



AI to redefine Antibody discovery
workflow

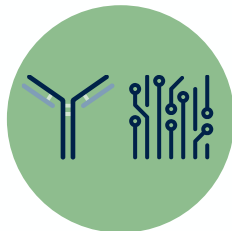


Who are we?

French TechBio company

Spin-off from CNRS/INRAe

2017



Artificial Intelligence for antibody drug

Unique technology and expertise in Europe for applying AI/ML for drug discovery

Early adopters purchased our products

Based in EU, US, South Korea and Israel, biotech & pharma companies

40

20M

Antibodies characterized

Applied within 9 therapeutic areas, can be used for other biodrugs

1st Artificial Intelligence based vaccine

AI used to design peptide for CoVepiT, OSE Immunotherapeutics vaccine

COVID
19

26.04.21

Our DNA is to combine Computational and Biology

A team of 15 people dedicated to your success

- Y 10+ years of research in AI/ML in drug discovery
- Y International experience working on US (DARPA) and European programs
- Y 100+ peer reviewed scientific publications and 4 patents
- Y KOLs in immuno-oncology (French hospital, Medtech, Biotech and pharma companies)
- Y Make antibody faster, better and safer using AI

POWERED BY:





We transform years into 1 month with digitalization

MAbFactory – AI & ML



- Y Decrease the risk, Accelerate drug discovery by x500, all therapeutic areas
- Y Pick and design candidates ready for biological functional assays
- Y Parallelization of billion of simulations to design the best candidate to the target



Digitalization of drug discovery

Only antibody sequences and target name required

No new data training/ML required

Epitope binning of panel of 1000 antibodies in 3 days

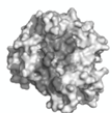
Epitope mapping in 5 min



selection



characterization



Target



Artificial Intelligence and databases

optimization



Forecast off-targets in minutes



Final lead Ab

- Y Accelerate 500x drug discovery
- Y Increase 5x the success rate of market approval
- Y Reduce 10x drug discovery costs
- Y Expand IP protection
- Y Validated by industry (pharma & biotech)

26.04.21

MAbSilico assets & achievements

MABSilico

Databases – proprietary and public

- Y 4000 structures
- Y 70M sequences
- Y 400k Abs, 3k targets
- Y 1300 Abs with kd



- Y Patents, publications
- Y Next generation sequencing (NGS)
- Y Public databases

3 algorithms

Docking
Protein-protein docking



Similarity
CDR similarity measurement



Affinity
KD prediction



5

Antibodies drugs in preclinic and clinic

2 Abs in preclinic, 2 Abs in clinic (phase 2 or 3) and 1 peptide-based vaccine in phase 1 from early adopters

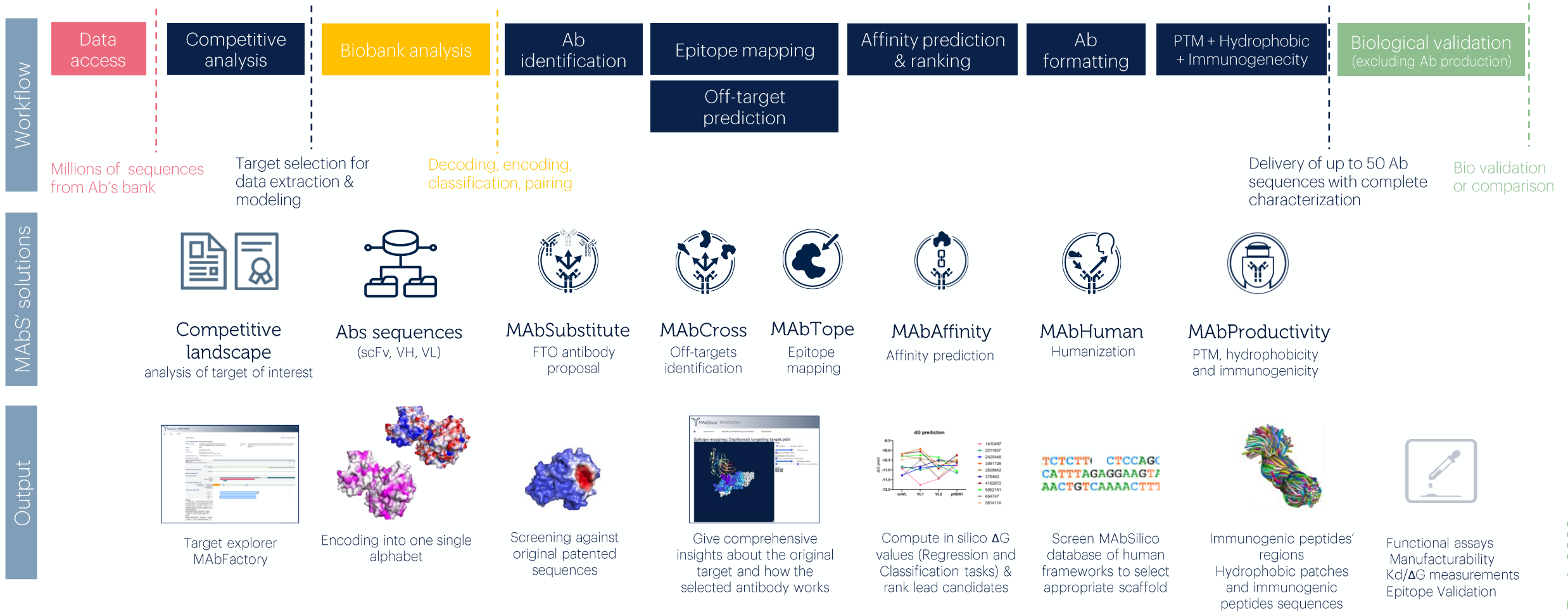
1 EU patent (WO2018087494A1) with exclusive licence
20+ scientific publications

