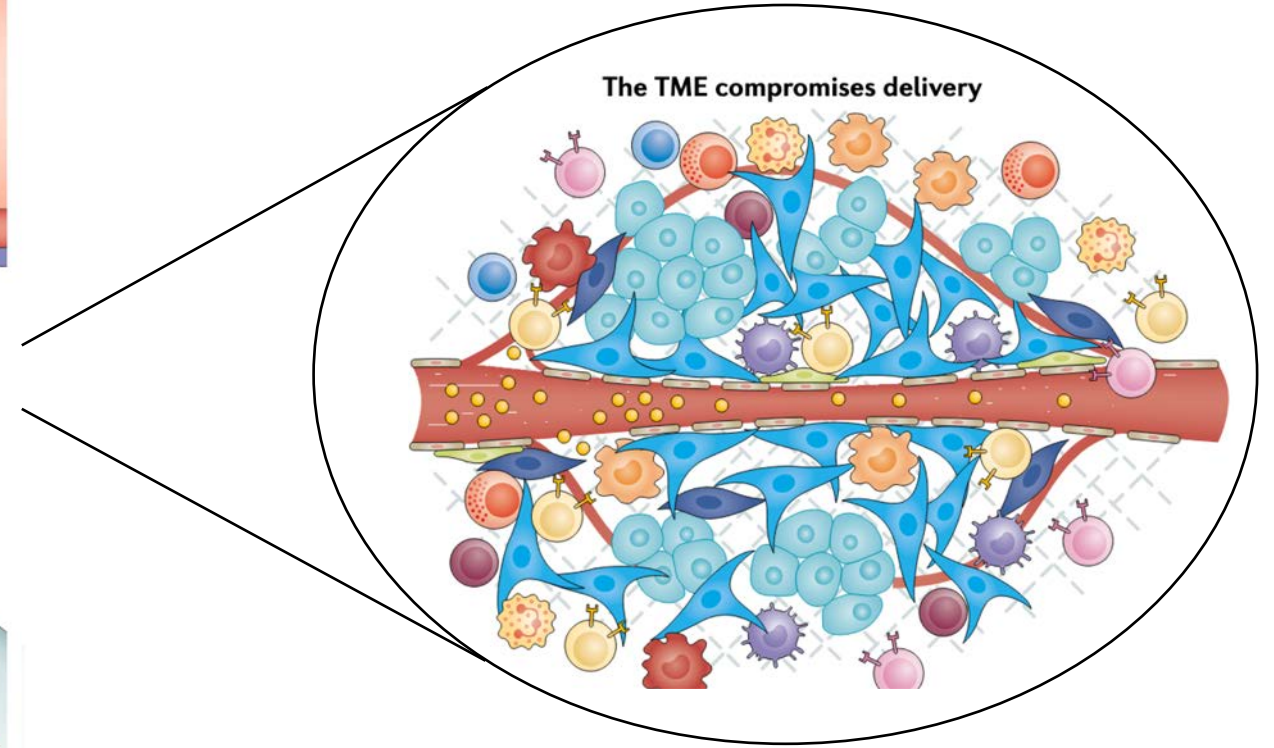
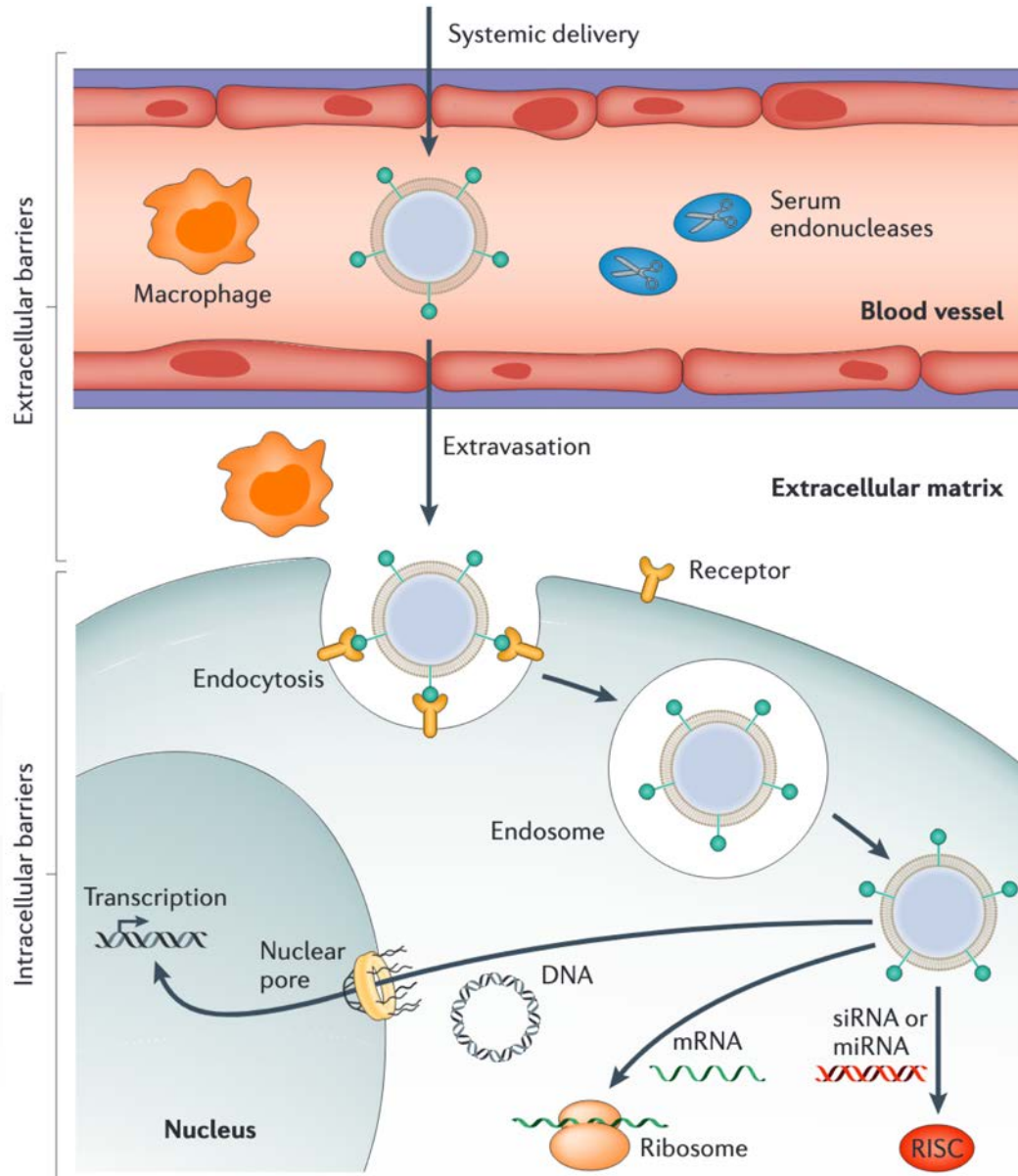


