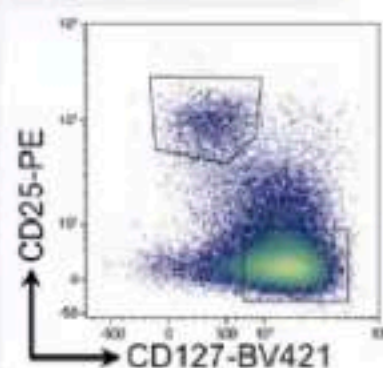
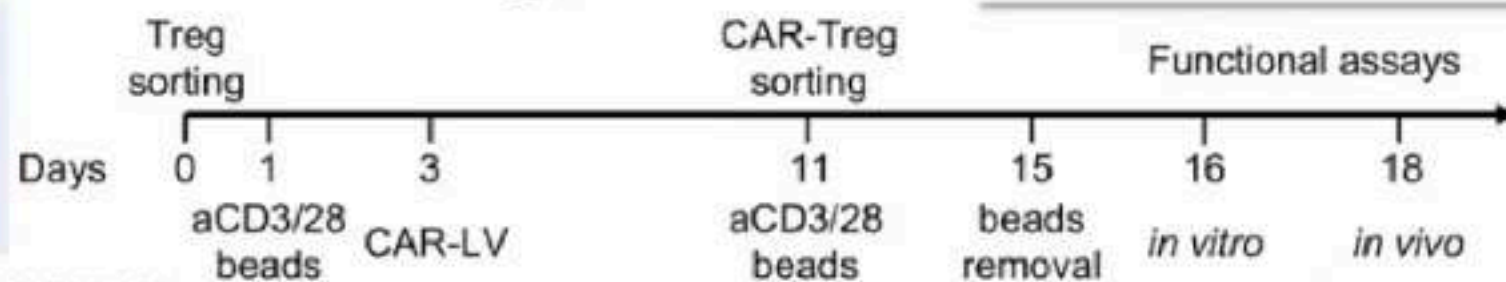
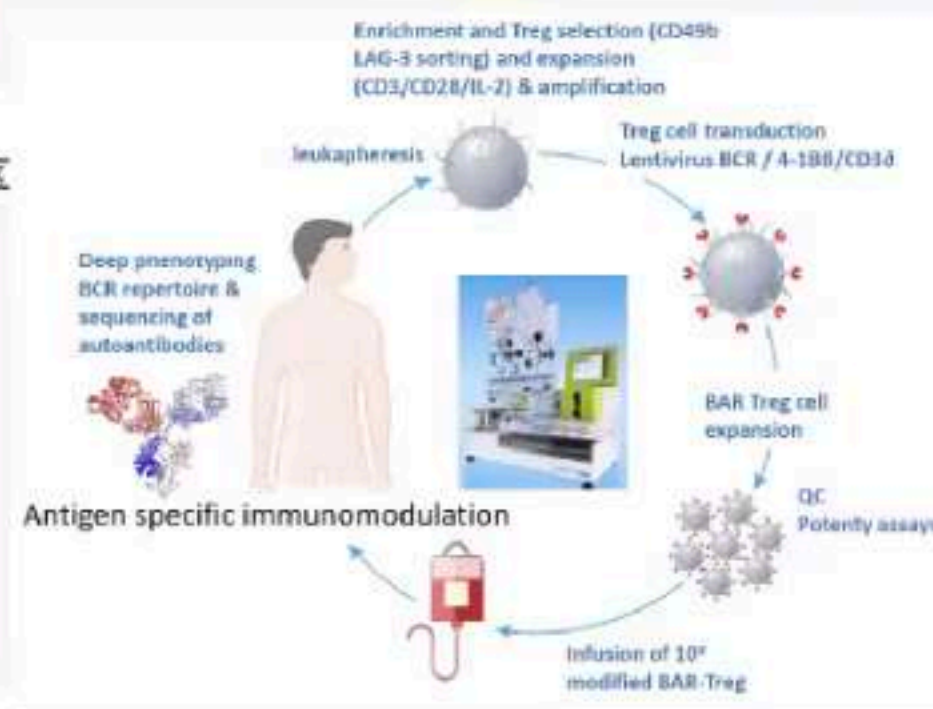
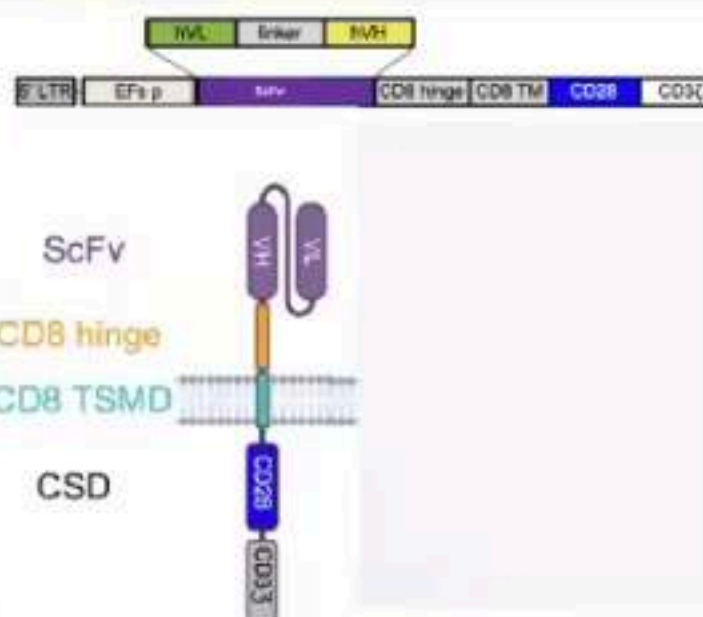