5

Tech Deck 2022



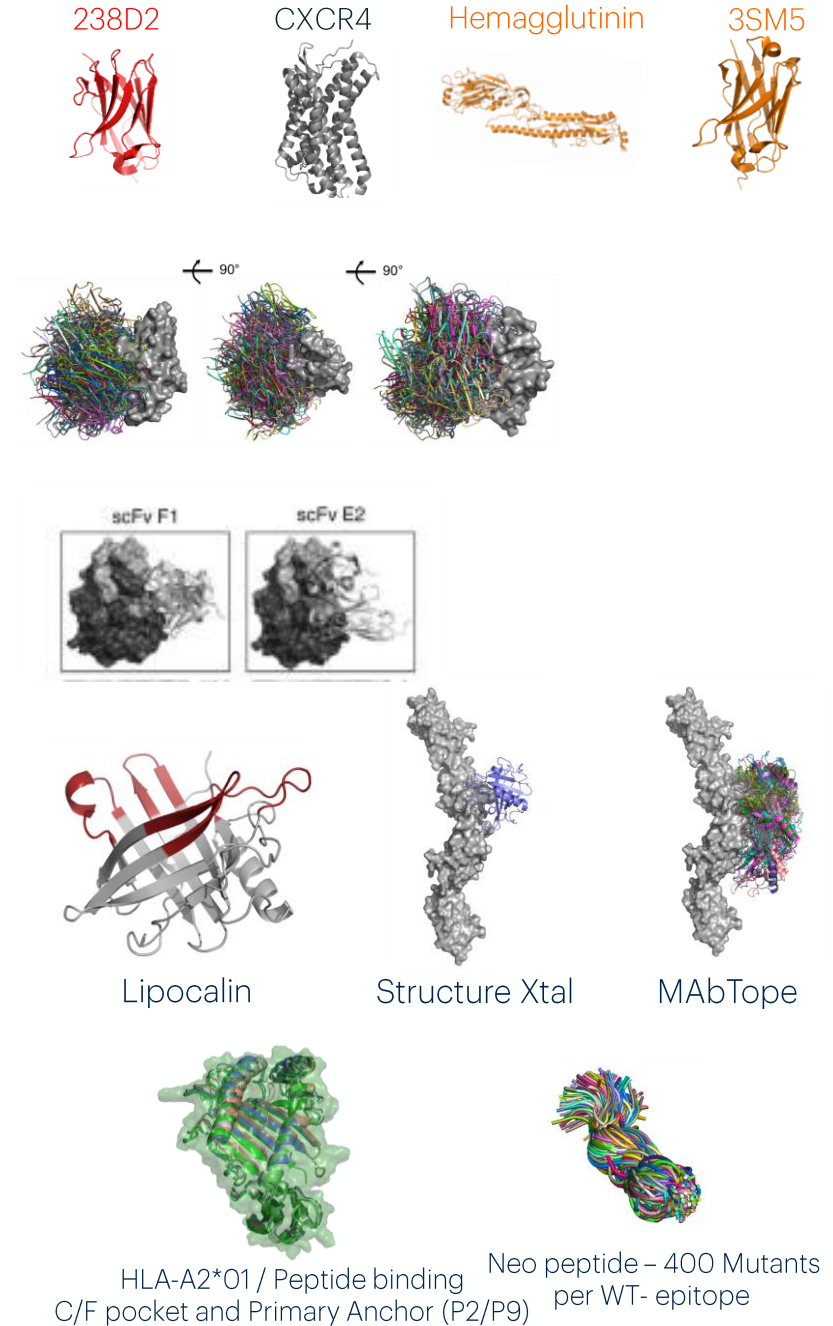
Parallelization of million of simulations in days





AI used for biologics drug discovery

- Y **VHH:** method of CDR similarity developed on VHH against CXCR4 (off-target prediction and binder replacement)
- Y **Bispecific Ab:** BiCKI® platform of OSE Immuno with anti-PD-1 as central skeleton (OSE-279)
- Y **CAR-T:** ScFv can be used for CAR-T, work done on anti-cath-D
[A. Yahya et al., BMJ 2019](#)
- Y **Novel format:** proof of concept for epitope mapping on lipocalin (4 hyper-variables loop ~ 4 CDRs)
- Y **Peptide:** in silico affinity maturation for CoVepiT (covid19 vaccine in clinical trial) [V. Gauttier et al., BioRxiv 2020](#)



05 Use cases of drug design & discovery programs

Computational peptide design for covid-19 vaccine – CoVepiT clinical phase I



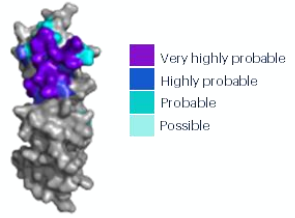
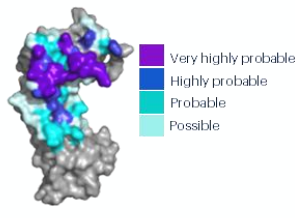
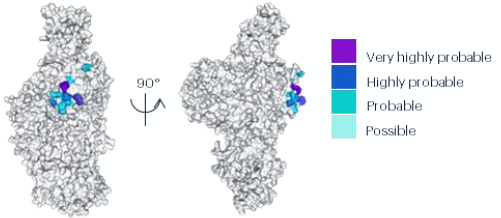
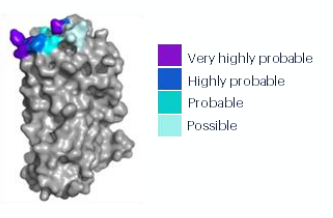
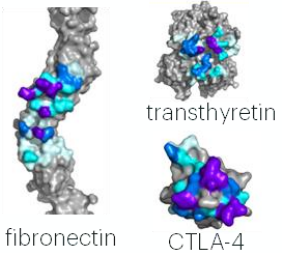


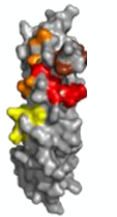
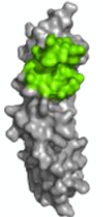
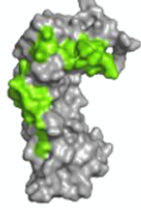
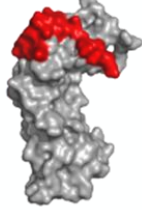
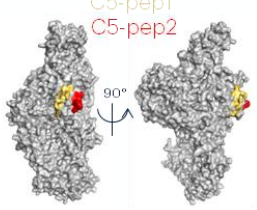
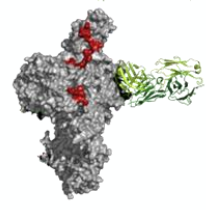
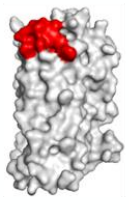
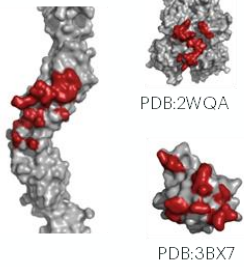






