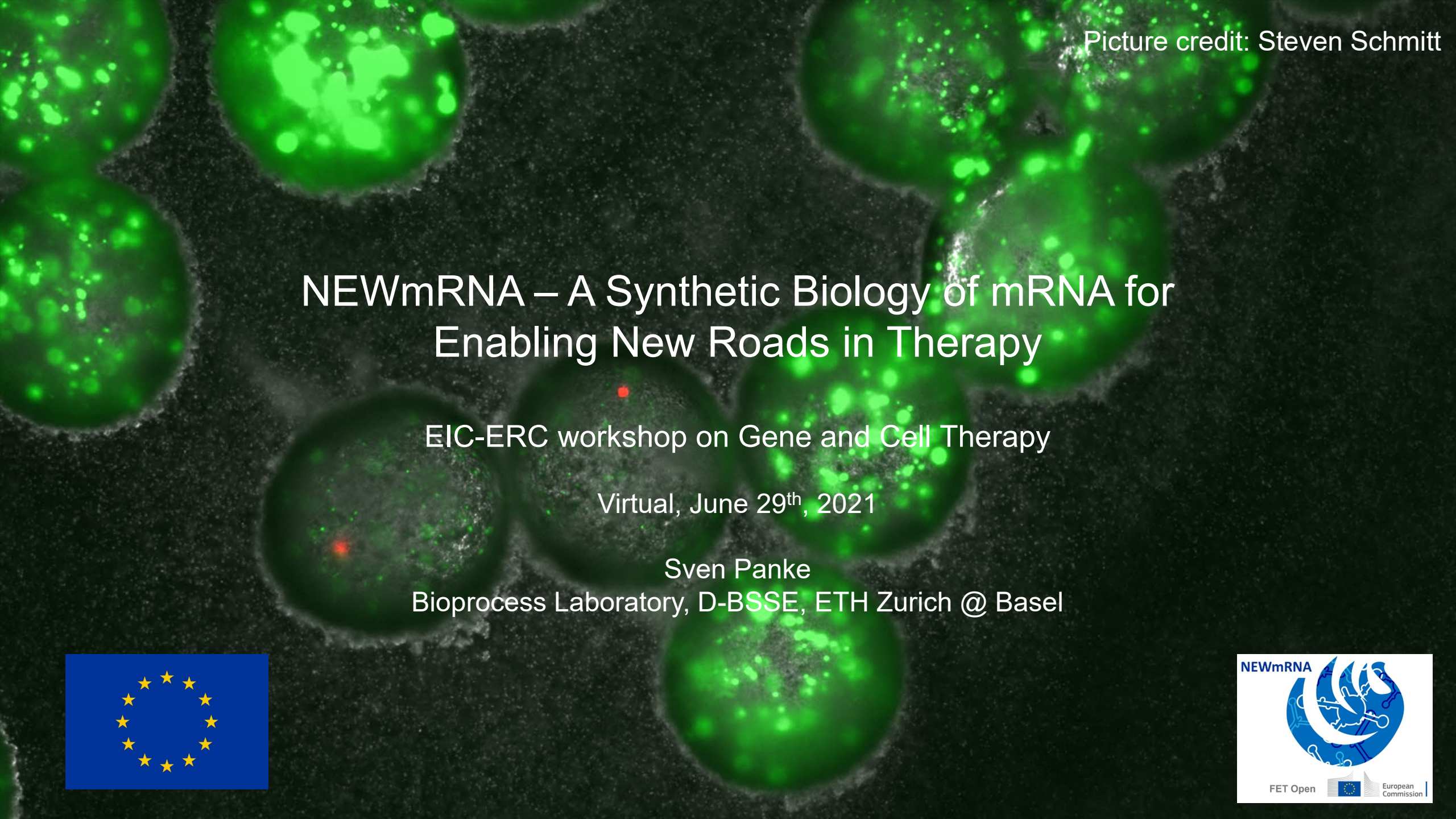

Picture credit: Steven Schmitt

NEWmRNA – A Synthetic Biology of mRNA for Enabling New Roads in Therapy

EIC-ERC workshop on Gene and Cell Therapy

Virtual, June 29th, 2021

Sven Panke
Bioprocess Laboratory, D-BSSE, ETH Zurich @ Basel

NEWmRNA

FET Open

European Commission

NEWmRNA – A Synthetic Biology for mRNA

Universität Konstanz

NEWmRNA

KATHOLIEKE UNIVERSITEIT LEUVEN

cea

FET Open

European Commission

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

THERAXEN

Universität Zürich[UZH]

Mastering the manfacturing paradigm is crucial for the transition from science to innovation

Proteins/peptides

1960: Insulin extraction from 50 pig pancreas/diabetic person

2020: (Eg) Sanofi Lantus plant provides recombinant insulin to millions of diabetic people

