



for the

CANCER
PROGRESS
by Defined Health

Nigel Horscroft D.Phil

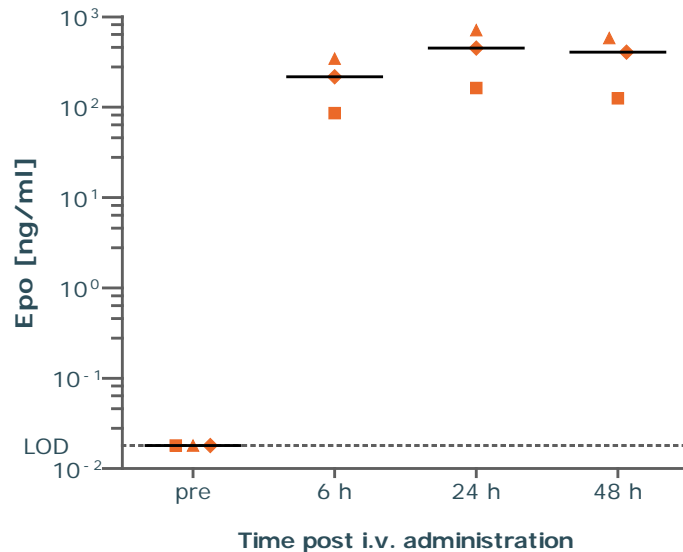
Cancer Progress by Defined Health
New York, NY | March 8-9, 2016



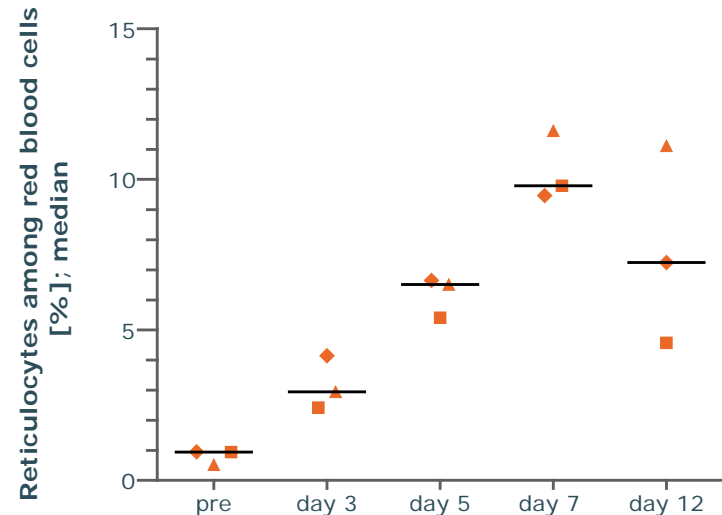
CureVac's mRNA can elicit systemic biological effects in pigs

- Single intravenous dose of formulated Epo mRNA results in high levels of Epo and pronounced biological effects in domestic pigs