# Génération de CAR-Treg ciblés

## Treg cell sorting

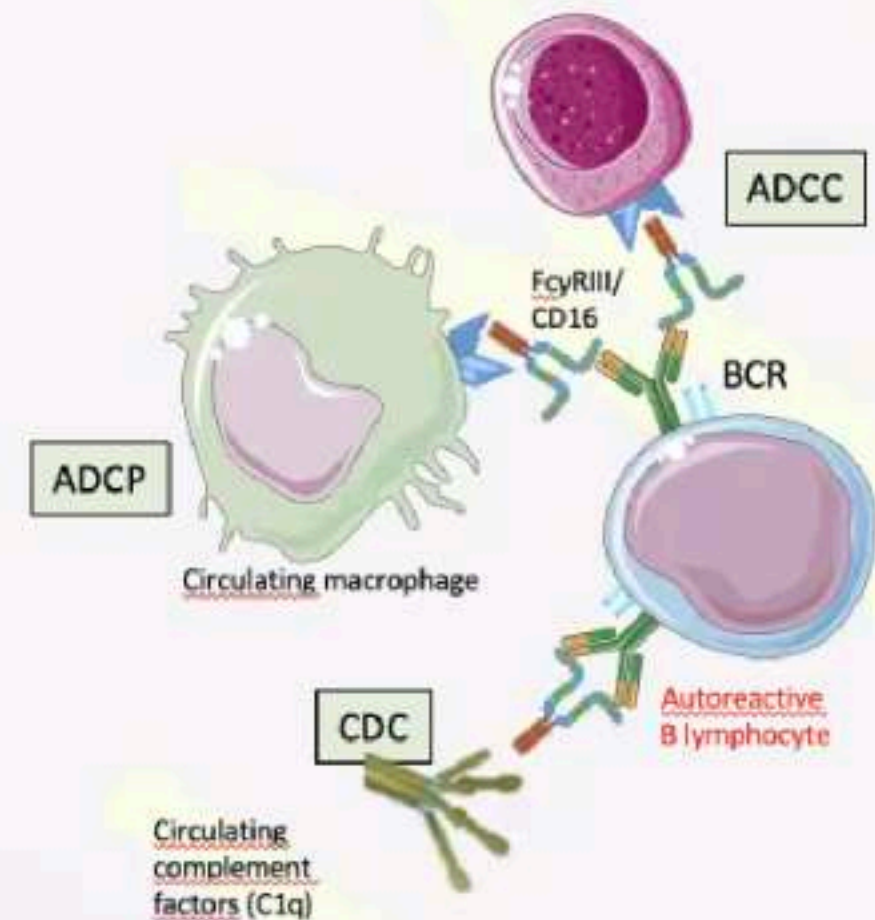


## Lentiviral vector manufacturing



## NK armés pour une IMMUNOTHÉRAPIE SPÉCIFIQUE

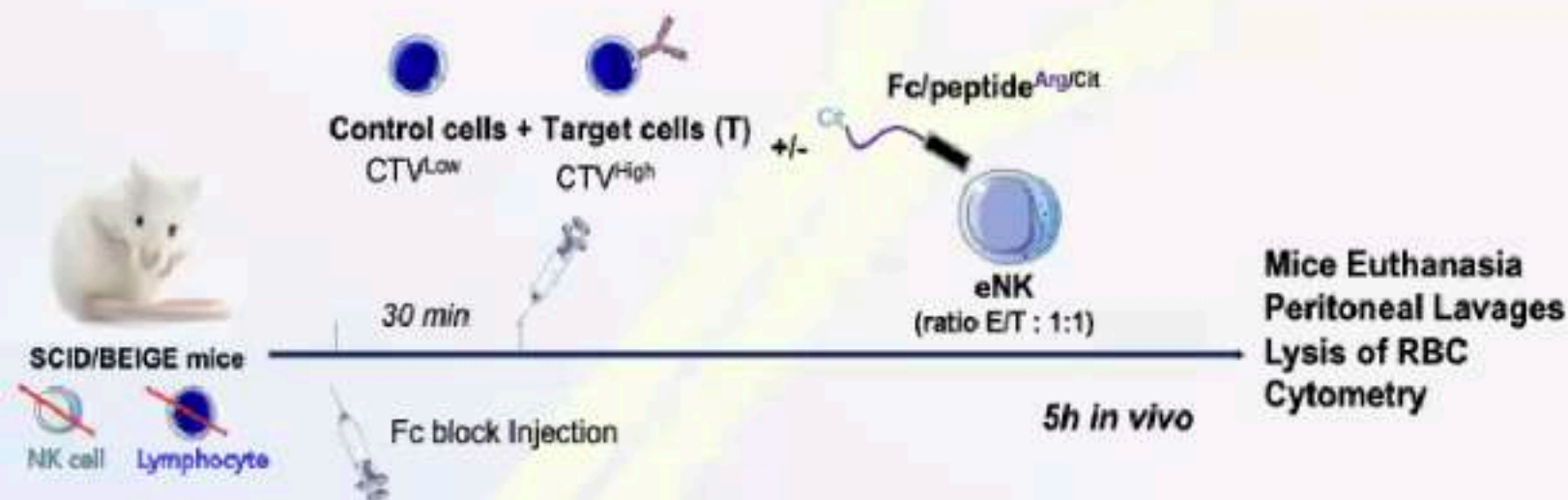
- basée sur la destruction spécifique des lymphocytes B immatures et des lymphocytes B mémoires par ciblage du BCR par recrutement des cellules effectrices NK et macrophages
- le fragment Fc d'IgG1 se lie au CD16 des cellules effectrices pour induire une ADCC et/ou une ADCP



