Developing personalized Synthetic RNA for the selection of next generation therapeutics

Prof. Dr. Lorenzo Franceschini

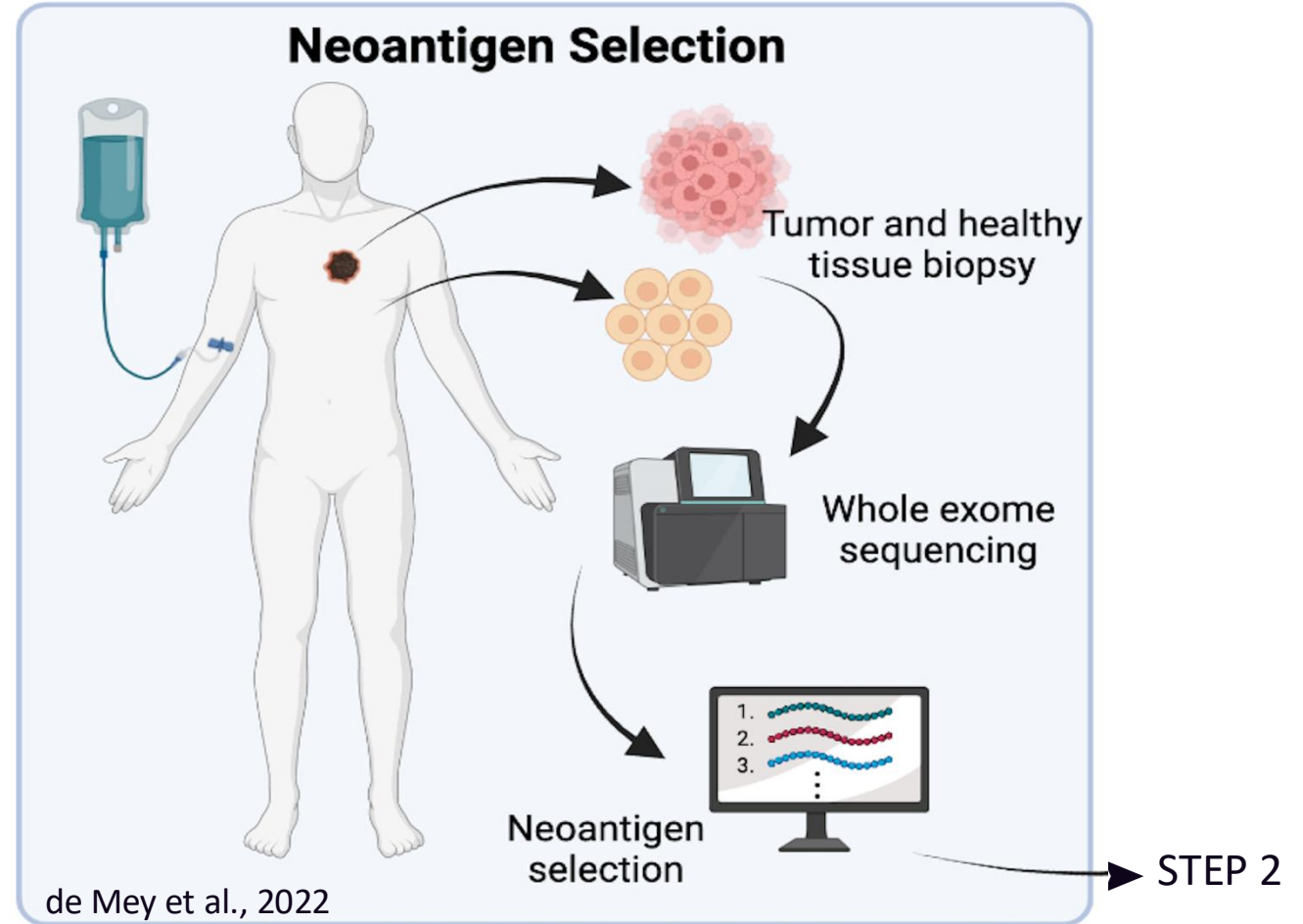Translational Oncology Research Centre (TORC) VUB

mRNA-based therapeutics: <u>selection</u>, production & validation

STEP 1
Choose your Therapeutic target:

➤ **TAA**
  Tumour associated antigen

➤ **Neo-antigen**
  Patient-specific epitope
  generated in one tumour

➤ **NHD antigen**
  Non-human-derived epitope

➤ **TCR**
  T cell receptor

➤ **CAR**
  Chimeric antigen receptor

TECH
TRANSFER
OFFICES
FLANDERS

Neoantigen Selection

Tumor and healthy tissue biopsy

Whole exome sequencing

Neoantigen selection

de Mey et al., 2022

STEP 2

mRNA-based therapeutics: selection, production & validation

STEP 2

Manufacture your synthetic RNA:

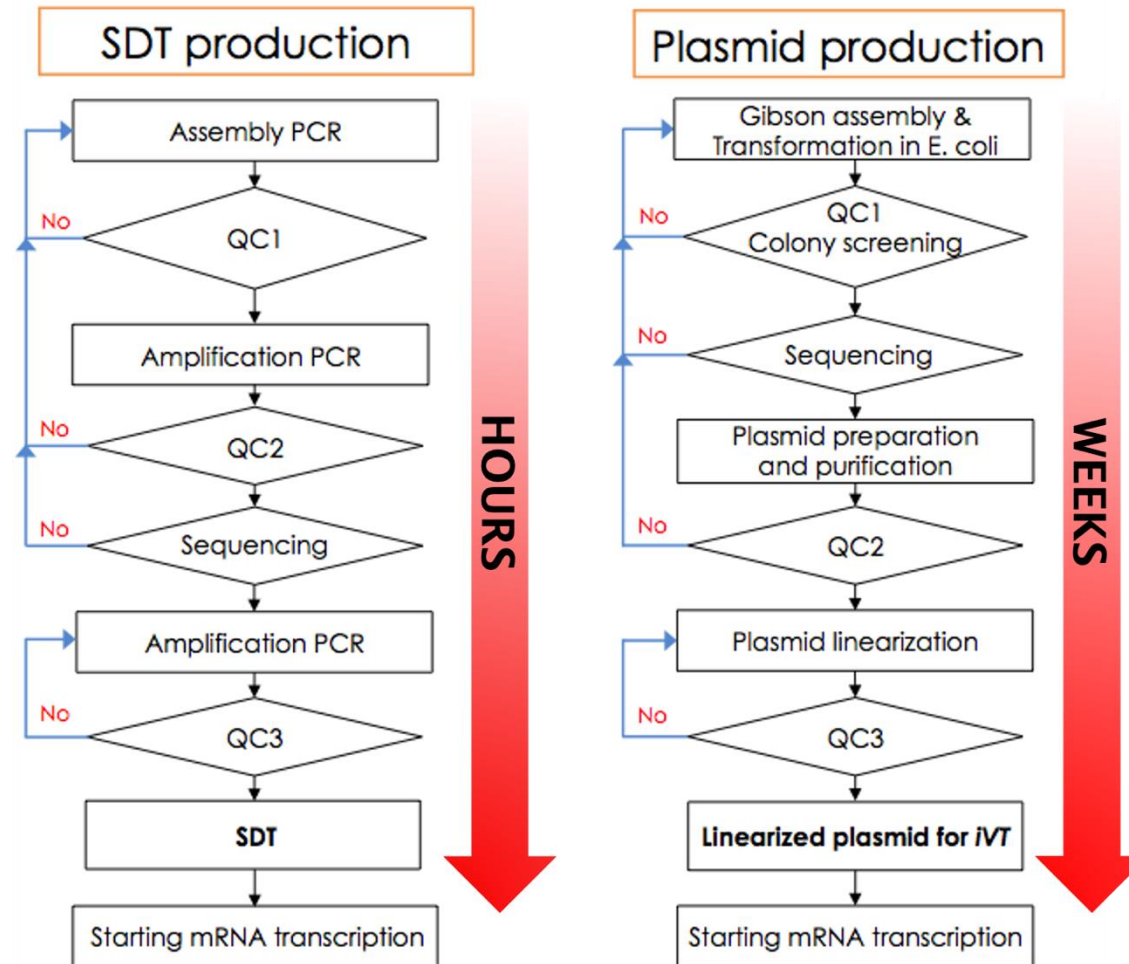- Oligonucleotide-based process

- PCR assembly and amplification

- Custom fidelity and purity

- Application-based design

Prompt mRNA production

de Mey et al., 2022
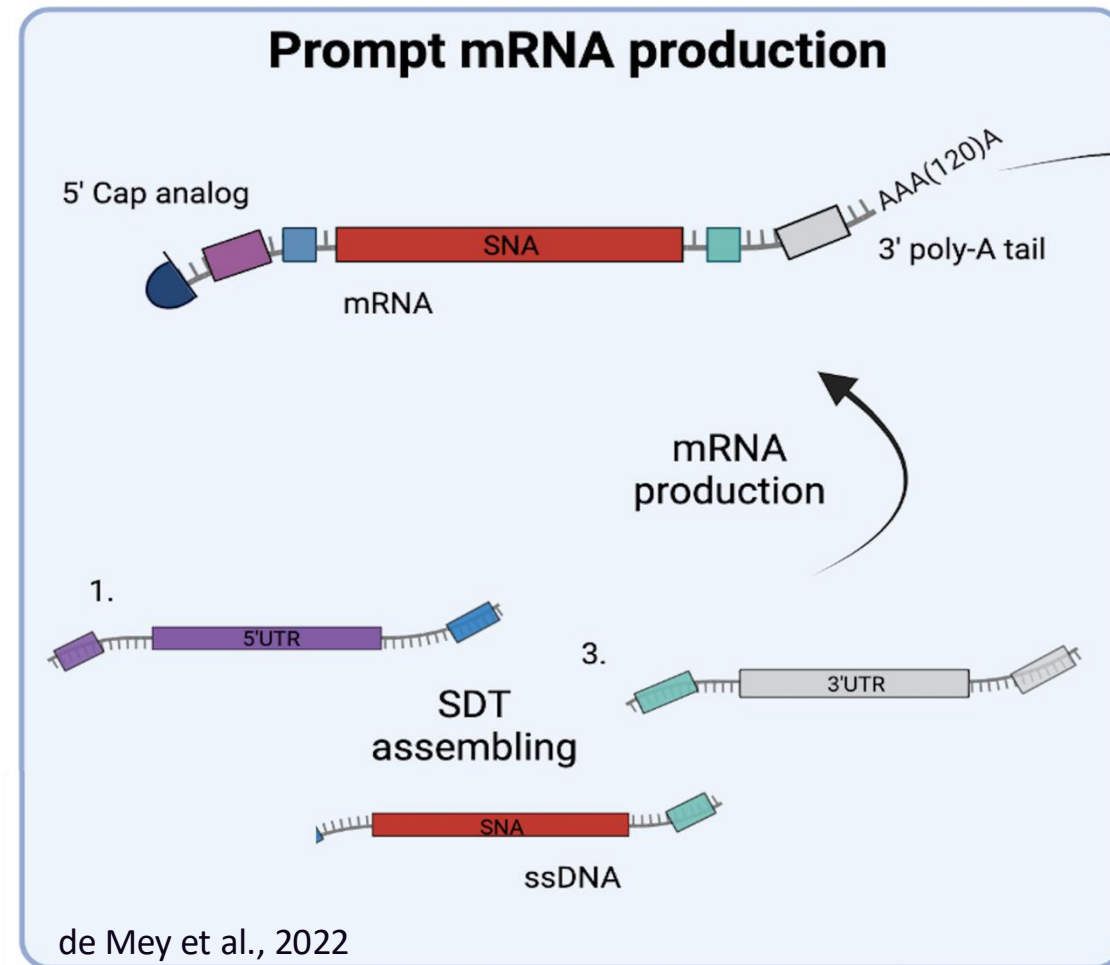
STEP 3

mRNA-based therapeutics: selection, production & validation

SDT- derived mRNA

- Fast & flexible