Design new lead candidates against RBD from SARS-CoV-2

End-to-end framework that can serve as anti-pandemics platform

Design of an anti-A2A design using MAbSubstitute

Design new lead candidates to replace a breast cancer triple negative drug

Use of MAbFactory to select and design of anti-TIGIT

	Dupilumab / IL4R α	OSE-127 / IL-7R α	Eculizumab / C5	OSE-230 / ChemR23	Lipocalins	Time
	<ul style="list-style-type: none"> The Dupilumab (DUPIXENT[®]) is targeting the IL4Rα and is FDA-approved for Eczema, Atopic dermatitis, Several forms of severe asthma. Epitope was not known until 2020 	<ul style="list-style-type: none"> New Ab targeting the IL-7Rα to prevent the expansion of pathogenic memory immune cells and chronic autoimmune attacks. 	<ul style="list-style-type: none"> Eculizumab targets the complement C5 and is indicated in nocturnal paroxysmic hemoglobinuria (NPH) and in atypical hemolytic and uremic syndromes (aHUS). The epitope was only partially solved and did not explain the biological observations (absence of interspecies crossreactivity) 	<ul style="list-style-type: none"> New Ab targeting ChemR23 (GPCR) which is overexpressed at the inflamed site of IBD, Arthritis, CLE, ANCA vasculitis, Asthma, Sepsis, COPD, ARDS, CHP, COVID-19 New concept in the management of severe & chronic inflammation 	<ul style="list-style-type: none"> Lipocalins are a novel class of binding molecules with 4 hyper-variables loops (~ 4 CDRs) which transport small hydrophobic molecules 	<ul style="list-style-type: none"> AI vs. biology, from minutes to months
 MAbTope					 fibronectin transferrin CTLA-4	 Minutes
 Biological assays	Experimentally validated residues (cytometry)  Crystallography (PDB: 6wgl) 	Peptide array  HDX 	Experimentally validated residues (peptide array)  HDX  Crystal. (pdb 5i5k)	Experimentally validated peptide (ELISA) 	Crystallography  PDB:2WQA PDB:3BX7	 Months
 Publications	 Tahir et al., 2021	 Lyssia et al., 2018	 Brachet et al., 2017	 Trilleaud et al., 2021		

05 Computational peptide design for covid-19 vaccine

Clinical phase 1

Problem

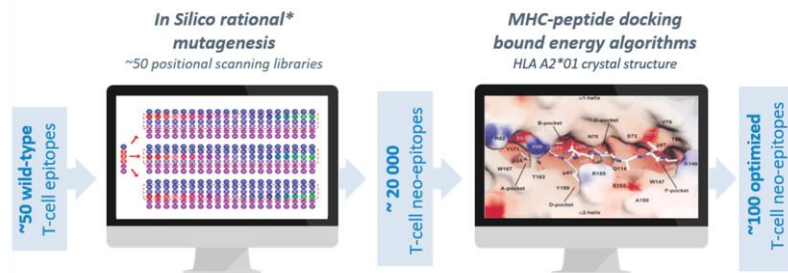
- Design a multi-target CD8 T cell peptide COVID-19 vaccine targeting for design targeting several structural (S, M, N) and non-structural (NSPs) SARS-CoV-2 proteins.
- Find potential universal vaccine against future coronaviruses.

Approach

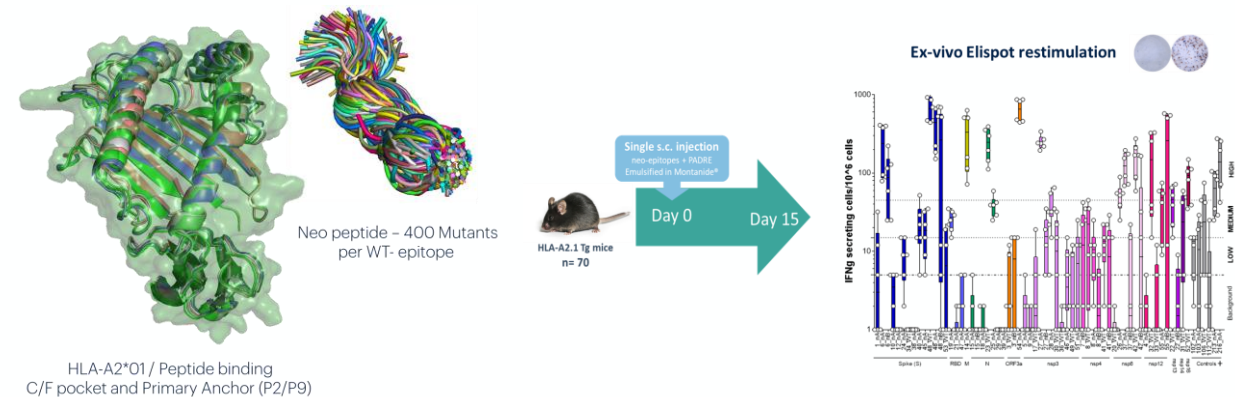
- Adapt an immunologically optimized multi-neoepitopes-based peptide vaccine platform for SARS-CoV-2.
- Identify and optimize peptides' immunogenicity using computational approach.

Results

- 55WT epitope out of 35.000 identify as best HLA-A2 binder with strong immunogenicity.
- Design of 55 neoepitopes validated experimentally (IFN γ measurement) which induce strong proportion of virus specific CD8 T-cells.
- First human data: Immunodominant epitopes tested positively in COVID-19 convalescent versus unexposed subjects.
- In clinical development – phase 1