Propriété du consortium CURE RA

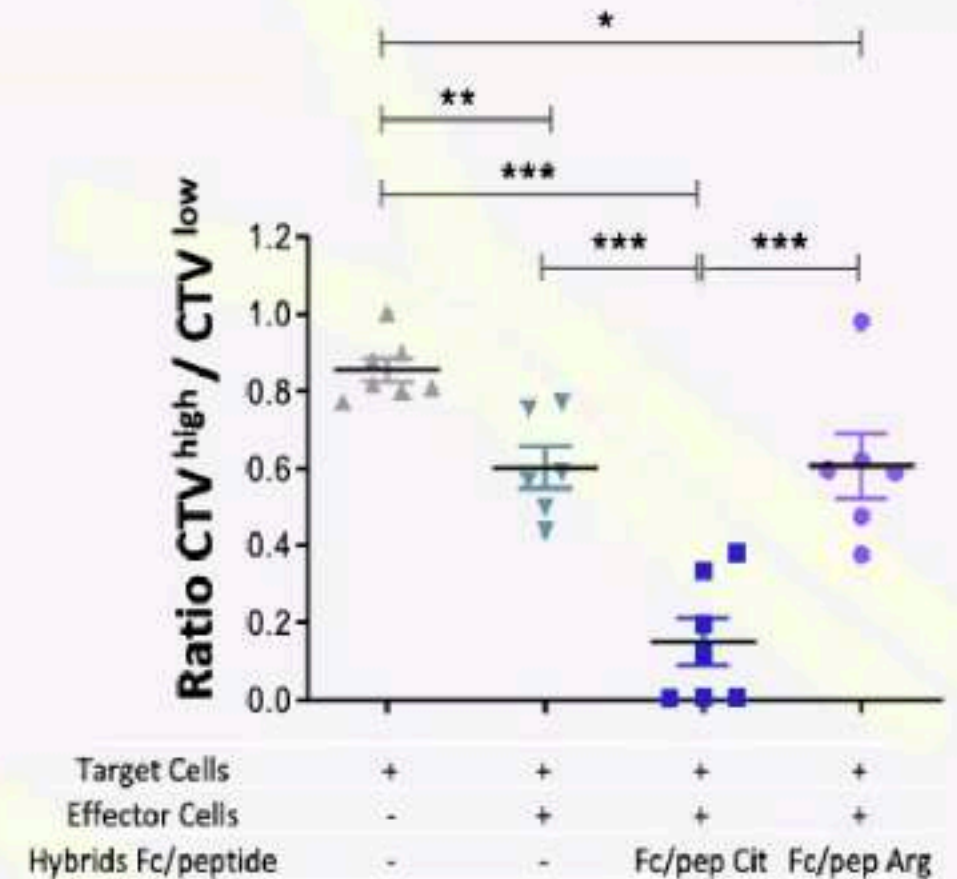


# Armed NK-T cells : Selective B cells targeting



**NK cells armed with hybrid molecules  
Induce ACPA<sup>+</sup> B cell lysis**

- Efficient in vivo
- Specific
- Dose effect
- Reproducible



3 patents  
1 spin-off ARTHRITIS4CURE

ARTHRITIS  
Recherche & Rhumatismes