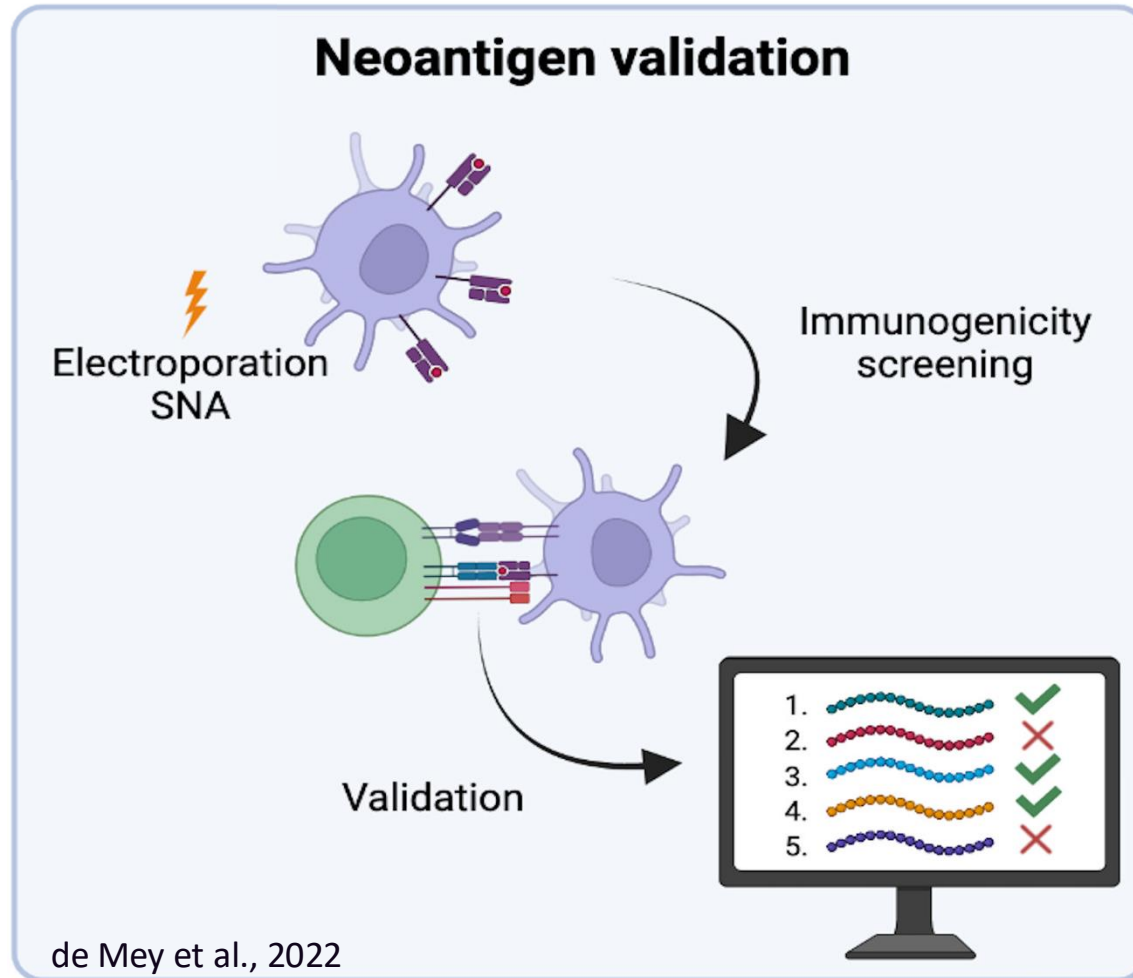- Scalable (down)
- No bacteria
- No antibiotics
- Fit for automation

TECH
TRANSFER
OFFICES
FLANDERS

mRNA-based therapeutics: selection, production & validation

STEP 3

Validate your candidates:

➢ Prompt

in vitro, ex or *in vivo* testing

➢ Flexible

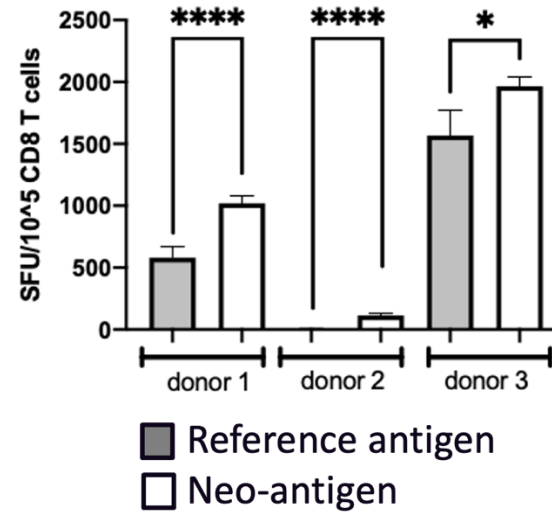Quick fix, change composition, formulation, design or candidate prior therapy

