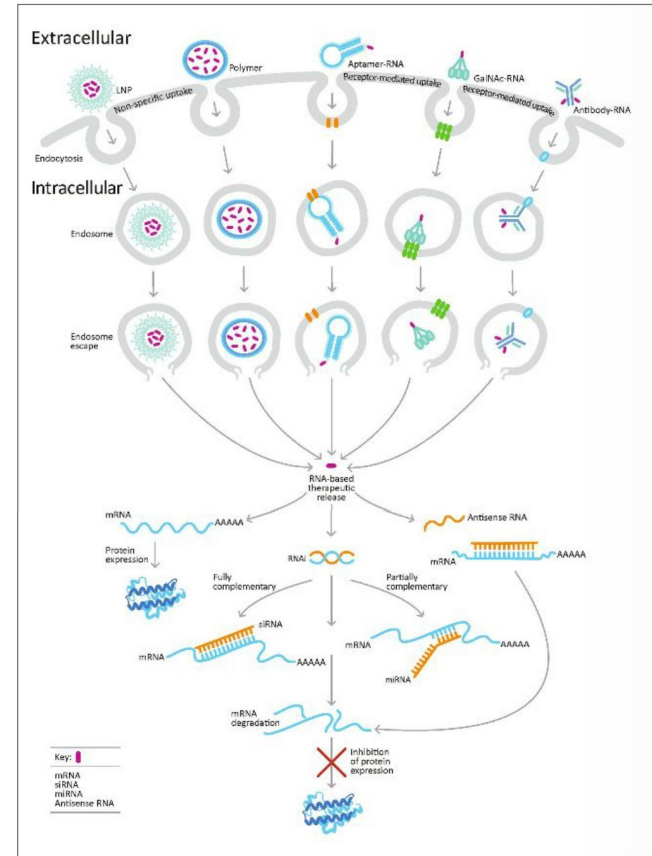

***In Vitro* Reconstituted Plant Virus Capsids for
Delivering RNA Genes to Mammalian Cells**

Case: 2014-111

Executive Summary

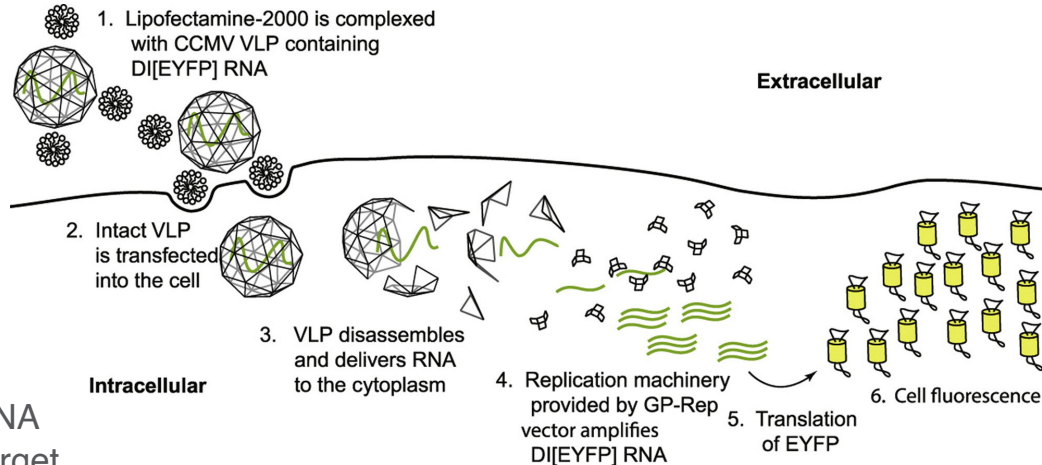
High Level Overview

- RNA viruses are a largely untapped resource
- RNA viruses have many uses including
 - Forming therapeutic proteins
 - Modifying DNA, RNA, and protein already found in the cell
- The development of RNA-based drugs faces a few challenges
 - RNase enzymes present in cells degrade RNA
 - Inefficient targeting of the RNA to cells of interest
 - Limited expression of RNA



Technology Overview

Cowpea chlorotic mottle virus (CCMV) capsid proteins have the unique ability to spontaneously **self-assemble** around RNA molecules of widely varying length and sequence.



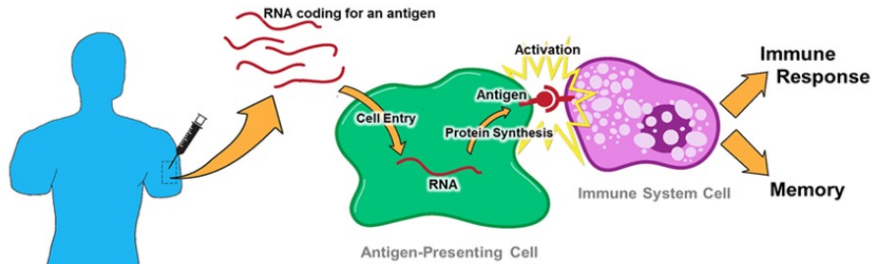
RNA in these nucleocapsids are **protected from degradation** and are able to release the RNA in the cytoplasm of target mammalian cells.