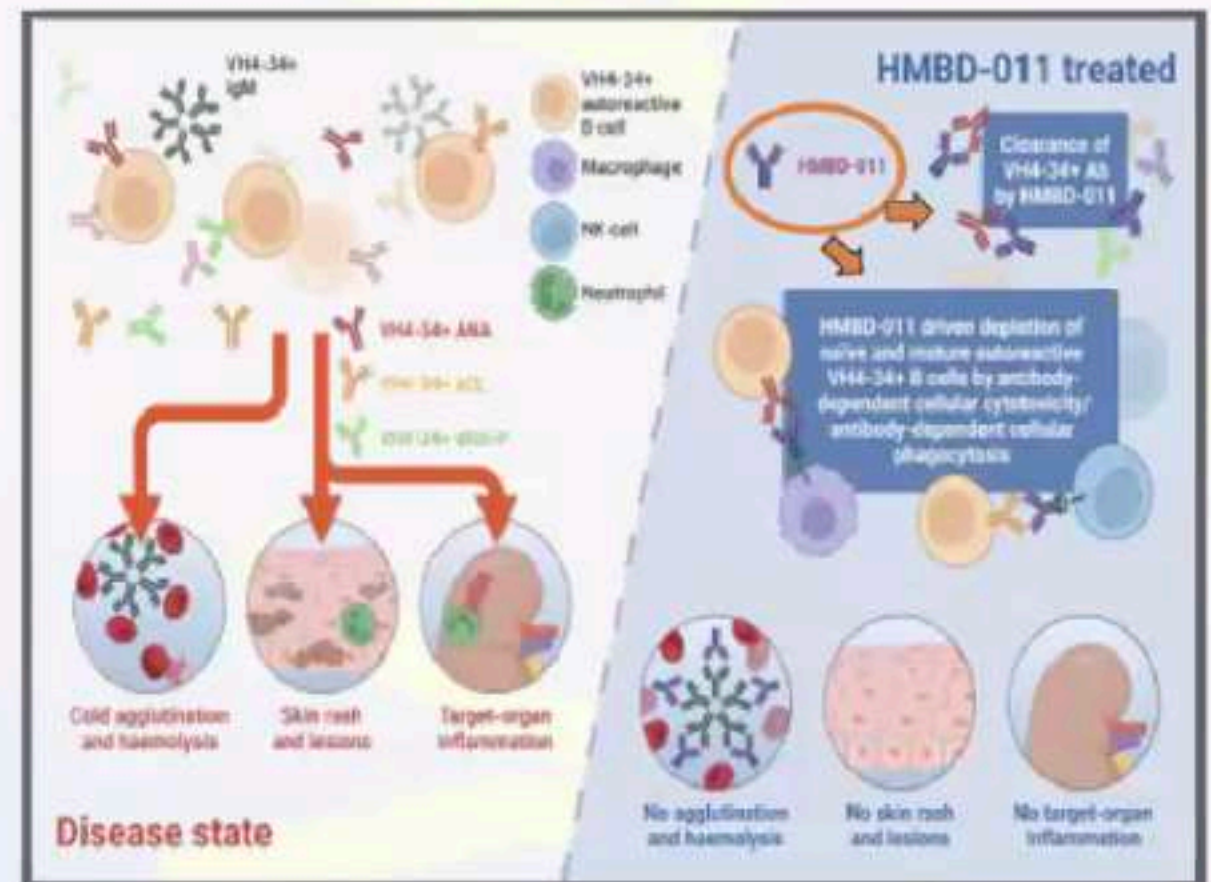


bpi france Inserm

## mAb anti-idiotypic VH4-34+ in SLE

- VH4-34 is an intrinsically autoreactive antibody **heavy chain**
- **Variable region** with a germline-encoded in framework region (FR1) (normally excluded from the mature B cell repertoire)
- In SLE, VH4-34+ B cells undergo expansion and affinity
