

# Inauguration Chaire UCB

## Rhumatismes inflammatoires et systémiques



9 mai 2012



# Inauguration

***Professeur Jacques Melin***

Vice-recteur  
Secteur des Sciences de la santé

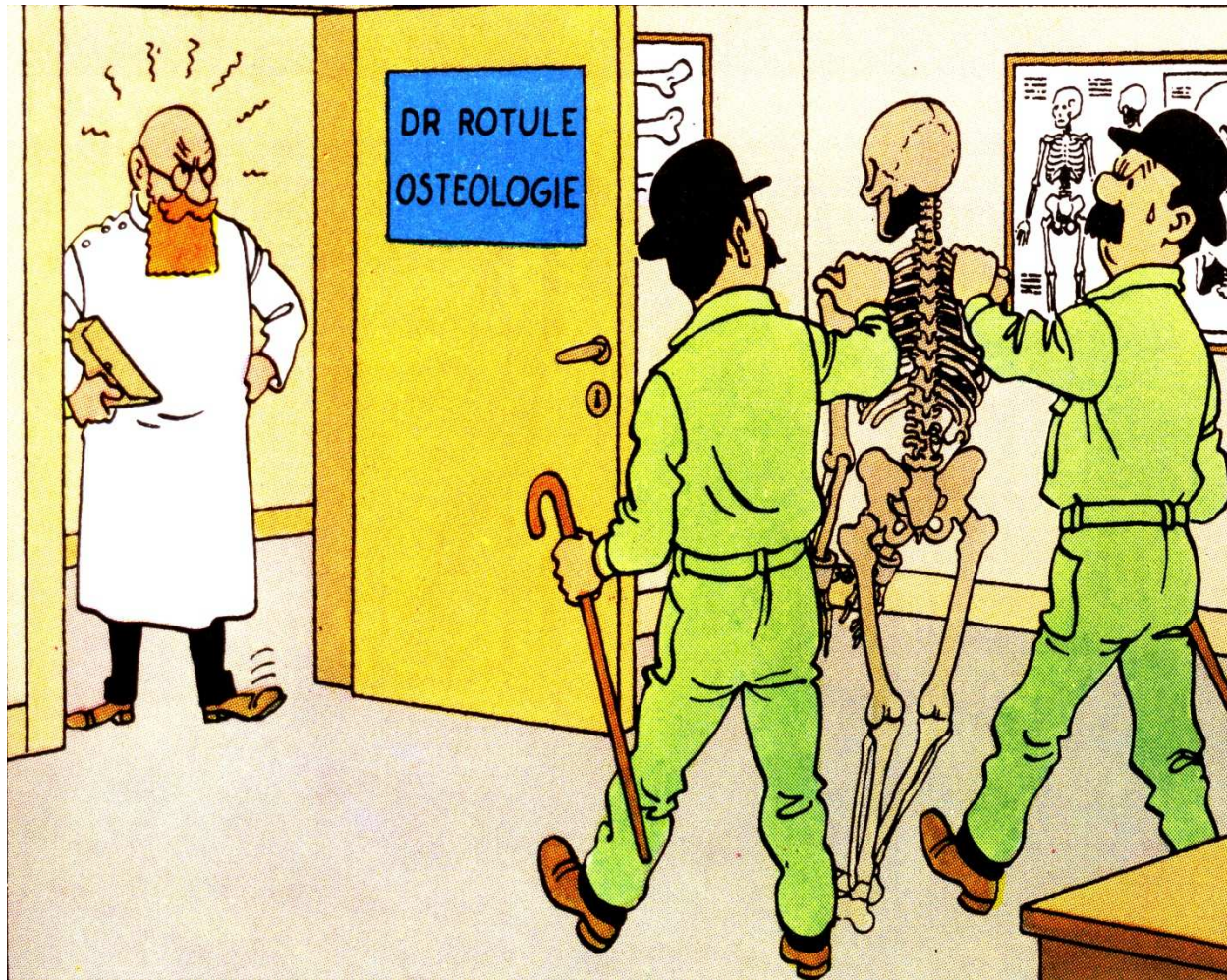


# La rhumatologie au XXI<sup>e</sup> siècle: une science clinique

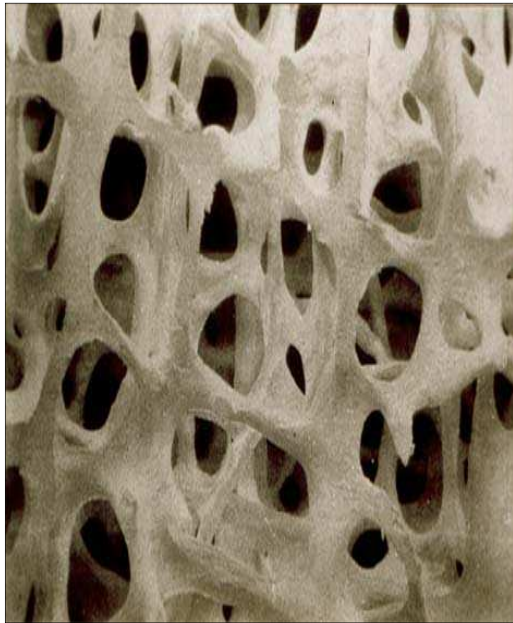
***Professeur Frédéric Houssiau***

Faculté de médecine et médecine dentaire  
Institut de recherche expérimentale et clinique  
Pôle de Pathologies rhumatismales