New generation ionizable lipids

Routes of administration for RNA delivery



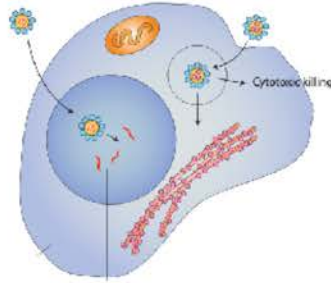
The Challenges of RNA Delivery



clearance + targeting
+ penetration

Approaches to address challenges in RNA Delivery

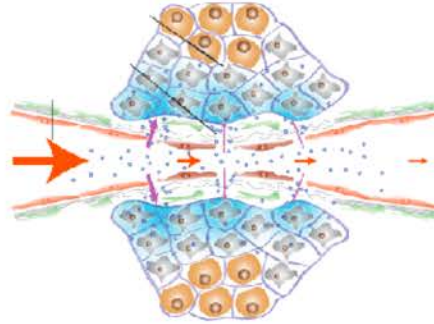
intracellular
barriers



membrane
penetrating

endosomal
escape

extracellular
barriers

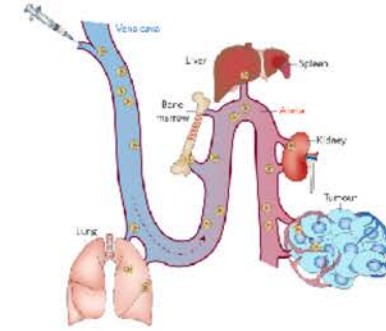


active
targeting

particle
size/shape

TME
normalization

systemic
barriers







stealth
nanoparticles

differential
organ targeting

nanoprimering

What needs to happen for RNA delivery to make a difference in oncology?

-  Delivery vehicle improvement
-  Scale up challenges
-  Patient stratification
-  Other challenges?