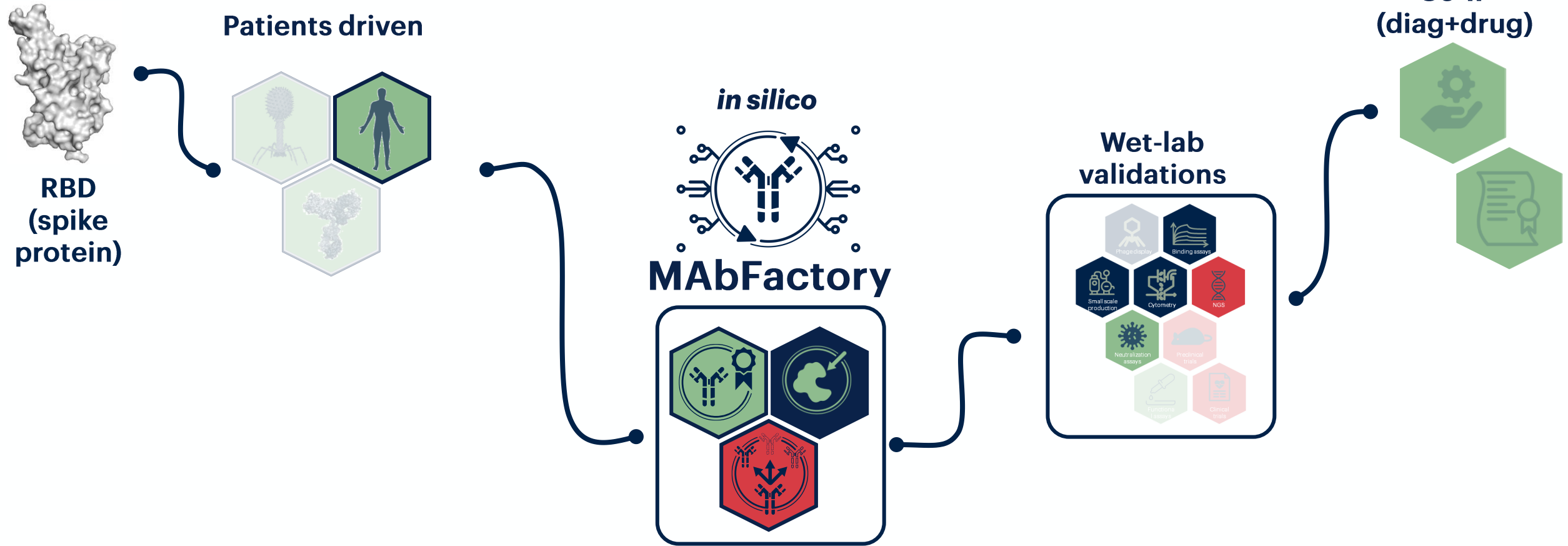


* Random mutagenesis -> 28 000 billion peptides possibilities !
Rational design based on OSE Know-How -> 20 x 10³ peptides



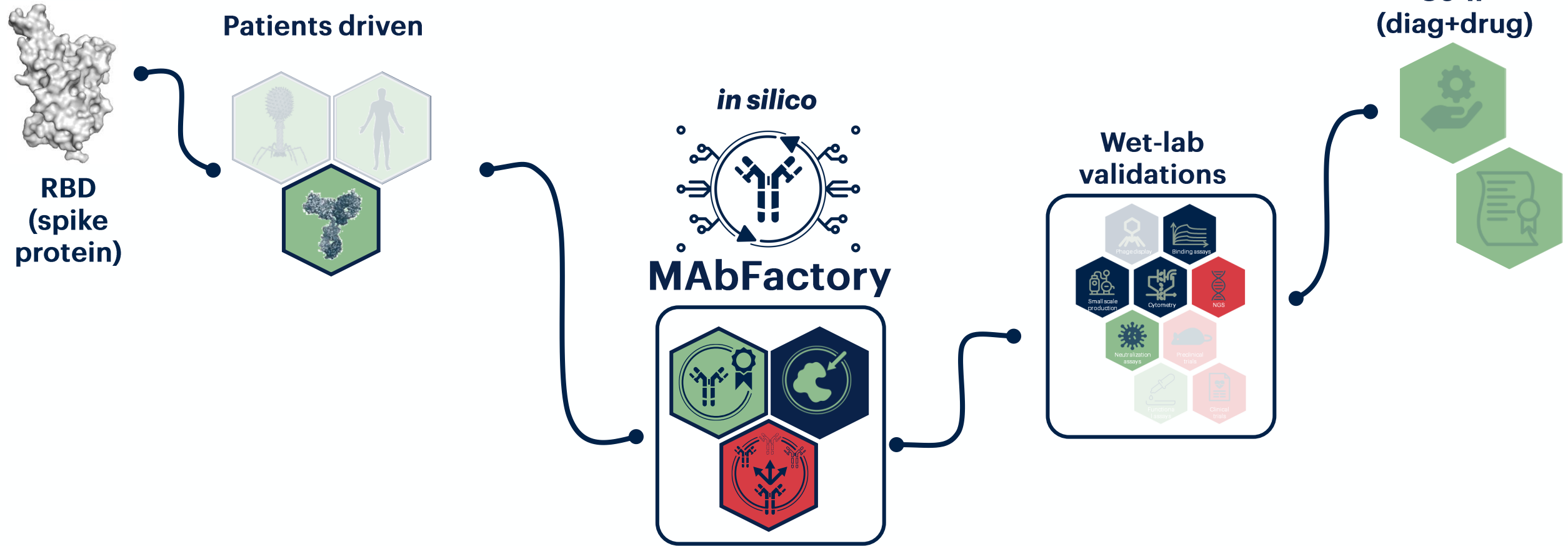
05 End-to-end framework that can serve as anti-pandemics platform, from patients to lead candidates

Humabdiag [project](#) - ongoing



05 End-to-end framework that can serve as anti-pandemics platform, from patients to lead candidates

MabCOVID- ongoing



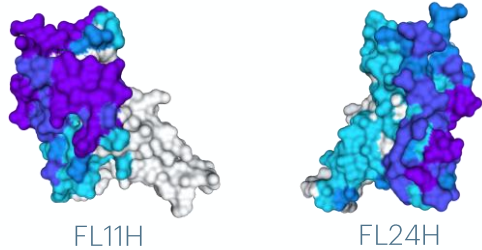


RBD

- Wuhan-neutralizing IgG isolated from patients as starting Ab
- Design of FL11H and FL24H using NGS sequences