## La rhumatologie par Hergé



# Ostéoporose



**Os normal**



**Os porotique**



**Tassement  
vertébral**

# Arthrose



**Polyarthrose**

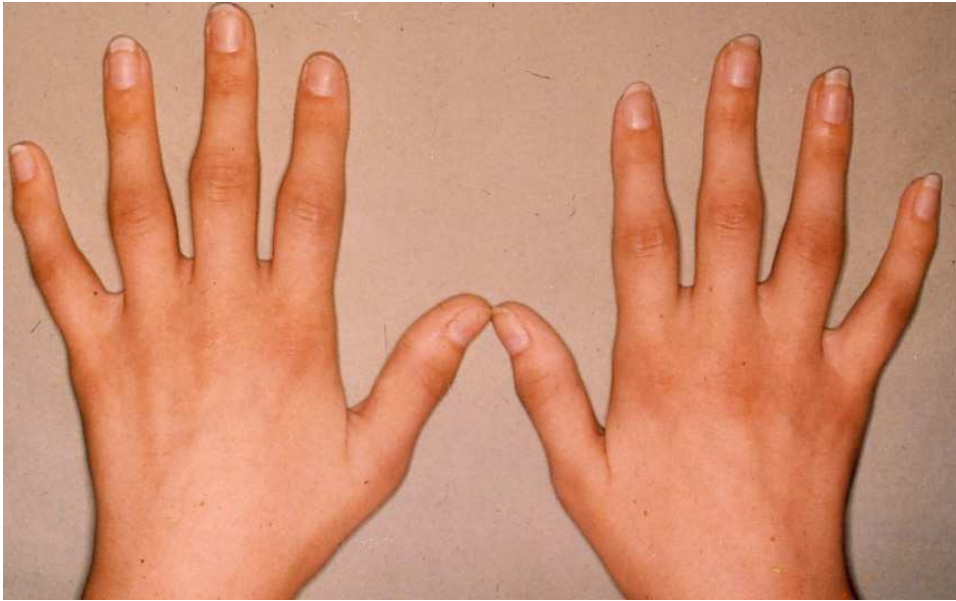


