Providing tailored technological innovative solutions to efficiently address vaccines needs through:

- Co-construction of focused project including relevant academic, private partners and BIOASTER experts
- Technology research units with multidisciplinary innovative strategies
- Integrated pre-clinical, multi/meta OMICs and Immunomonitoring data analyses
- Cost effective implementation
TECHNOLOGY UNITS
from sample preparation to data analysis

- Biological collections & Microbiology
- Pre-clinical models & Imaging
- Protein & Expression systems engineering
- Metabolomics & Proteomics
- Immunomonitoring
- Biological microsystems & Advanced optics engineering
- Genomics & Transcriptomics
- Data Management & Analysis
SYSTEM VACCINOLOGY AS THE KEY TO SUCCESS FOR FUTURE VACCINES

- **System engineering**
  - OPTIMIZE expression systems
  - PREDICT efficacy through population stratification

- **System delivery**
  - TARGET antigen optimal presentation
  - DEVELOP new in vitro/ex vivo models

- **System analytics**
  - DECIPHER adjuvant mode of Action
  - STREAMLINE quality control processes

- **System adjuvantology**
  - DEVELOP new in vitro/ex vivo models

- **System biology**
  - OPTIMIZE expression systems
  - TARGET antigen optimal presentation

- **System manufacturing**
  - STREAMLINE quality control processes
  - DECIPHER adjuvant mode of Action
## Examples

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NEW AND IMPROVED EXPRESSION SYSTEM THROUGH METABOLIC ENGINEERING

Example
System engineering

GAME XXL: Genomic And Metabolomic Engineering for controlled and robust antigens lipidation

INTEREST
Potential applications:
- Improve lipoprotein lipidation
- Non native lipidated proteins engineering
- Universal lipidation tool for addition of TLR2 agonist activity

ADVANTAGES
- Improve robustness of production process
- Decreased CoGs
- Streamlined analytical tools
- Generation of self-adjuvanted antigens

KNOW HOW
- Vector optimization
- Multiomics & functional analysis workflow
- Host system engineering and optimized process

IMPLEMENTATION OF INNOVATIVES TECHNOLOGICAL APPROACHES

Engineered production strain
Genomic engineering
Engineered strain improved for lipoprotein production

Original strain
Targeted approach
Yield improvement
Signatures
Multiomic approach

by BIOASTER
NEW AND OPTIMIZED VACCINES DELIVERY

Example
System delivery

NANOCAGE: versatile protein cage nanoparticles for target epitope surface display & heterologous protein packaging

INTEREST
- Target surface presentation & internal cargo loading
- Epitope repetitiveness (high immunogenicity)
- Versatile nanocage tool

ADVANTAGES
- In vitro auto-assembly
- Generation of nanoparticles in E.coli as well as other expression systems
- Wide array of applications

KNOW HOW
- Industrial USP & DSP process
- Biochemical & physical characterization
IN VITRO TOOLS AND EX VIVO MODELS FOR BIOLOGICAL READ OUTS

BIND IT: rapid reagent development for targets of interest

INTEREST
- Rapid access to protein binders/effectors specific for relevant biological targets
- Potential applications: in vitro diagnostics, therapeutics, vaccines, research

ADVANTAGES
- Continuous affinity improvement loop
- Fast and versatile (days to weeks)
- No need for immunization
- Low cost & reproducible in vitro production process (E. coli)
- No post-translational modifications
- Affinities to the picomolar range

KNOW HOW
- Protein expression and engineering
- Technology display
- Cell free production
- Next generation sequencing
ADJUVANT MODE OF ACTION DECIPHERING

MS-IMAGING: DESI-MS for in situ adjuvant tracking and inflammation monitoring

**INTEREST**
- *in situ* system vaccinology
- Application of metabolomics and proteomics, for the local characterization of vaccine and adjuvant inflammation/reactogenicity

**ADVANTAGES**
- Imaging by mass spectrometry (MSI) allows to analyze antigens, adjuvants and inflammatory lipids simultaneously
- High Resolution MSI allows both targeted and untargeted analyses for monitoring and mechanism comprehension
- DESI is a non-destructive technology compatible with histology

**KNOW HOW**
- DESI platform coupled to a Q Exactive™ HF (Thermo Scientific™) for highest sensitivity and resolution
- Expertise in metabolomics and proteomics for high-value data generation and interpretation
- Histology and histochemistry capacities for global imaging approaches

Adapted from Y. Fujimura & D. Miura, 2014
PRODUCT QUALITY PREDICTION THROUGH PREDICTIVE BIOMARKERS