- About 50% of SLE patients have elevated levels of VH4-34+ IgG
- **Develop mAb anti-idiotypic (HMBD-011, 9G4)**

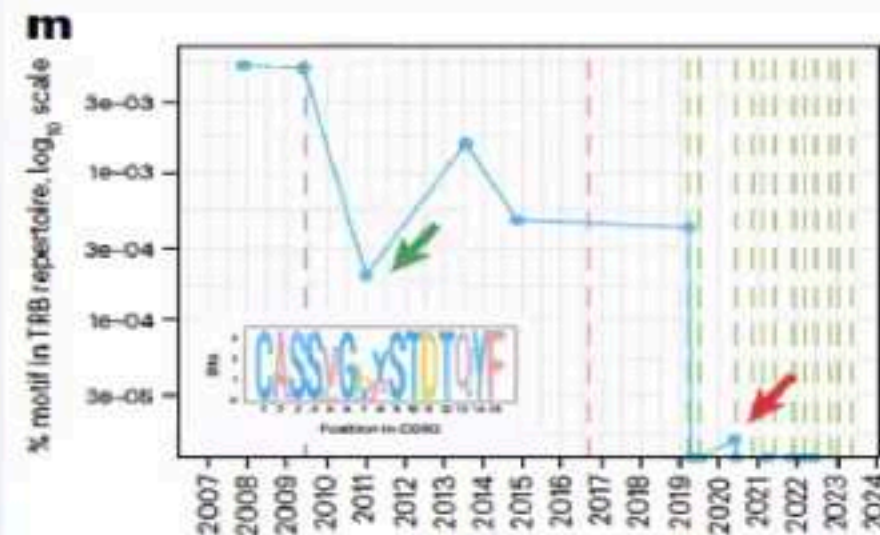
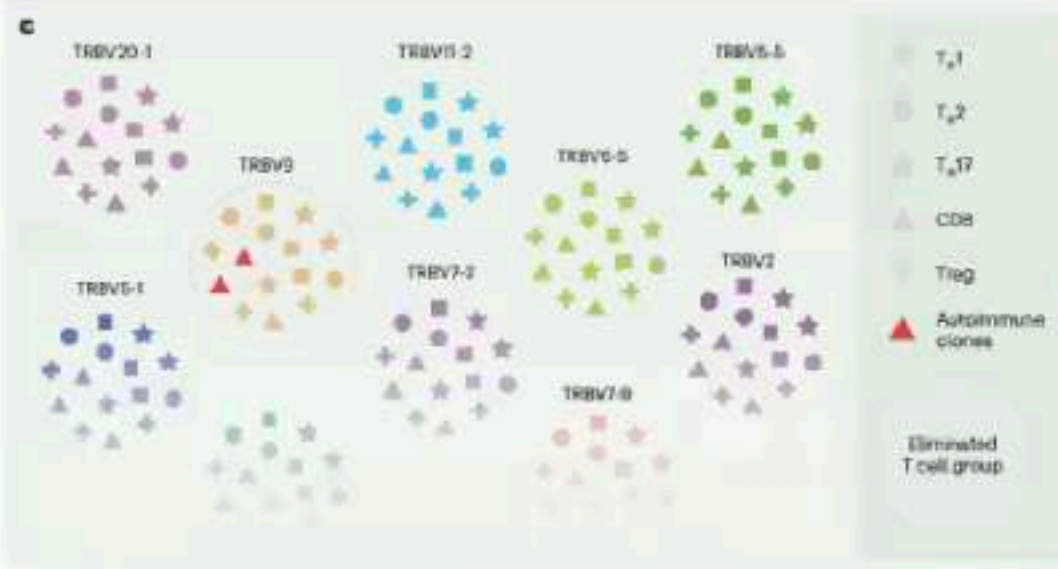
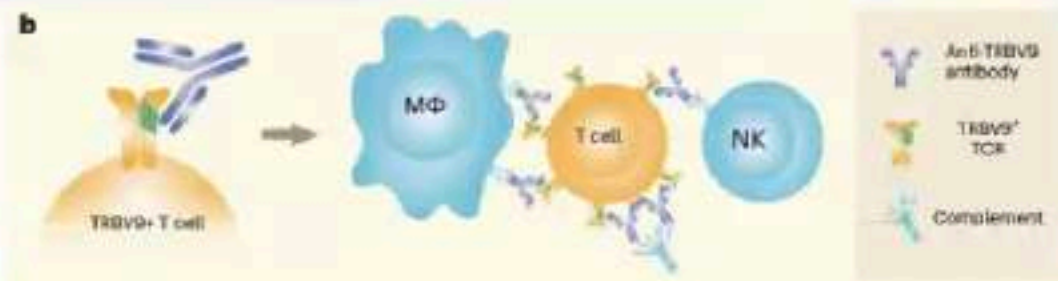
HMBD-011 can deplete VH4-34+ autoantibodies and autoreactive B cells to address underlying disease pathology in lupus and CAD