**Coxarthrose**

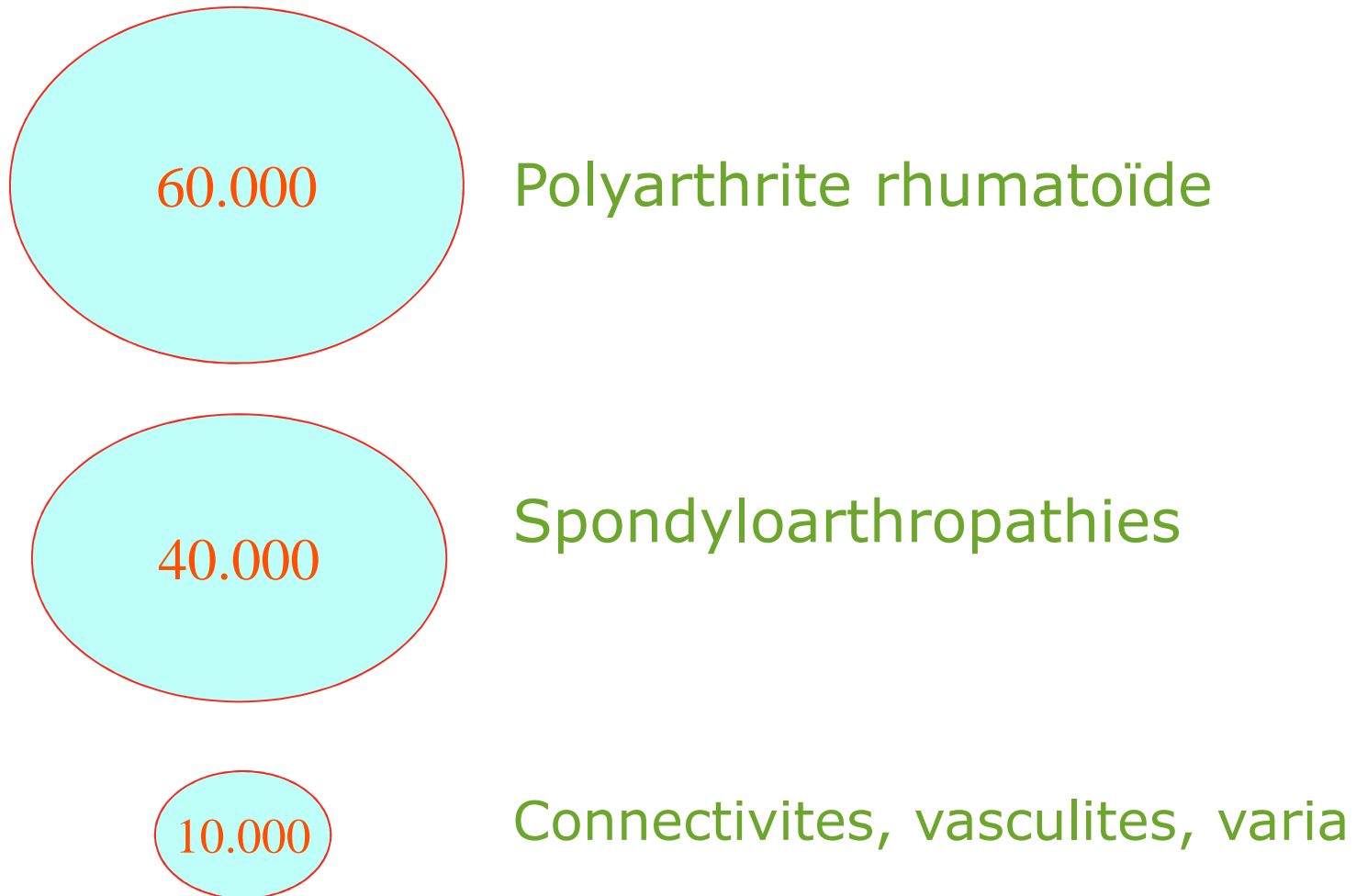


**Gonarthrose**

# L'arthrite enflamme les articulations

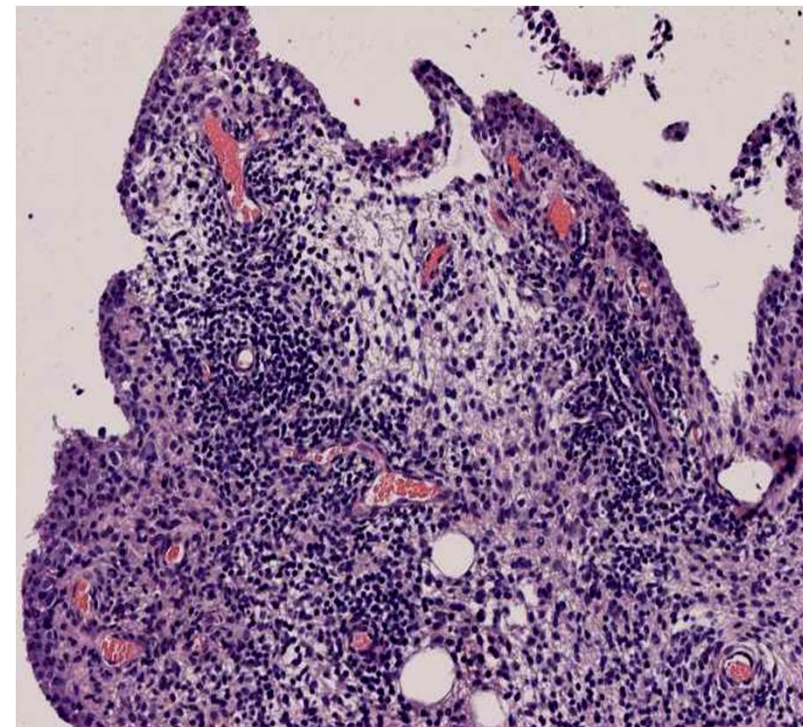
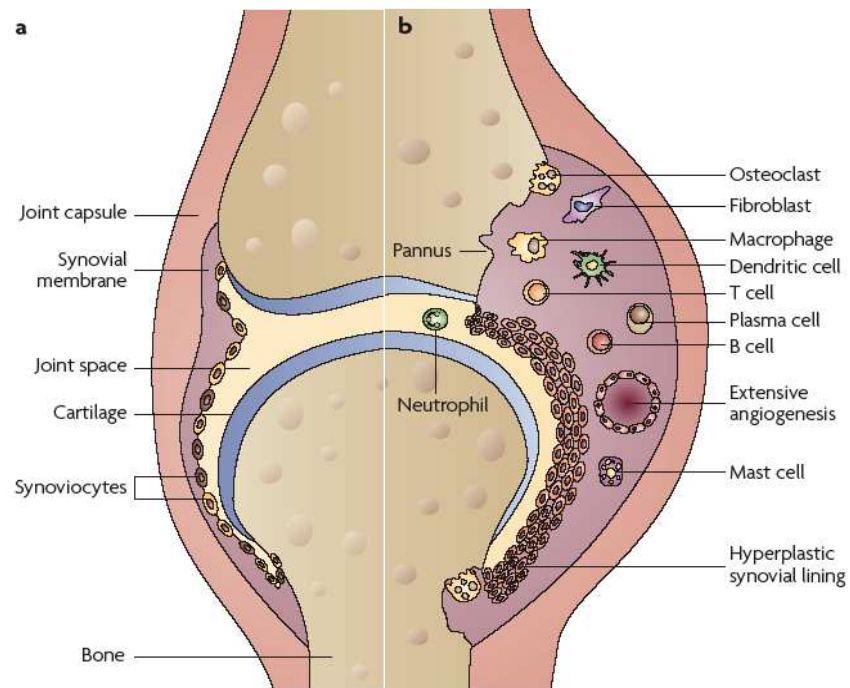


