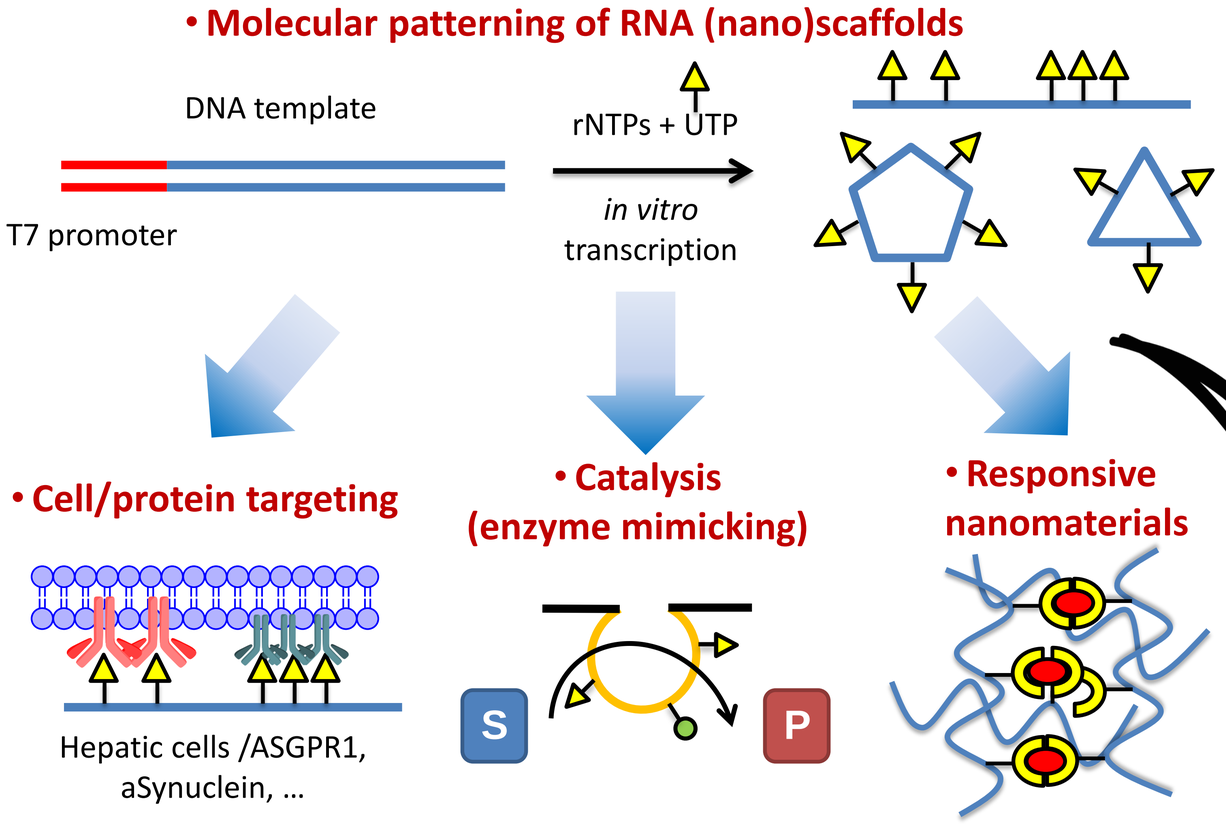
CHEMICALLY MODIFIED RNA FOR SYNTHETIC BIOLOGY AND BIOMEDICINE

Julián Valero

jvalero@inano.au.dk

- **Molecular patterning of RNA (nano)scaffolds**



RNA + CHEMICAL MODIFICATIONS: A WIN-WIN COMBINATION

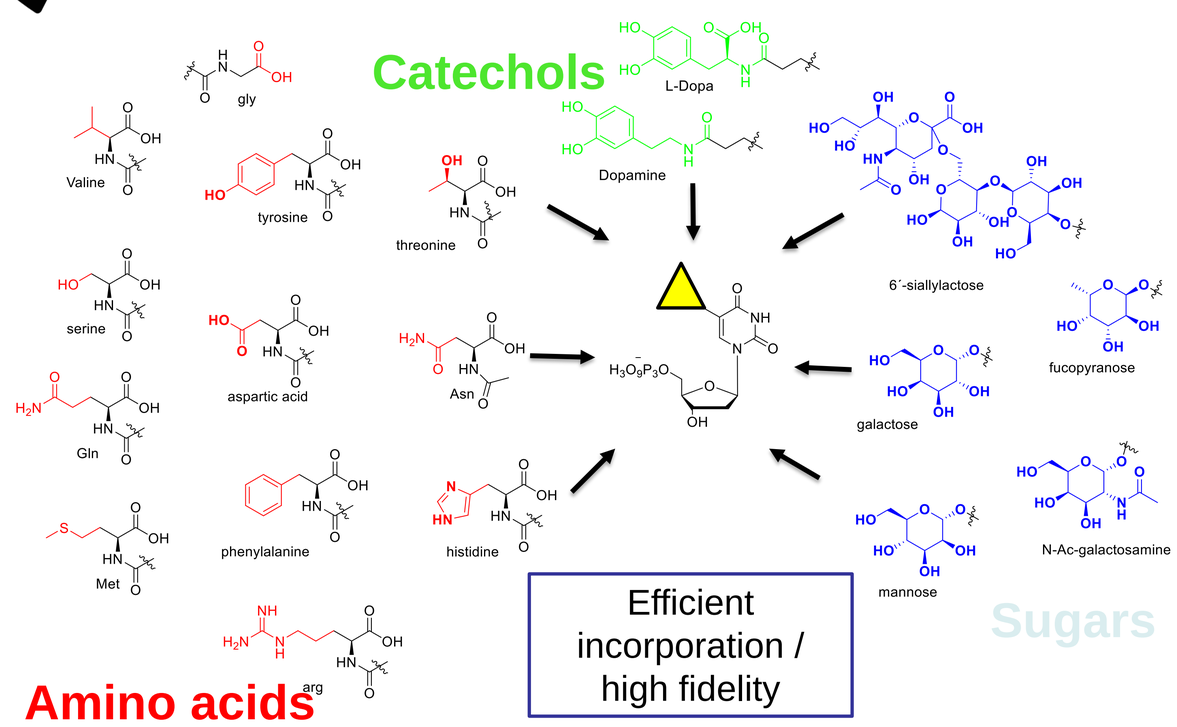
We use RNA to develop a new class of hybrid biomolecules for applications in synthetic biology and biomedicine. Chemically modified RNA displays novel features:

- ✓ Improved binding properties with high specificity for cell/protein targeting.
- ✓ Enhanced reactivity for catalysis (RNAzymes)
- ✓ Stable against degradation
- ✓ Enhanced cell uptake and pharmacokinetics
- ✓ Compatible with *in vitro* evolution

EXPANDING THE RNA LEXICON

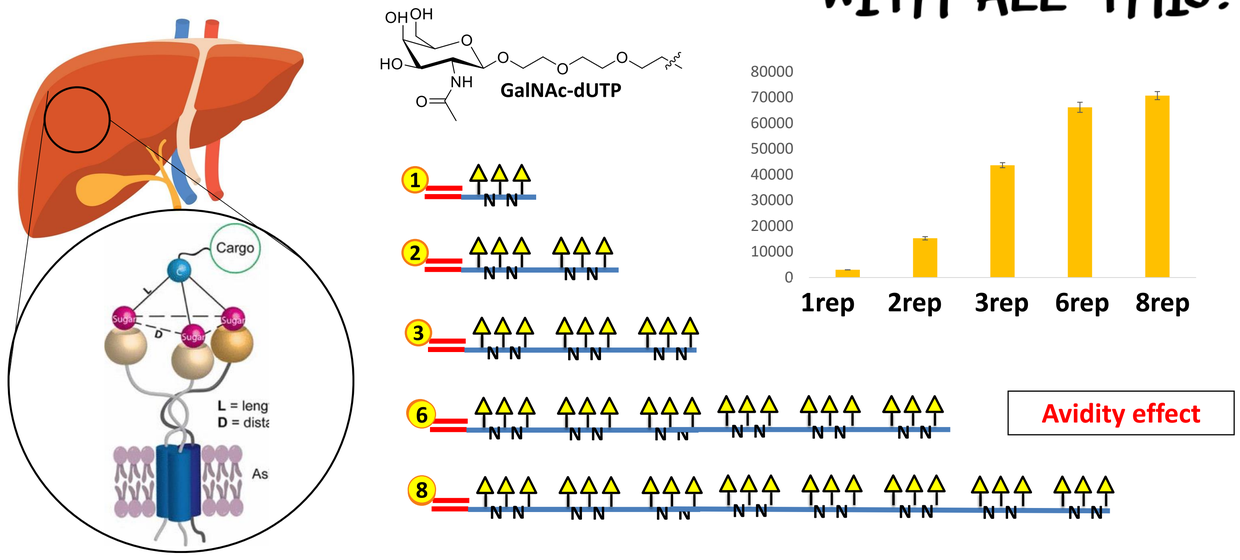
We have established a method for **co-transcriptional incorporation** of a wide variety of **chemically modified nucleobases** that is fully compatible with *in vitro* selection strategies.