Ligands attached to the viral capsid can **target** cells of interest

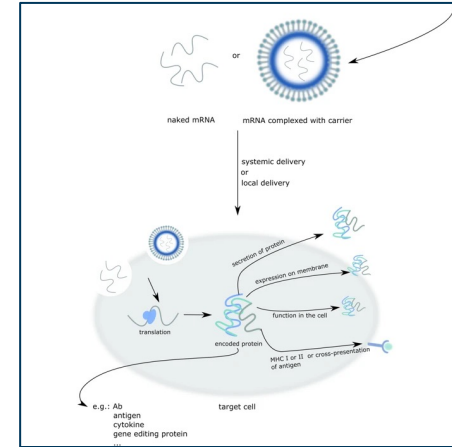
The RNA is **self-replicating**, leading to high gene expression

Potential Applications of Invention

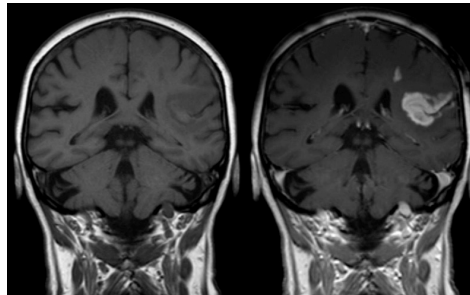
1. Targeted delivery of vaccines



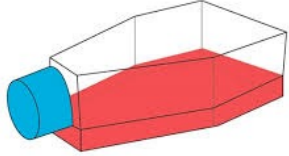
3. Therapeutic proteins in RNA form



2. MRI contrast imaging

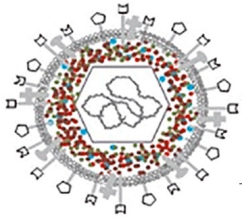


Advantages of Invention



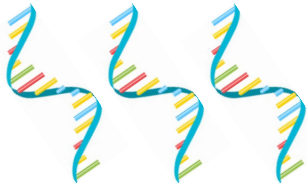
No costly cell culture

Using a capsid of a self-assembling plant does not require cell culture



Targeting

An RNA virus can be targeted by addition of ligand on capsid protein

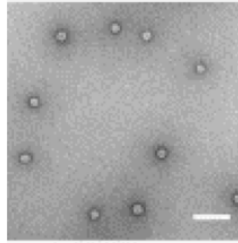


High Expression

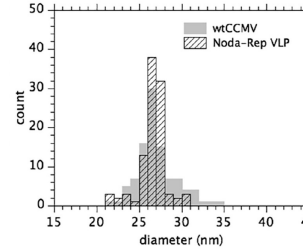
Self-replicating RNA allow for high expression in mammalian cells

Developmental Timeline of Technology

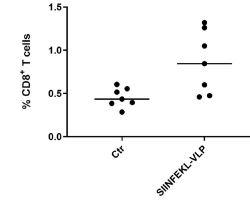
Dec 2009:
Initial
Conception



Virus-like particles have
size distributions similar
to CCMV viruses

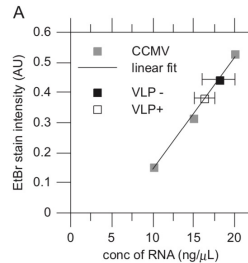


RNA within virus-like particles
are protected from RNases

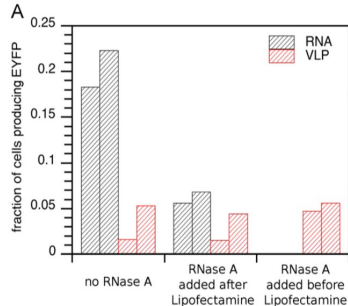


A packaged mRNA vaccine
increased CD8+ positive mouse
spleen cells

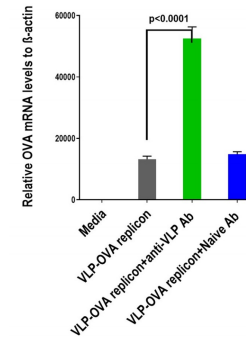
Virus-like particles have
a RNA carrying capacity
of ~18 ng/uL