# Les maladies rhumatismales inflammatoires ne sont pas rares

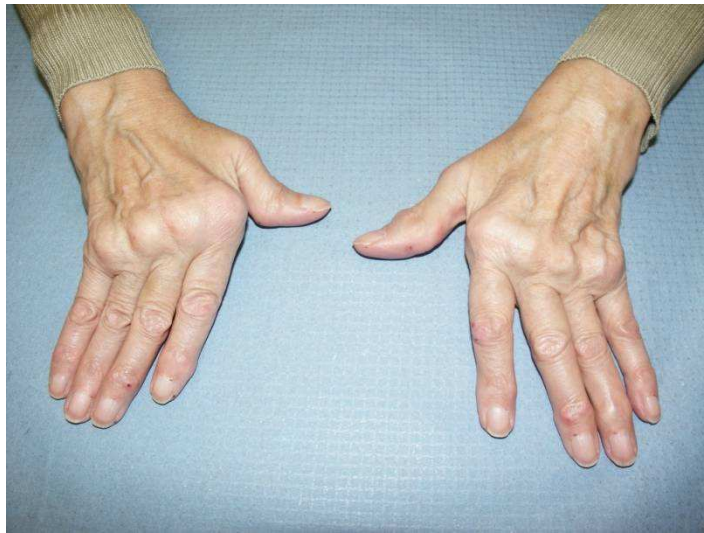




# Maladies inflammatoires de la synoviale



# L'arthrite déformante



# L'arthrite ankylose



# L'arthrite détruit les articulations



**Normal**

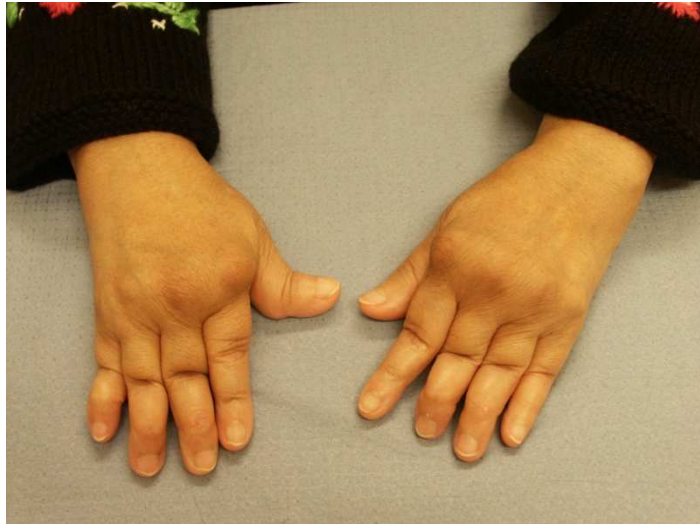


**Polyarthrite**

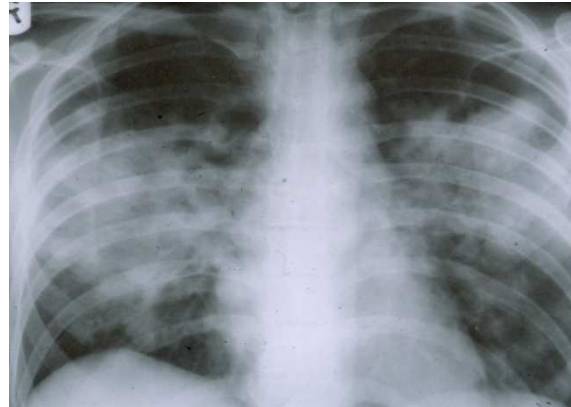
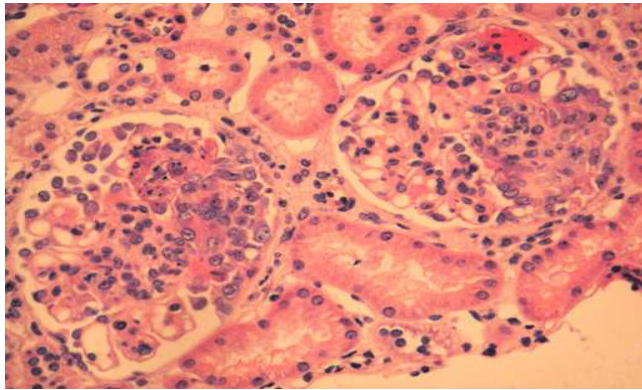
# L'arthrite détruit les articulations



# L'arthrite provoque du handicap



# Au-delà de l'arthrite...



**Rhumatisme  
s  
systémiques**



# L'arthrite concerne les enfants







## L'arthrite peut réduire l'espérance de vie

Lupus érythémateux disséminé sévère

80% survie à 15 ans

Mais, maladie qui concerne la femme jeune

Donc, 1/5 probabilité de décéder à 35 ans si la maladie commence à 20 ans...