- ✓Amino acid side chains
- ✓Cathecols and other polyphenols.
- ✓Sugars of different complexity.



WHAT CAN WE DO WITH ALL THIS?

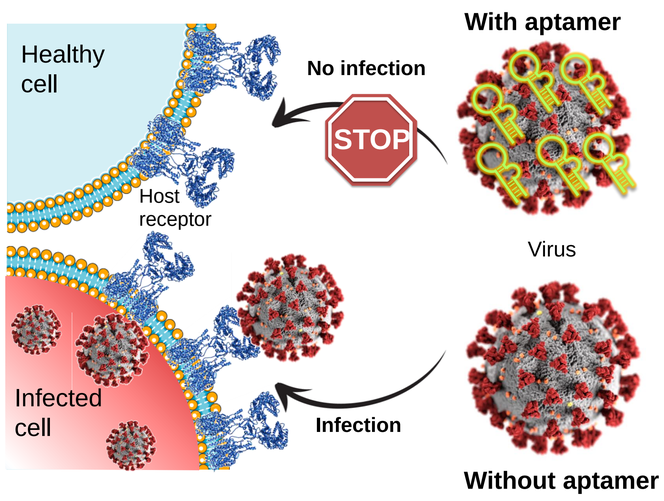
LIVER TARGETING



GalNAc-modified RNAs selective to the asialoglycoprotein receptor (ASGPR1) in hepatic cells **show potential to be used for liver therapy** as drug delivery vector.

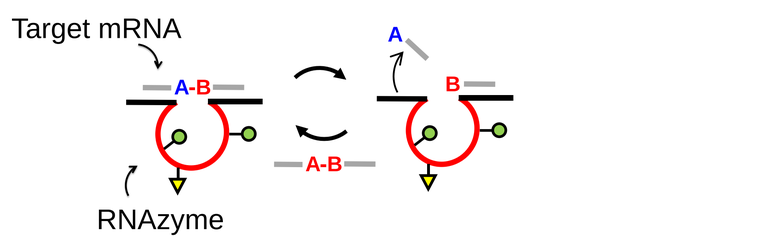
VIRUS TARGETING

We have developed a 2´-fluoro **modified RNA aptamer that is serum-stable** and **binds strongly to SARS-CoV2 spike** protein and can block viral entry. Current efforts are focused **on targeting other viruses (influenza , adenovirus) with sugar modified aptamers.**

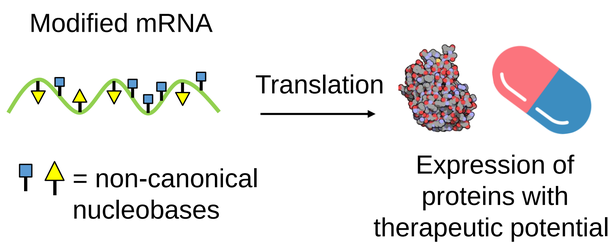


PROJECTS!!! FUTURE DIRECTIONS

- ✓ Novel **RNAzymes** to **control gene expression.**



- ✓ **Chemically enhanced mRNA** for efficient uptake and **prolonged protein translation**



- ✓ Expansion of **RNA alphabet** and **decoding** via nanopore sequencing.
- ✓ Designing **functional RNA:protein biohybrid nanosystems.**
- ✓ **Nanoinjection** of functional **non-coding RNAs** using synthetic nanopores.