candidates

- Two distinct predicted epitopes
- Production in diabody (VH-VH) format



FL11H

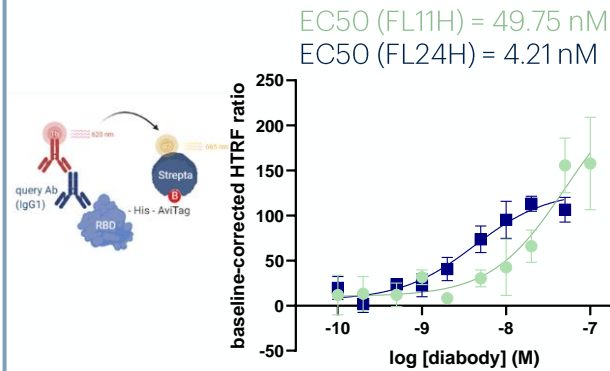
FL24H

Conclusions

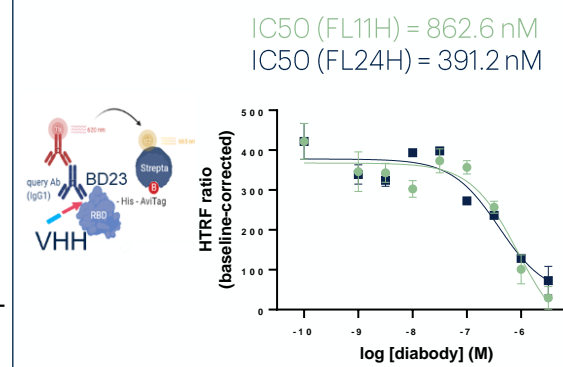
- Potential therapeutic mAb design by computer in days
- Format to optimized
- Effect on Omicron variant
- Ongoing: affinity maturation

In vitro validation of binding and neutralization effect

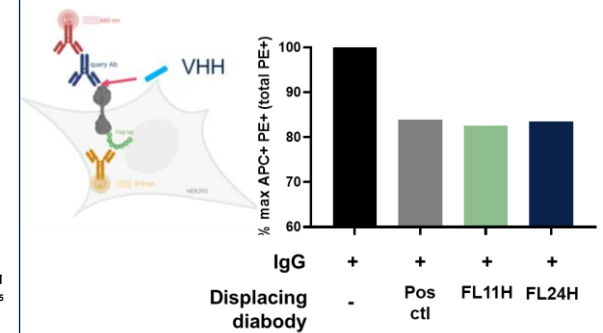
Direct binding : HTRF



Competition with IgG on RBD protein : HTRF



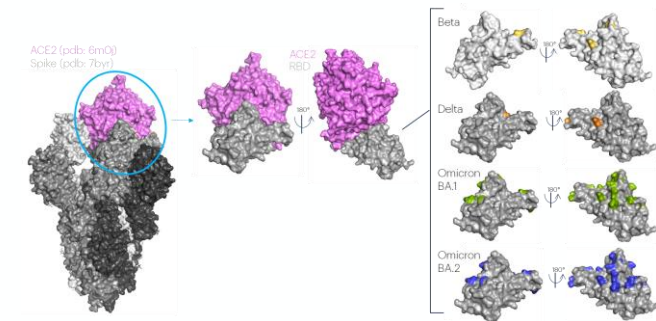
Competition with IgG on Spike : Flow cytometry



Neutralization assays (IC50 concentration in µg/ml)

Antibody	Wuhan	Delta	Omicron
FL11H (diabody)	4,3	1,4	Ongoing
FL24H (diabody)	28,6	9	Ongoing
Imdevimab (IgG)	0,006	0,006	Ongoing
Hyb. (IgG)	0,044	0,39	Ongoing

SARS-CoV-2 variants

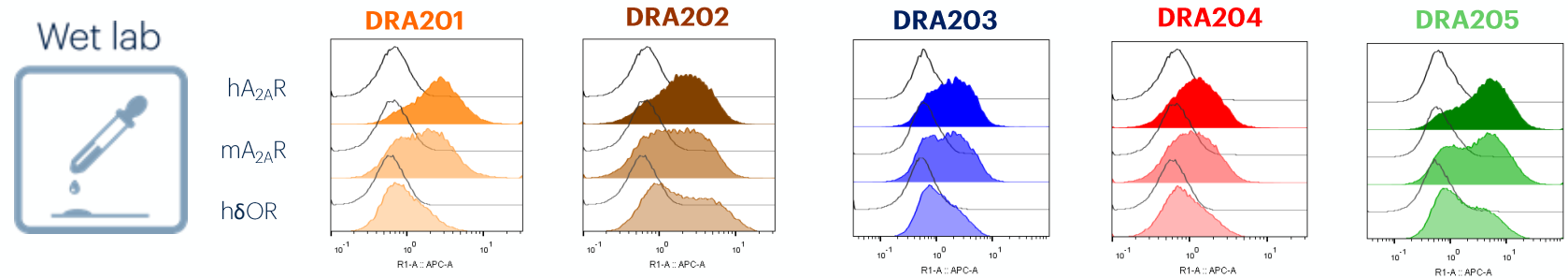




A_{2A}R (A₁, A_{2A}, A_{2B}, A₃)

- GPCR (Gi & β-arr)
- P1 class purinergic receptor, Autism Spectrum Disorder, Metastatic spread, Dementia, Sleep disorders

In vitro validation of new leads – binding validation

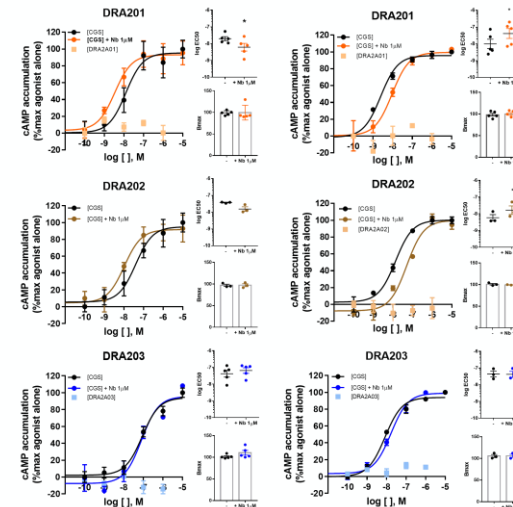


Leads

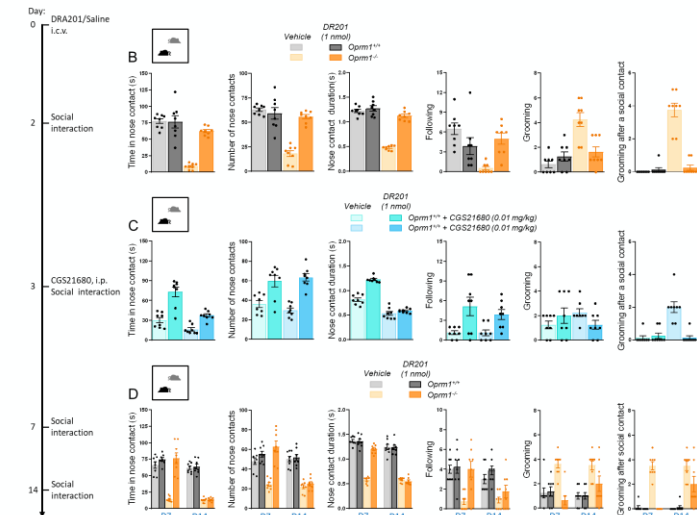
- Original: ScFv, Antagonist
- **New: 5 sequences VHH**