## Les progrès engrangés

Mieux mesurer

Mieux imager

Mieux comprendre

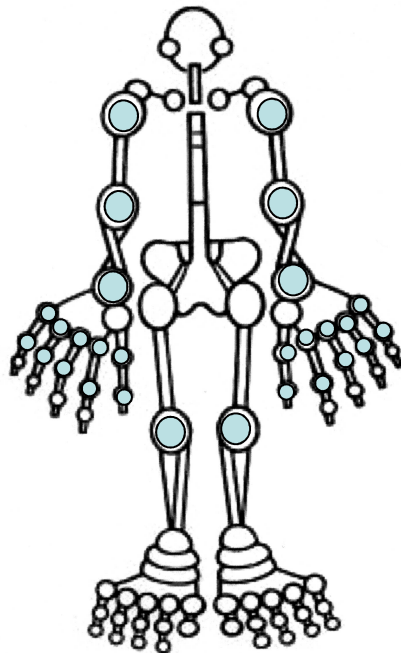
Mieux soigner

Approche globale

Mesurez tout ce que vous pouvez et rendez  
mesurable ce qui ne l'est pas encore  
Galileo Galilei

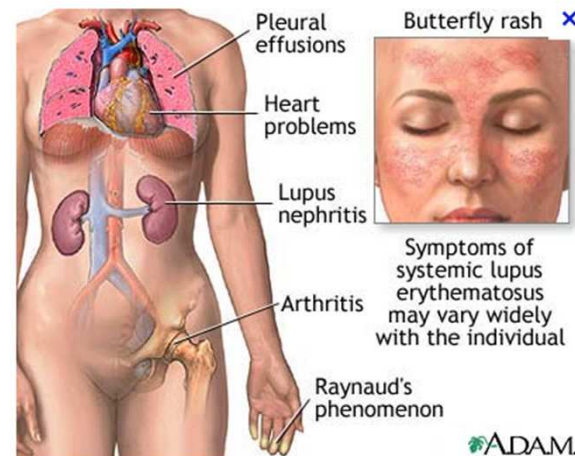
## Mieux mesurer

### Polyarthrite



DAS28  
CRP  
Handicap  
Score Rx  