# Targeted depletion of TRBV9<sup>+</sup> T cells as immunotherapy in a patient with ankylosing spondylitis

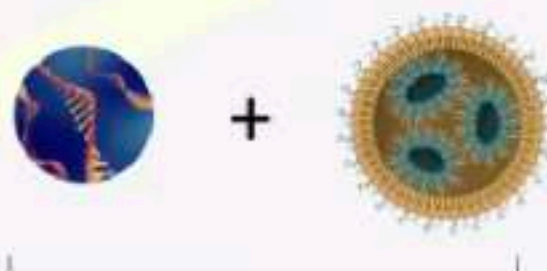


# Nanomédecine à base d'ARN



ARNs synthétiques  
modifiés

Formulation lipidique  
optimisée



Formulation non  
virale d'ARN  
thérapeutiques

ARNs  
biologiques

Particules lentivirales  
chimériques



Formulation  
lentivirale d'ARN  
biologiques

1

2



Ciblage in vivo des macrophages

## Partners:

INSERM

CHU Montpellier

Université Montpellier

Institut Charles Gerhardt Montpellier

Institut de Génomique Fonctionnelle

Flash Therapeutics



INSERM

ICGM  
Institut Charles Gerhardt Montpellier

flash  
THERAPEUTICS

IGF



# Modélisation de la réponse immunitaire et IA



- Modèles physico-mathématiques pour le test et la prédiction de la dynamique des populations cellulaires (L2C-IMAG) :

- modèles à compartiments (dynamique temporelle, systèmes d'EDO (ordinaires) sur les populations cellulaires (boîte à outils DSAIRM))
- modèles spatialisés (dynamiques spatio-temporelles sur les populations cellulaires, systèmes d'EDP (partielles))
- modèles de réseaux spatio-temporels pour identifier les rôles des cellules et leurs interactions réciproques dans le développement des maladies par rapport à l'homéostasie des tissus sains

$$\frac{\partial u}{\partial t} = D_1 \Delta u - k_1 u(\mathbf{r}, t) + k_2 v(\mathbf{r}, t) \sum_i S(\mathbf{r} - \mathbf{r}_i(t)),$$

$$\frac{\partial v}{\partial t} = D_2 \Delta v + k_1 u(\mathbf{r}, t) - k_2 v(\mathbf{r}, t) \sum_i S(\mathbf{r} - \mathbf{r}_i(t)).$$

**Modélisation physico-mathématique**  
**Collaboration CINÉS et HDS du CHU**



**Objectif : Développer des outils numériques pour le diagnostic et la prédiction des maladies auto-immunes**

**Données biologiques multi omics (microscopie, cytométrie de flux, ...) à partir de modèles expérimentaux (in vitro, organoïdes et animaux)**



**Données Bioinformatiques**

**Partners: IMGT, IRCM**

**Parmeggiani A.**

**IMAG-L2C CHARLES COULOMB**





# Clinical Centre dedicated to Autoimmunity

Centre Interdisciplinaire  
maladies auto-immunes



patient reception



Multidisciplinary consultation  
Information, consent

sampling



Patient education

Recruitment into a cohort

Personalized therapy  
Clinical trials

- ✓ Centre de soins : prise en charge **multidisciplinaire**
- ✓ accès **biothérapies**
- ✓ Accès au « **Deep phenotyping platform** »
- ✓ Mise en place des **cohortes**
- ✓ Education thérapeutique