In vivo validation of new leads and biological activities

Pharmacological profile of candidate antibodies on human and murine A_{2A} receptors



Effects of DR-2A-01 administered ICV on social interaction in the *Oprm1* knockout mouse model of autism



Conclusions

- Multiple alternative binders
- Allosteric Modulation & Cross specific
- In vivo validation

05 Design new lead candidates to replace a breast cancer triple negative drug

Ongoing project



TROP2

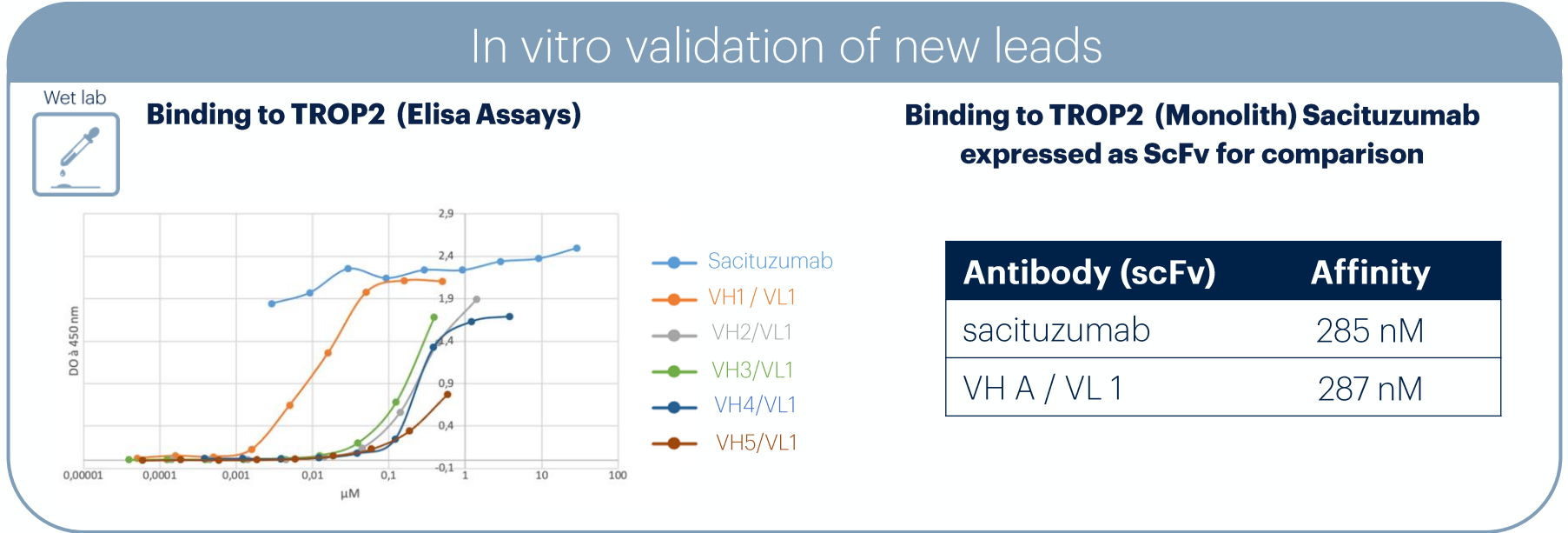
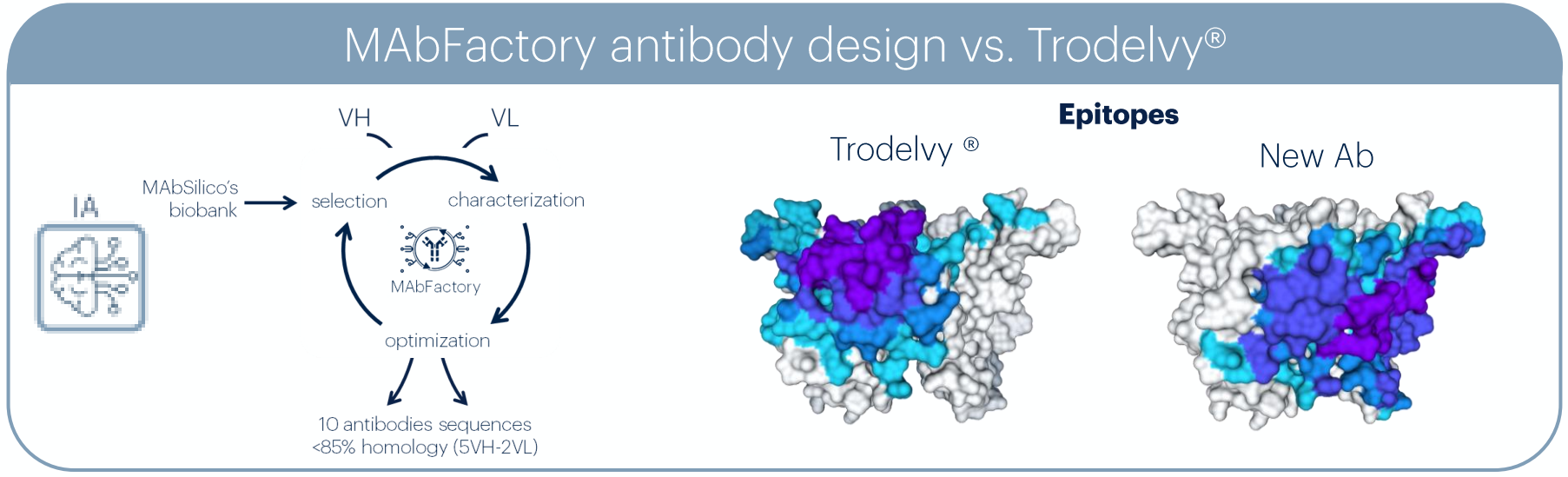
- Trophoblast cell-surface antigen 2 –TROP2
- Type I transmembrane glycoprotein, Triple Negative Breast Cancer, Valuable Biomarker in metastatic spread