Insulin plus variants with advantageous properties

DNA

1972: Khorana's paper series on Sc ala-tRNA gene synthesis

1983: PCR & short oligos

1999: Geneart & Friends - Solid phase mass synthesis

2004: Synthetic biology

20xx: DNA storage

RNA

Small RNAs

1977: RNA oligos from amidite synthesis

2016: Nusinersen, eteplirsen (ASO drugs)

mRNAs

1984/85: SP6/T7-based in vitro mRNA synthesis

2021: Roll out of anti-SARC-CoV2 vaccine

RNA

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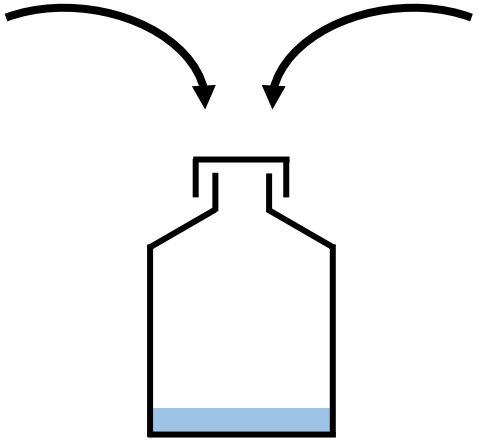
Short RNAs can be produced chemically

The chemical space of small RNA drugs is limited by chemistry

Long RNAs are produced enzymatically

The chemical space of mRNAs is limited by the substrate scope of RNA polymerases

Making mRNA is an *in vitro* affair



pDNA (1 mg for 20 mg of RNA)