## Deep phenotyping

- including BCR,
- NGS,
- VDJ,
- immunophenotype,
- epitope mapping

## Plateau bioinfo IHU

HDS CHU

Calculateur CINES ADAstra  
CRB





# Immun4Cure cohorts

## OBJECTIVES

### Identification of biomarkers

- Sub-group of patients
- Stratification of patients in each AID
- Predictive signature for treatment response
- Pronostic signature of the AID
- Comparison of signatures inter/intra AID
- Identification of sub-populations for treatment

### Design of biomolecules

### Modelling of auto-immunity

## METHODS

### Cohorts with 1 000 patients

- Systemic Lupus Erythematosus (SLE)
- Scleroderma (SSc)
- Early Rheumatoid Arthritis (RA)
- Early Multiple Sclerosis (MS)

### Annual follow-up for 5 years

- Less than one year of evolution
- No biotherapy
- 200 subjects with annual follow-up
- Collections of plasma, DNA, cells, RNA (CRB)
- Identification of B & T répertoires
- Analysis of VDJ rearrangement
- Immunophenotyping
- NGS
- RNAseq, epigenetics
- Auto-antibody chip

## Immun4Cure cohorts

### Early SLE cohort

- Symptom duration < 1 year  
or  
Start before 15 year
- 2010 ACR EULAR criteria
- ANA +, **rituximab naïve**
- Active lupus w/SLEDAI>6

#### Clinical data

Age, BMI, contraception, tobacco ...

Date diagnosis, disease duration,  
SLEDAI-2K score

**Therapies** : IS, steroids , belimumab, anafrolumab

**Biology**: creatinine, proteinuria

Immunology: AAN, C3 C4, antiADN ....