Score Echo  
Qualité de vie

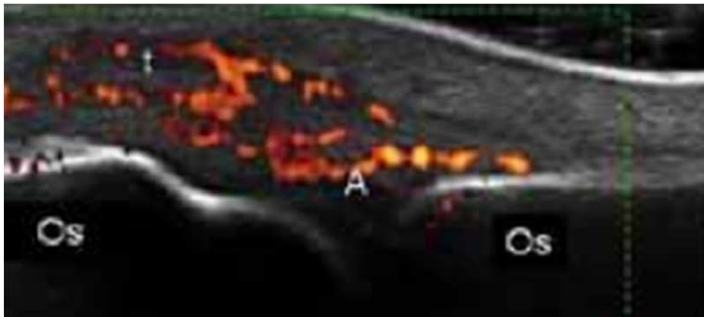
### Lupus



Sledai  
Bilag  
Slicc  
Eclam  
Anticorps

Activité *versus* dommage chronique  
Biomarqueurs diagnostic/pronostic

# Mieux imager



Echographie/D  
oppler



IRM

# Mieux comprendre



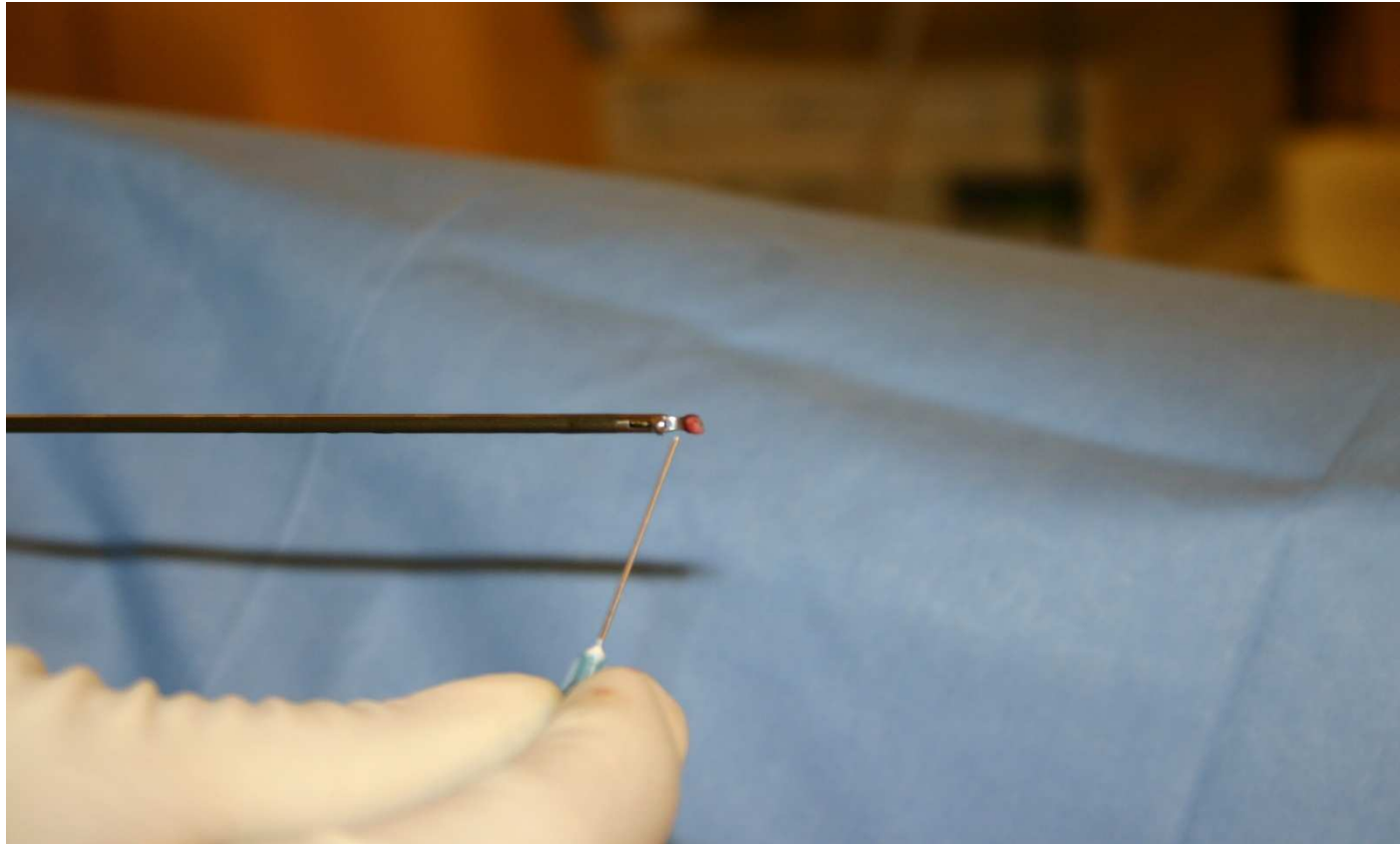
Mini-arthroscopie