INSIGHT CELLS: monitoring live cells growth through bioprocess biomarkers

INTEREST
- Dynamic monitoring of cell metabolism during vaccine production, for bioprocesses comprehension and optimization

ADVANTAGES
- Monitoring in real time of metabolites production and consumption, in a closed small-scale fermentation system
- Optimization of bioprocesses together with quality biomarker identification
- High-level NMR technology allowing dynamic metabolomics studies for bioprocesses comprehension

KNOW HOW
- Co-developer of the InsightCell approach, using the Insight MR™ probe from Bruker
- Expertise in NMR metabolomics, from wet lab to data interpretation
- Expertise in microbiology and bioprocesses
BIOMARKERS FOR POPULATION STRATIFICATION AND REACTOGENICITY/EFFICACY PREDICTION

Example
System Biology

Data management, infrastructure & algorithms

SUPERVISED ANALYSIS
- Multiomics analysis
- Cytometry analysis
- Interspecies analysis
- Temporal analysis

KNOWLEDGE DISCOVERY
- Signature
- Mechanism of action
- Pathway
- System biology

Deployed strategy & methodologies depend on biological questions

TECHNOLOGICAL APPLICATION
- Biomarker
- Clinical decision tools
- R&D decision tools
- High dimensional data visualization

Genomics
Transcriptomics
Proteomics
Metabolomics
Clinical data
Cytometry

Clustering
Unsupervised analysis
**Collect**
Biological samples

**Analyze**
Biological samples

- Immune cells
- Cytokines
- Antibodies

- Commensal/
  Infectious agents
- Microbiome

- Genomics
- Transcriptomics
- Proteomics
- Metabolomics
- Immunomics

**WE CONDUCT PROJECTS INTEGRATING CLINICAL STUDY DESIGN AND TECHNOLOGIES FOR TARGET VALIDATION**

- Executed in dedicated preclinical/clinical animal/human studies capitalizing on our network of experts and clinicians
- With adapted monitoring and study management overseen by our Clinical research associates
- Leading to traceable specimens of high quality capitalizing on advanced data management tools and storage and processing infrastructures
- With adapted monitoring and management of study
- Leading to traceable specimens of high quality
- Analysis through omics pipeline adapted to your needs
- Developed as reliable and validated methods from sample preparation to data generation
- Vaccine composition in function of the targeted population and pathogen characteristics
- Identify innovative biomarkers of medical value
- Improve/control/predict your biological production performance
- Existing or proposed vaccine composition

- Optimum signature for showing the highest prognostic/stratification/performance adapted to industry constrains
- Within an advance infrastructure and algorithms for time to results optimization (Machine Learning)
- That can be delivered as a visually integrated clinical multi/metric data
MOSAIC – PROJECT SCOPE 2.2
Understanding the mechanism of action of adjuvants to help select successful vaccine candidates earlier in the development process

- Preclinical studies
- Pivotal tox study
- Clinical study
- Blood

3 adjuvants
Model antigen
Blood

Multi-omics technologies
- Metabolomics, Proteomics, Transcriptomics, MS Imaging, Flow cytometry

Conventional analysis
- ELISA/ELISPOT, Neutralization assay
- Biochemical parameters, Histology

System vaccinology outcomes

Data integration & advanced data analysis

ADJUVANT MODE OF ACTION
60 MONTHS

COLLABORATIVE PROJECT
Probiotics represent an interesting source of immune modulators to increase resistance to respiratory tract infections. In this study, mice fed with L. Paracasei CNCM I-1518 showed reduced susceptibility to the influenza infection, associated with less accumulation of inflammatory cells in the lungs, faster viral clearance and general health improvement.

A UNIQUE MODEL

INDUSTRIAL APPLICATIONS

BIOASTER, a partner of choice from early stage to pre-industrial development

We develop specific technologies, ready for industrialization
- Standardized and automated processes
- Appropriate methods for samples collection and storage (Iso 9001)
- Automated sample preparation
- Complex signature translation to commonly used detection tools
- Expression systems optimization, including genomic strain engineering
- Upstream and downstream production process optimization

We handle and interpret complex data
- Integrated & expert data sciences
- Data management facilities ruled by tracking and control policies
- High data storage and cloud computing capacities
- Custom bioinformatic pipelines development
- Tailor-made visualization tools

BIOASTER, Technology Research Institute, to better share innovation
- International scientific network & partners
- 80+ scientific experts, technology platforms, unique state of the art equipments
- Professional projects management and tools
- Opportunity of sharing costs and risks of your innovation projects
- Research and development collaborative projects or services
- A multidisciplinary team of experts dedicated to diagnostics projects

BIOASTER PROGRAMS
Diagnostic
Antimicrobials
Vaccines
Microbiota

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