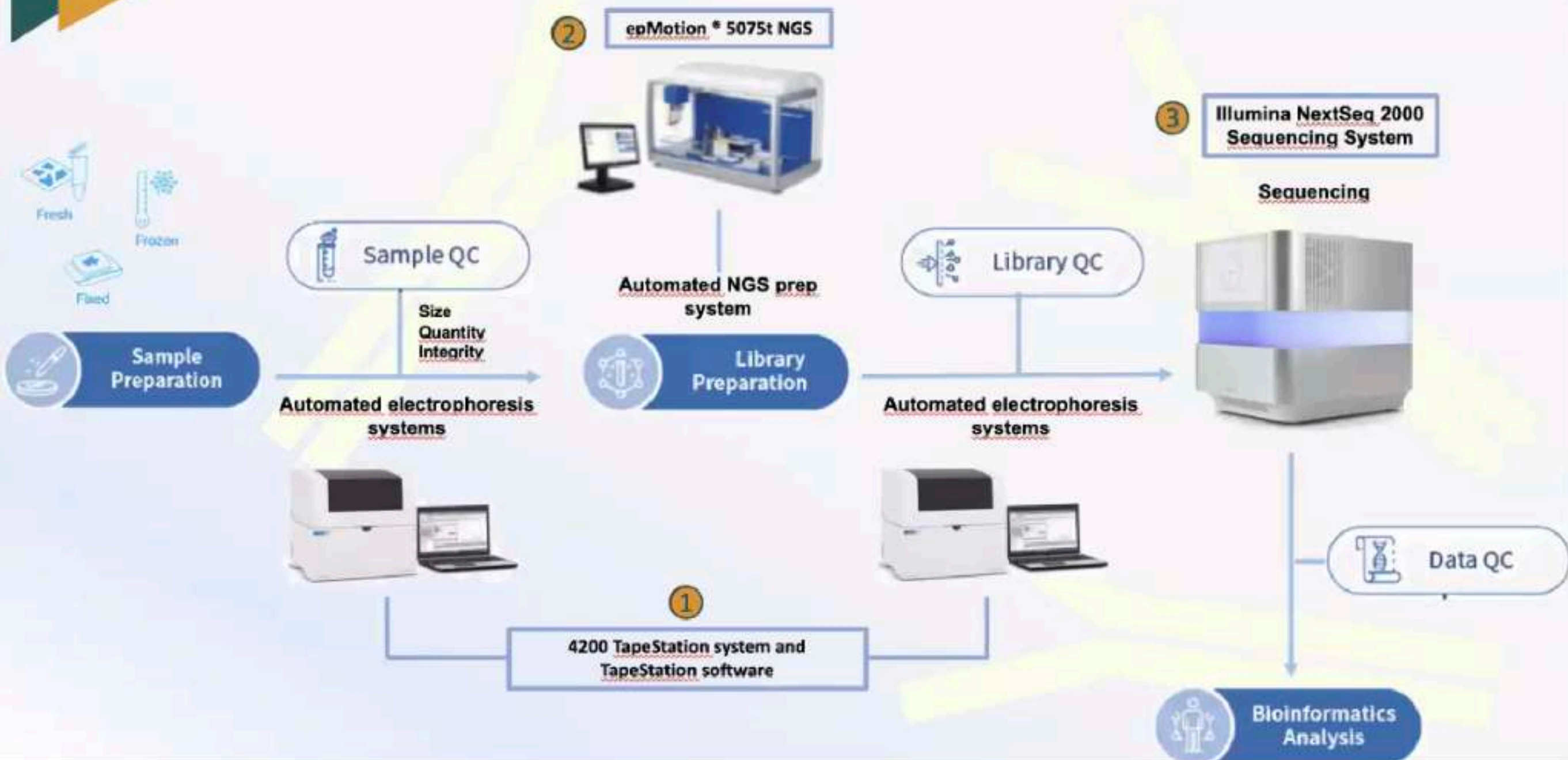
Imaging: CNS, kidney

Biopsy: kidney, CSF

...



# Automated solution for RNAseq & DNAseq workflows



## Samples



- **Blood 7 tubes 7 ml** for PBMC, serum,
- RNA → Paxgene tubes
- Bcult tubes **B cells** → for cell sorting
- Depending on availabilities
  - Saliva
  - copro
  - Skin biopsy
  - Other tissues: kidneys, lungs, ...

### Deep phenotyping

- BCR
- NGS
- VDJ
- Immunophenotyping
- Epitope mapping

### Bioinformatics & AI

- IHU Bioinfo Platform
- CHU Health Data Hosting
- IHU Biological Resources Centre





## Training & Education



UNIVERSITÉ DE  
MONTPELLIER



### Professional training : BioOcc, training programs for bioproduction

- ✓ TRAINING PLATFORM FOR BIOPRODUCTION in GMP facilities
- ✓ 4 SPECIALIZED HEALTH PROFESSIONAL MASTERS
- ✓ EUROPEAN MASTER'S PROGRAM - CHARM-EU ALLIANCE  
Trinity College Dublin, Universities Barcelona, Montpellier, Utrecht, Budapest



### MD, Pharmacy

- ✓ TEACHING UNIT dedicated to cell & immuno therapies in the MD & pharmacist's cursus
- ✓ DIGITAL HEALTH SCHOOL for medical training (ESN by UM)



### IMMUN4CURE PhD program

- ✓ In partnership with UM doctoral school
- ✓ 20 PhD / year : training by research

Call « Compétences et Métiers d'Avenir »

- Bio'Occ : Biotherapy and Bioproduction in Occitania

- Digital Health School (Ecole de Santé Numérique (ESNbyUM))

Bio'Occ



Support 8 M€

## Governance

## INSERM FOUNDATION

### ADMINISTRATIVE COUNCIL of the IMMUN4CURE FOUNDATION

Chaired by Pr A FISCHER

InsERM CHU  



## COMEX



C. JORGENSEN

DIRECTOR

Scientific coord.  
S. Kremmer



Administrative  
Division

C. LACOMBE

- Finances
- Human Ressources
- IHU Manager
- Support services
- Technical service
- Infrastructure



Scientific  
Division

F. DIQUAD

- Cellular Immunotherapy
- Molecular Medicine
- Regenerative Medicine
- Immunology & Immunotherapy
- Bioinformatics & Molecular Modelling



Medical  
Division

G. CARTRON

- Clinical trials
- Regulatory Issues
- Ethical issues
- Cohorts
- Coord. CRB & data
- CIMA clinical centre



Training  
Division

J. DE VOS

- Call for PhD
- European Master
- Integration of teaching Unit in medical & pharmaceutical curriculum
- Traineeship coordination
- Organisation of technicians training



Valorisation  
Division

TO BE RECRUITED

- Business Developer
- Interaction with SATT
- Legal issues
- Sourcing
- Valorisation and patents
- Contracts