rATP
rGTP
rCTP
rXXXX

Chemistry
Biotechnology

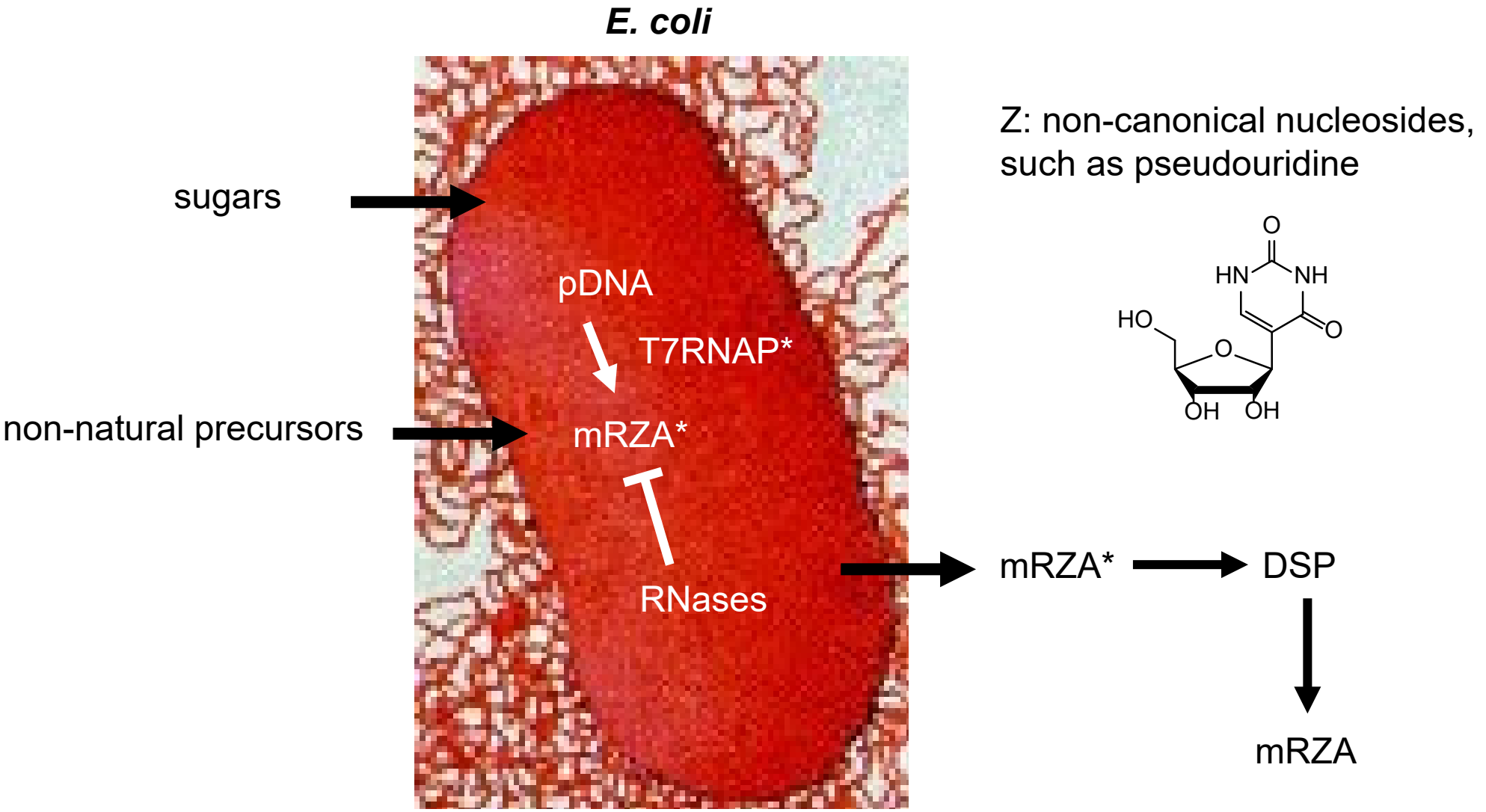
ARCA-cap

T7 RNAP:
Some flexibility but at mRNA scope only for selected rNTPs

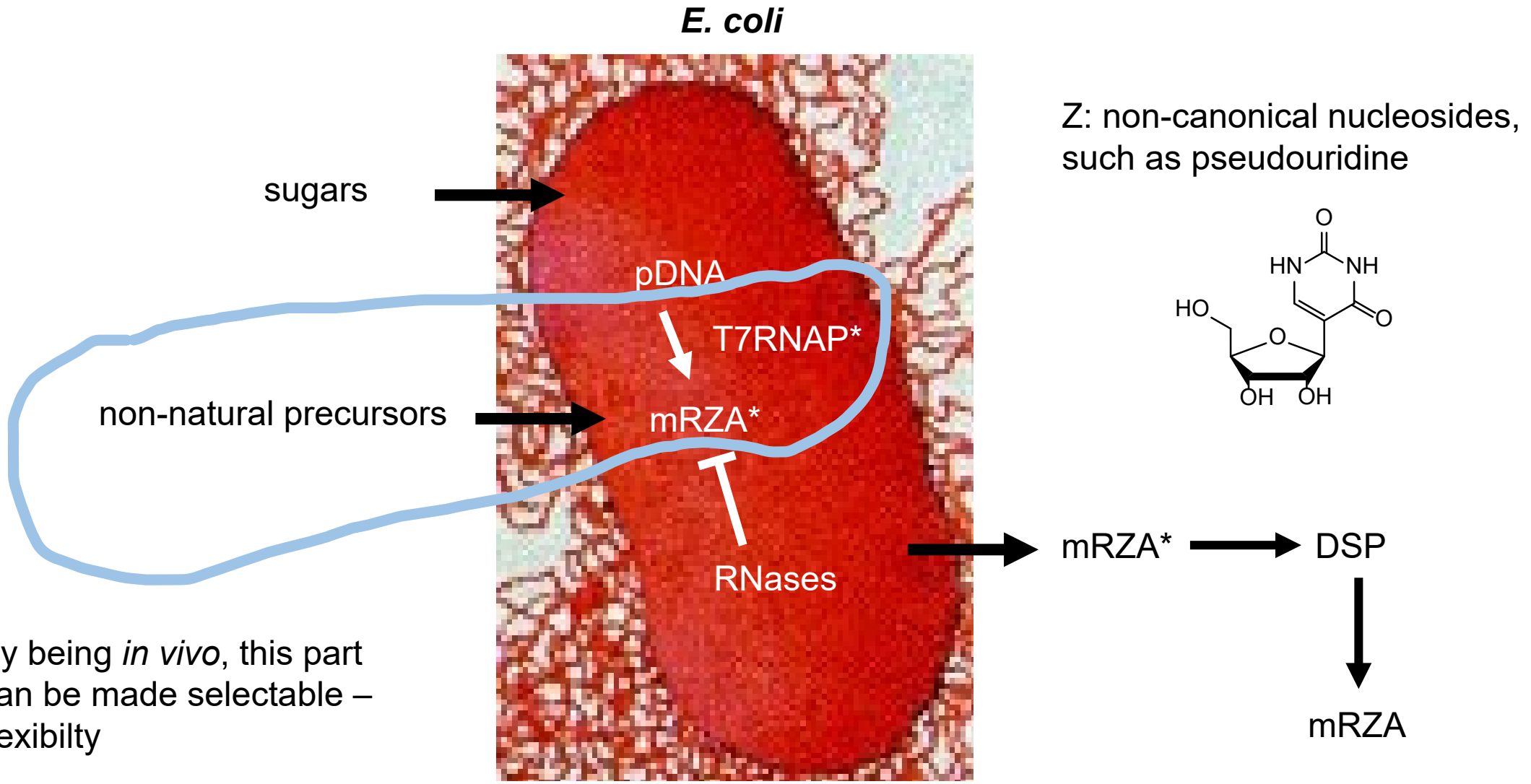
Total amount vs dose size

Dose size: approx 30-100 µg

NEWmRNA: From *in vitro* to *in vivo*



NEWmRNA: From *in vitro* to *in vivo*



in vitro versus *in vivo*

in vitro

- Highly controlled
- GMP (relatively) simple
- Scalable 1st order
- Solution to capping
- Sectorial
- Very little potential for endotoxins (via pDNA)

in vivo

- Scalable 2nd order
- Critical functions become selectable
- From sugars and cheap precursors to complex informational polymers
- Highly flexible
- Foundational

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