Epo expression from CureVac's mRNA



Increase in reticulocytes

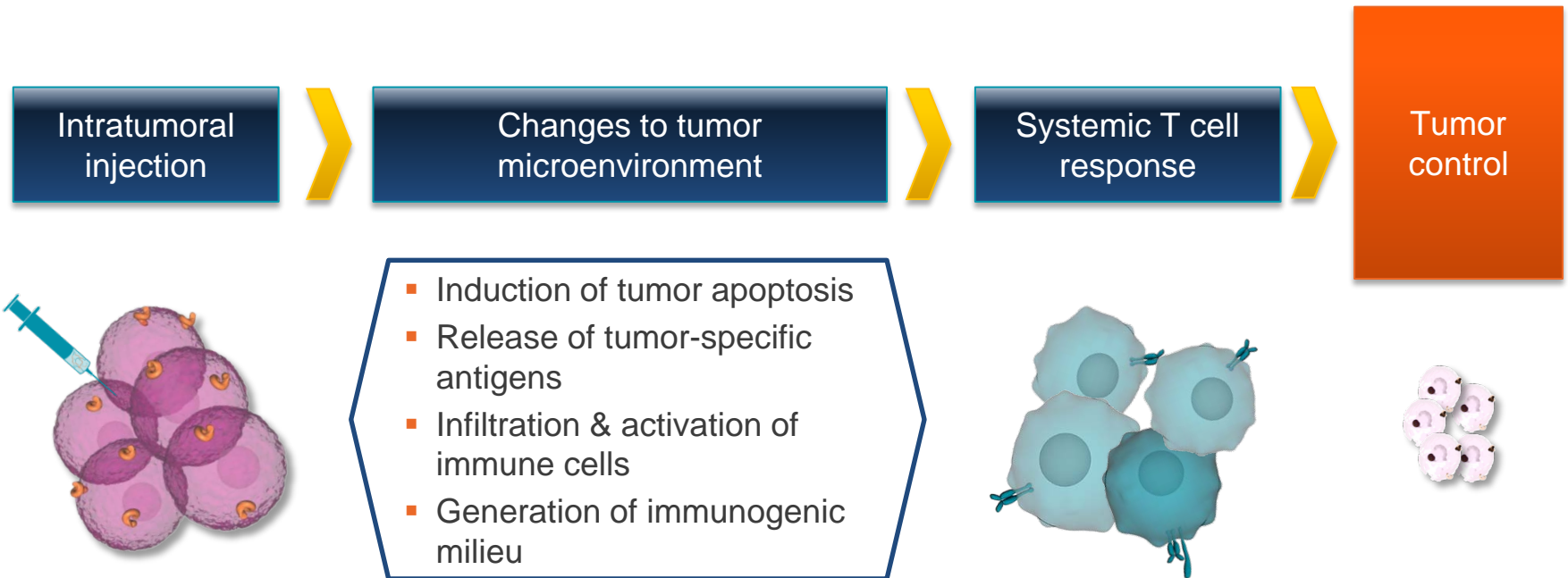


mRNA dose: 1.3 mg corresponds to 0.065 mg/kg
LNPs supplied by Acuitas

Andreas Thess et al: **Sequence-engineered mRNA without chemical nucleoside modifications enables an effective protein therapy in large animals.** *Molecular Therapy*. 2015 Sep;23(9):1456-64.

Intratumoral RNA therapy

From local treatment to systemic memory response:



→ RNA therapy targets multiple pathways to induce a systemic response

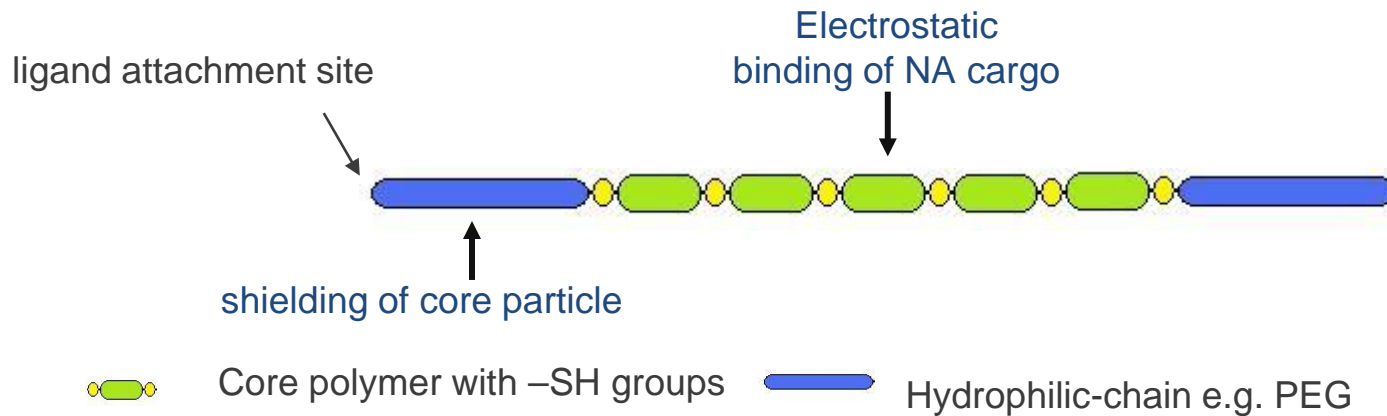
Efficacy of intratumoral mRNA therapy based on multiple targets

- Intratumoral delivery of two targets results in the immediate stagnation of tumor growth followed by a complete tumor eradication in majority of animals
- Mice cured from tumors after intratumoral mRNA therapy are protected against tumor rechallenge



CureVac's Carrier Molecules (CVCMs)