# L'arthrite en direct



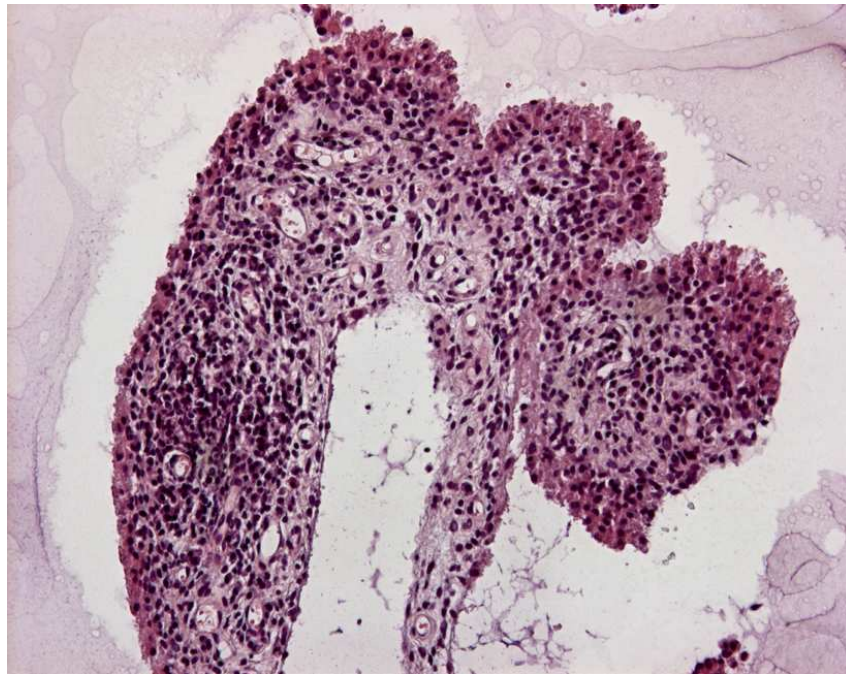
Hyperplasie synoviale

# Biopsies synoviales

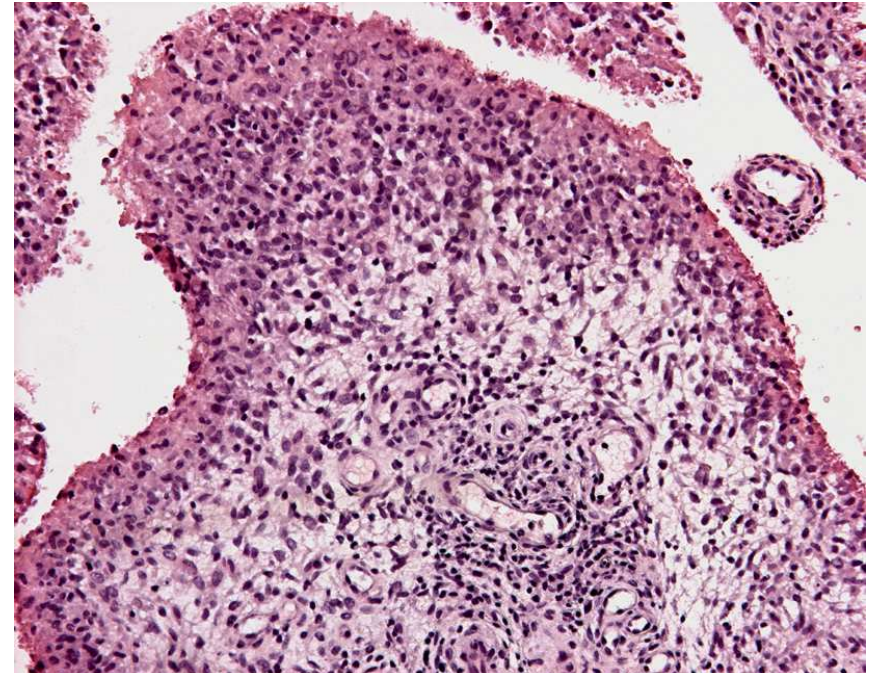


# Biopsies synoviales

Lupus



Polyarthrite



La même image





# Signature moléculaire

Gènes



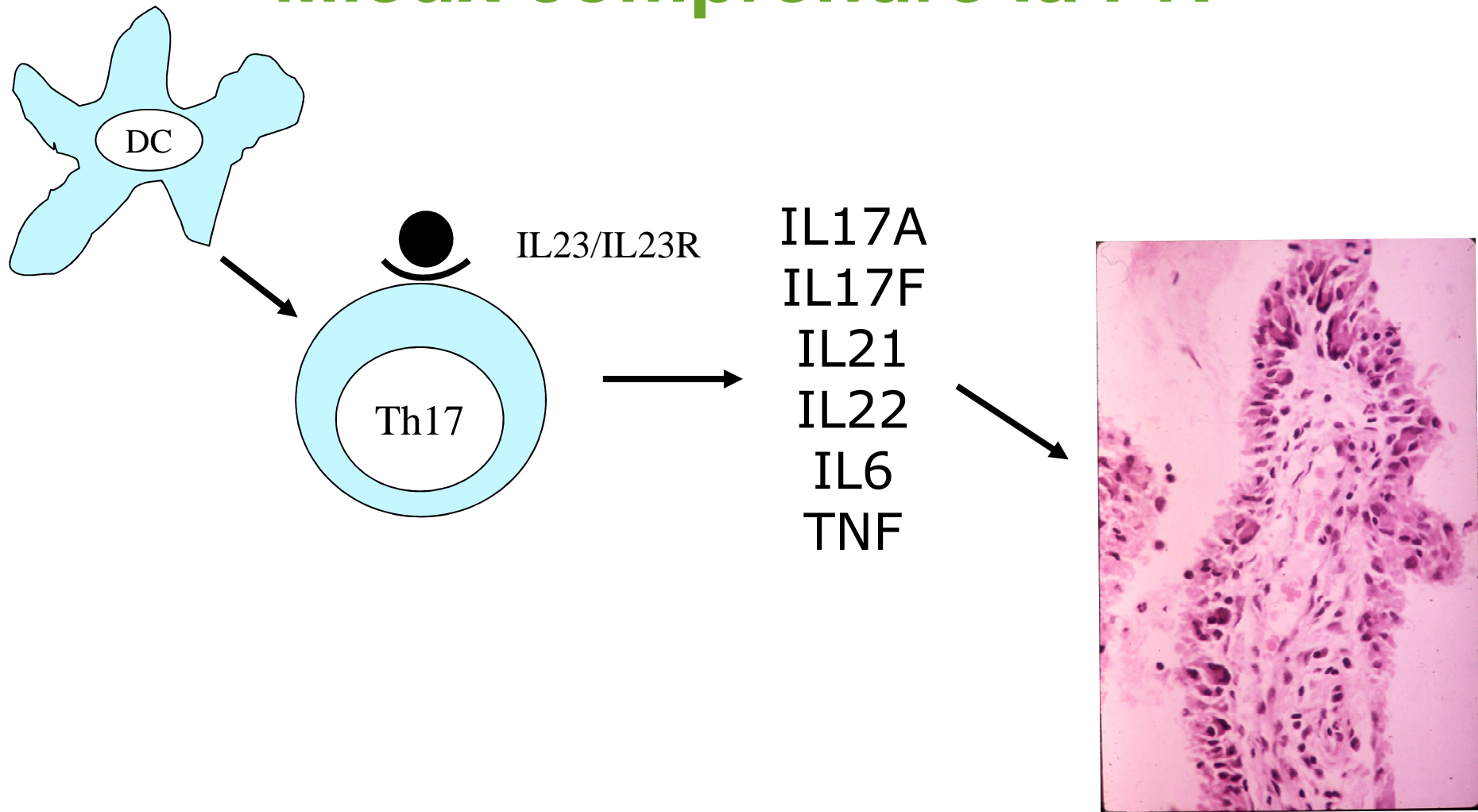
Profil d'expression de nos  
40.000 gènes peut être  
étudié sur... un cm<sup>2</sup>!