Neoantigen validation

Electroporation SNA

Immunogenicity screening

Validation

de Mey et al., 2022

TECH TRANSFER OFFICES FLANDERS

Dedicated SDT platforms for individualized therapeutics

- **Neo-antigens**

- TCR

- CAR

➢ **Immunogenicity evaluation**

➢ **Membrane presentation**
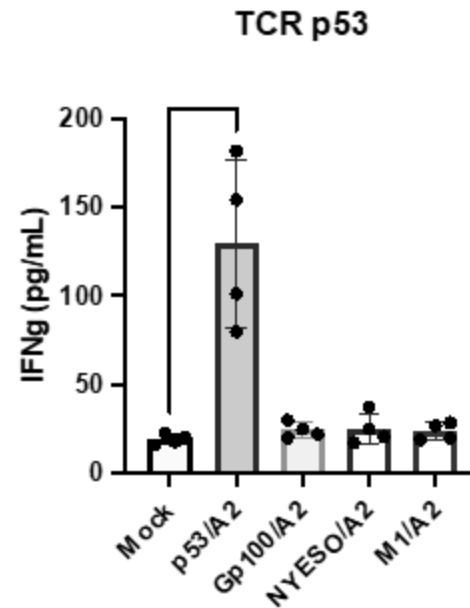
➢ **Check *in silico* false "positive and negative" predicted candidates**

de Mey et al., 2022

Dedicated SDT platforms for individualized therapeutics

- Neo-antigens

- **TCR**

- CAR

TCR p53

- ➤ **T cell receptor activation with cognate NA**
- ➤ **TCR engineering**

Esprit et al., 2025

Dedicated SDT platforms for individualized therapeutics

APPLICATIONS:

- Neo-antigens

- TCR activation

- **CAR reactivity**
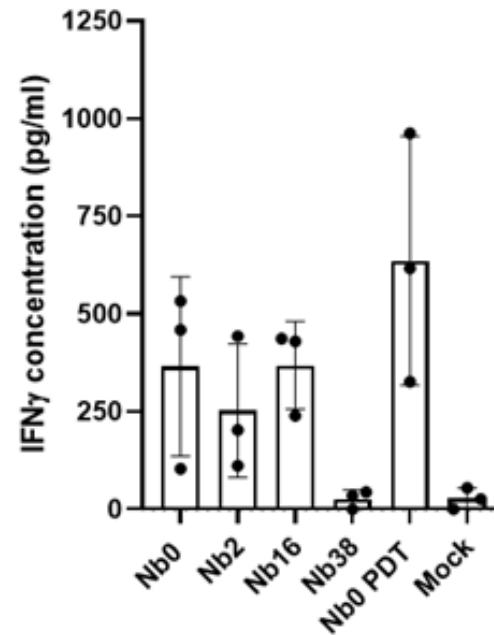
➤ **Nanobody library screening**
➤ **Antigen receptor engineering**

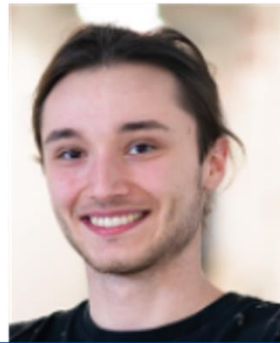TECH
TRANSFER
OFFICES
FLANDERS

Bertazzon et al., 2025

Take-home message

➤ **Therapeutic potency** evaluation:

  ✓ Screening

  ✓ Validation

➤ Molecular design characterization:

  ✓ Coding sequence

  ✓ Non-coding elements

➤ **Target engineering**:

  ✓ Improved therapeutic performance

TECH
TRANSFER
OFFICES
FLANDERS

Thank you!

SCAN ME

Karine Breckpot   Arthur Esprit   Dorien Autaers   Giada Bertazzon   G. Van Craesbeek

Visit **TORC.research.be**

or drop an email @
Lorenzo.Franceschini@vub.be

TECH
TRANSFER
OFFICES
FLANDERS

Questions?

SCAN ME

TECH
TRANSFER
OFFICES
FLANDERS

Visit TORC.research.be

or drop an email @
Lorenzo.Franceschini@vub.be