Virus-like particles
release RNA in the
cytoplasm



Pre-incubation of virus-like
particles with antibodies
enhances RNA uptake



Market Opportunity

Market Overview: Gene Therapy Market

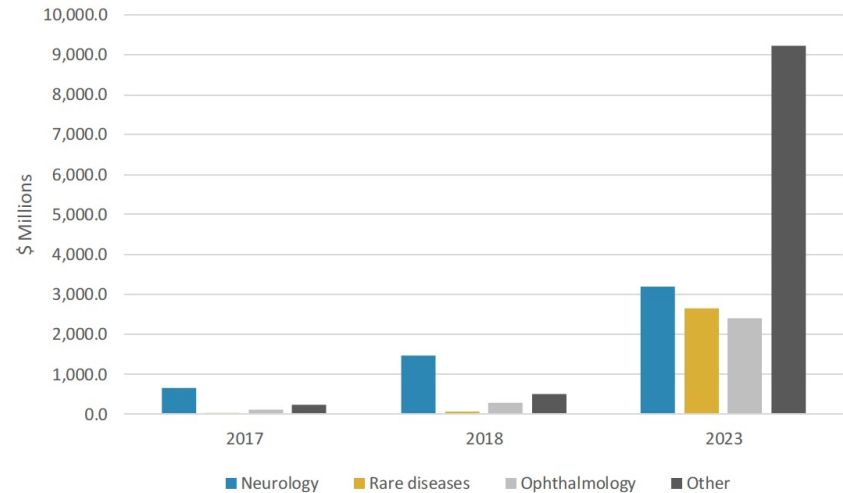
Since this therapeutic involves introducing genetic material into a cell, the market will be considered the genetic modification therapies market.

- Global Market - \$2.3 billion in 2018
- Forecasted to reach \$17.4 billion by 2023
- CAGR of 49.9% by 2023

There are three main gene therapy treatments currently utilized:

- DNA viruses (including AAV vector and lentivirus)
- Lipid-based RNA
- Nanoparticle-associated RNA

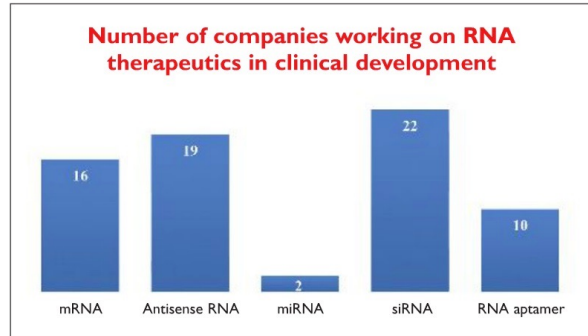
Global Market for Genetic Modification Therapies
2017-2023



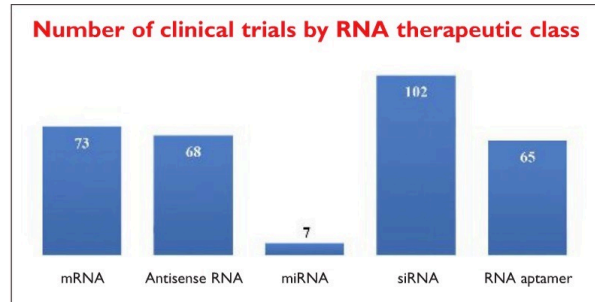
Competition to Invention

| Competition Type | Expression | Safety | Targeting | Ease of Production |
|------------------------|------------|--------|-----------|--------------------|
| Plant Virus | HIGH | HIGH | ✓ | HIGH |
| DNA virus | HIGH | LOW | ✓ | LOW |
| Lipid-based RNA | LOW | HIGH | ✗ | HIGH |
| Nanoparticle-based RNA | LOW | MEDIUM | ✓ | MEDIUM |

Market Stakeholder Profiles



Graph 1: Companies developing RNA-based therapeutics in the clinic (as of July 2018). Data provided by GlobalData Plc



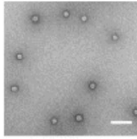
Graph 2: Number of RNA-based therapeutics in clinical trials (as of July 2018). Data provided by GlobalData Plc

- The industry is highly fragmented, however, each of the three segments in this market is led by a single company. Those companies are Ionis (ASO market segment), Alnylam (RNAi segment) and Moderna (mRNA segment).
- Companies that have clinical stage mRNA projects include Argos (Phase III), CureVac (Phase I, Phase II recently failed), BionTech (Phase II), Moderna (Phase I/II), and eTheRNA (Phase I/II).
- Key applications for mRNA medicines include vaccines, protein replacement and regenerative medicine.

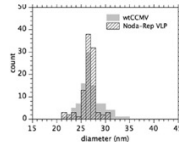
Commercialization Potential

Commercialization

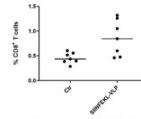
Initial Conception



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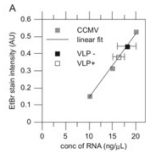


RNA within virus-like particles are protected from RNases

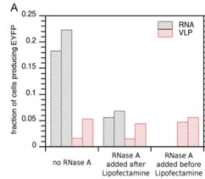


A packaged mRNA vaccine increased CD8+ positive mouse spleen cells

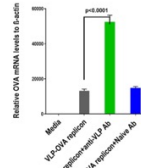
Virus-like particles have a RNA carrying capacity of ~18 ng/uL



Virus-like particles release RNA in the cytoplasm



Pre-incubation of virus-like particles with antibodies enhances RNA uptake



Issued Patent:
US10,221,399

Licensing

UCLA Technology Development Group

Thank You

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