Leads

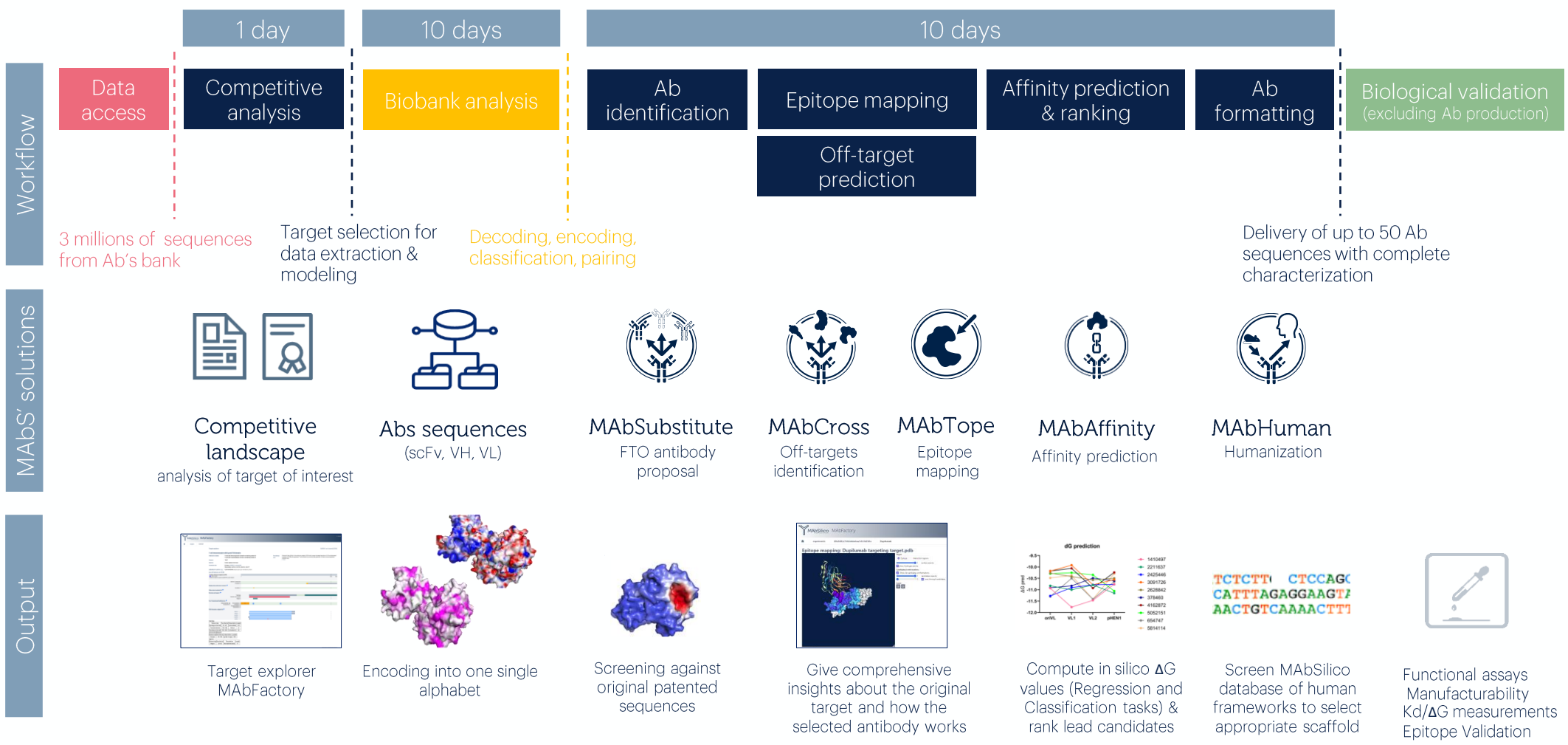
- Sacituzumab; therapeutic ADC antagonist Trodelvy®
- **New: 10 sequences (5 VH and 2 VL, in scFv)**

Conclusions

- Multiple alternative binders
- Allosteric Modulation & Cross specific
- In vivo validation



New leads against TIGIT selected & designed from a naïve bank of 3M antibodies



05 Use of MAbFactory to select and design of anti-TIGIT (part 2)

Ongoing project

TIGIT

- T-cell immunoreceptor with Ig and ITIM domains
- Immune check-point

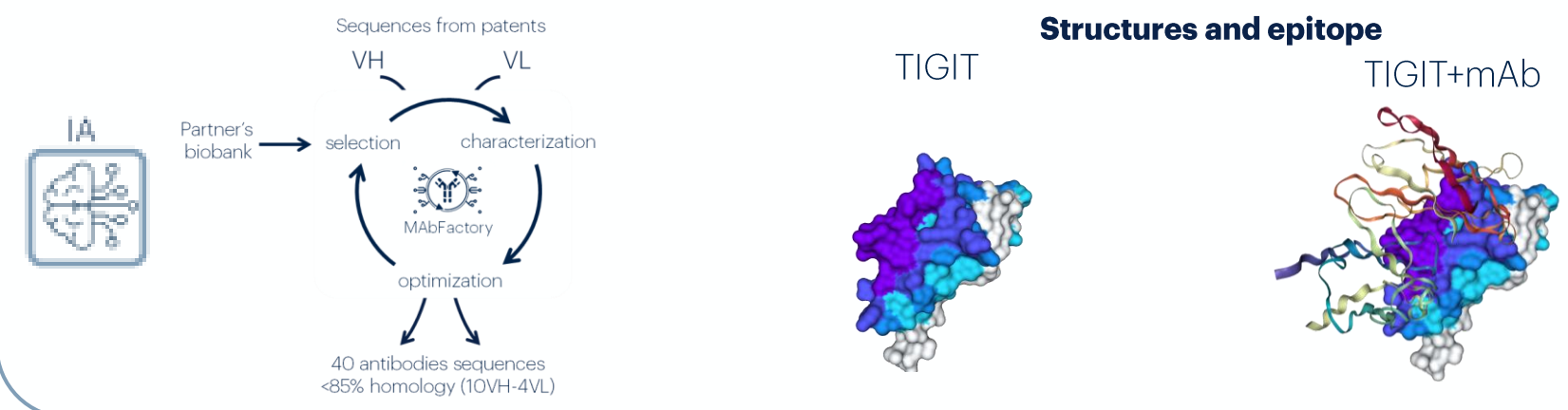
Leads

- 10 anti-TIGIT disclosed in patents
- **New: 40 sequences (10 VH & 4 VL, in scFv) from 3M sequences**