Architecture of CVCMs

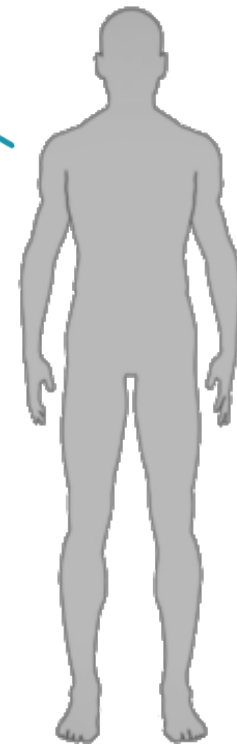


Mode of Action

- Formation of nanoparticles via electrostatic binding of nucleic acid to core polymer
- Cellular uptake via endocytosis
- Fast decomposition of the carrier in reducing environment
- mRNA release into the cytosol

RNAntibody[®] – The body makes its own functional antibodies without vaccination

mRNA can encode any therapeutic antibody

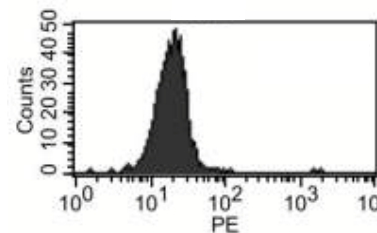
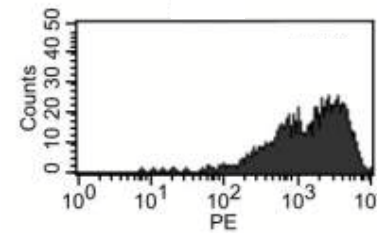
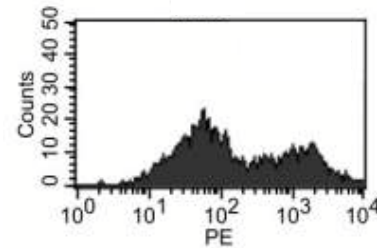
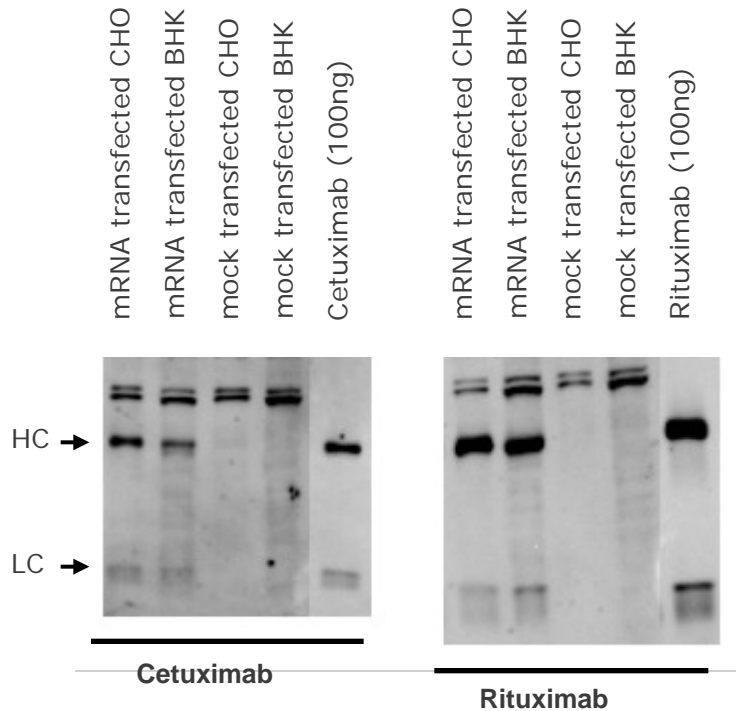


CureVac's mRNA can encode functional antibodies

- Antibodies encoded by mRNA are correctly expressed, secreted and bind specifically to the appropriate target protein

Western Blot analysis of cell lysates

Flow cytometric analysis of supernatants for the presence of target-binding antibodies



Similar data obtained also for Rituximab

In vivo efficacy of mRNA encoded antibodies

- Significantly reduced tumor growth in mice treated with mRNA encoding for Antibody X

Percent survival

median tumor volume [cm³]

RNAntibody[®] protects mice from lethal toxin challenge

- RNAntibody[®] encoding a bi-specific single chain antibody targeting BoNT/A
- Single dose on d-1
- Challenge with 10xLD₅₀ dose of BoNT/A on d0
- Daily monitoring for survival
- VNA-Stx2 = negative control