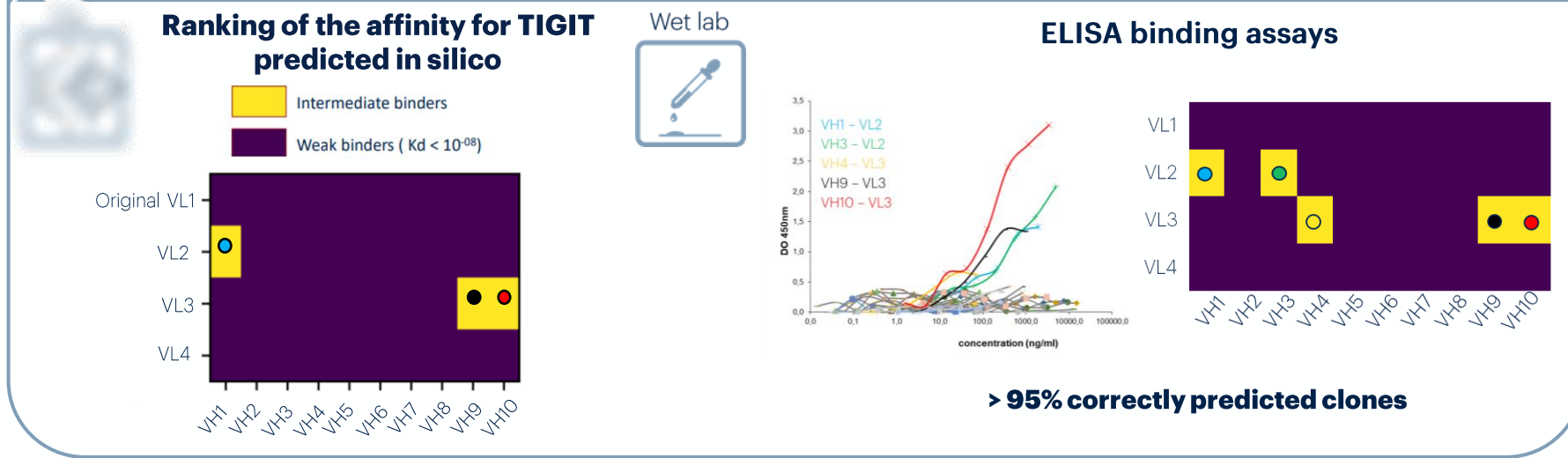
Conclusions

- Selection of binders from biobank in days
- in silico humanization of murine lead candidates
- Affinity predicted validated by biological assays

Antibodies designed using MAbFactory

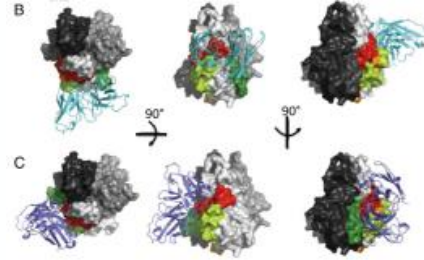


In silico followed by in vitro validation of new leads

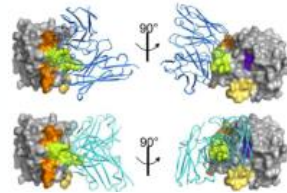




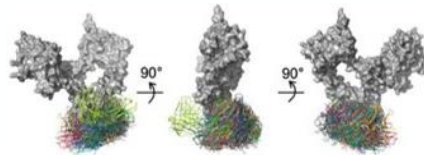
Y [MAbTope: A Method for Improved Epitope Mapping](#), **J Immunol**
October 15, 2018



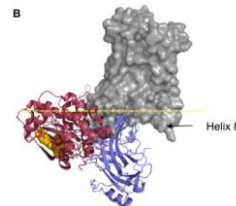
Y [4C3 Human Monoclonal Antibody](#) [...], **Front. Immunol.**, 25
September 2020



Y [Biasing human epidermal growth factor receptor 4](#) [...], **Cancer Sciences**, 16 May 2020

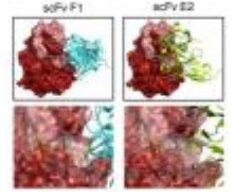


Y [G protein-dependent signaling triggers a \$\beta\$ -arrestin-scaffolded](#) [...]
FASEB J. 32,1154-1169 (2018)

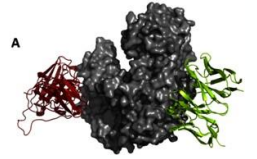


Y 1 EU patent ([WO2018087494A1](#))

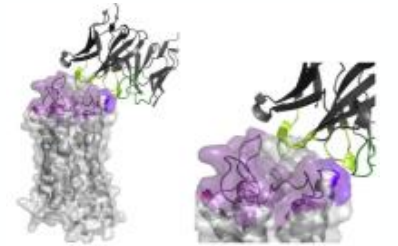
Y [Immunotherapy of triple-negative breast cancer with cathepsin D-targeting antibodies](#), **Journal for ImmunoTherapy of Cancer** - Feb 2019, 05th



Y [A recycling anti-transferrin receptor-1](#) [...], **mAbs** - 15 Dec 2018

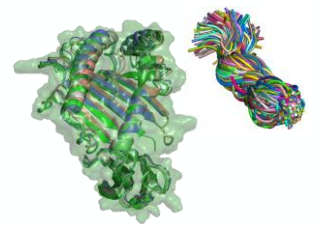


Y [Agonist anti-ChemR23 mAb](#) [...], **Science Advances**, 02 Apr 2021



Y [IL-7 receptor blockade blunts antigen-specific memory T cell](#) [...], **NATURE COMMUNICATIONS** (2018)

Y [...] [a multi-target COVID-19 vaccine](#), **BioRxiv** (2020)



Ready to use the AI-driven solutions for
antibody discovery faster, safer and better



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