Protéines



Inflammation  
Destruction

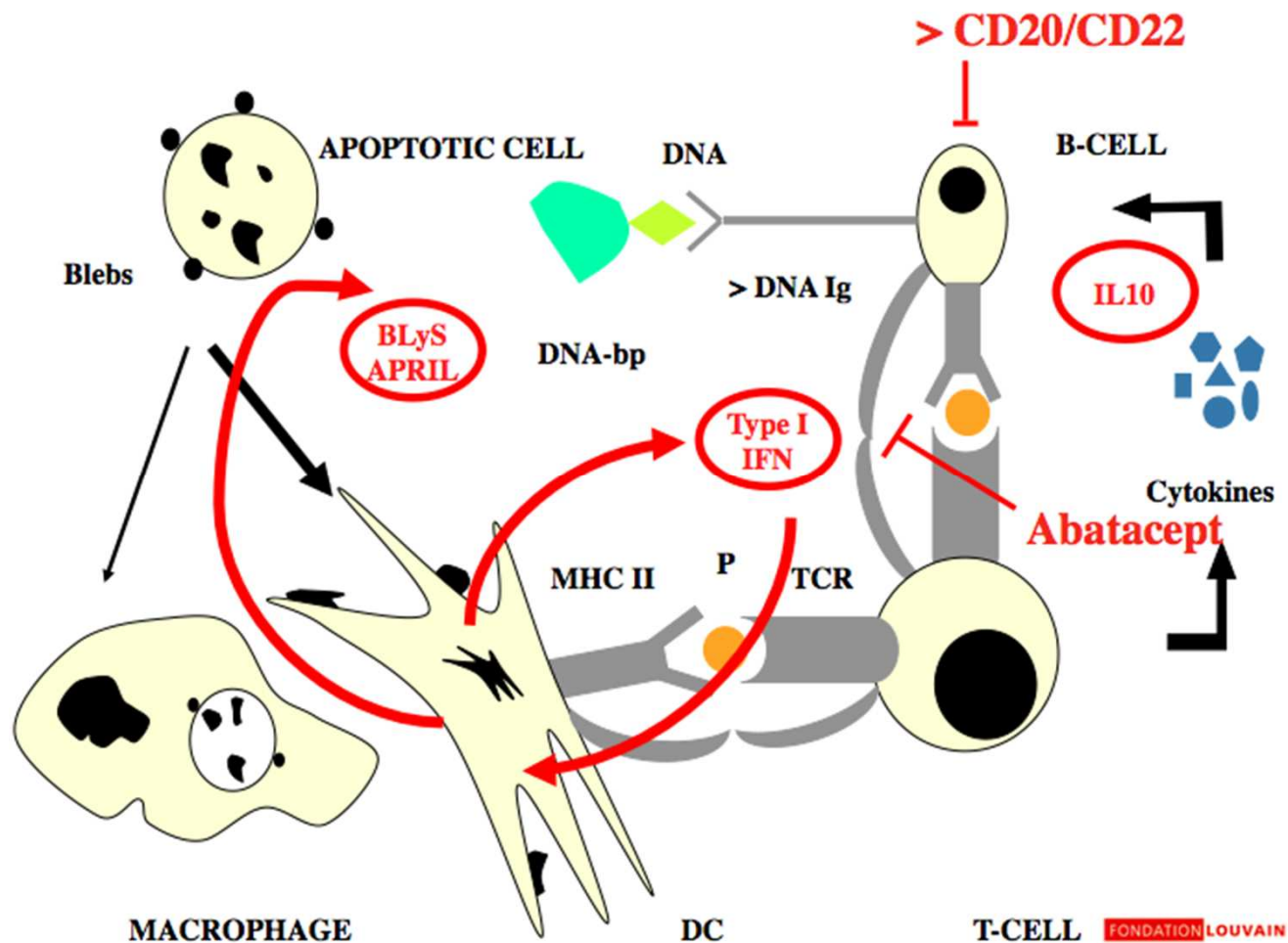
# Mieux comprendre la PR



# Une déferlante thérapeutique

Cible	Nom générique	Nom déposé	Industrie
IL1	anakinra	Kineret	Amgen
	canakinumab	Ilaris	Novartis
IL6	tocilizumab	RoActemra	Roche
TNF	infliximab	Remicade	Merck
	etanercept	Enbrel	Pfizer
	adalimumab	Humira	Abbott
	golimumab	Simponi	Merck
	certolizumab	Cimzia	UCB
CD20	rituximab	MabThera	Roche
CD28	abatacept	Orencia	BMS

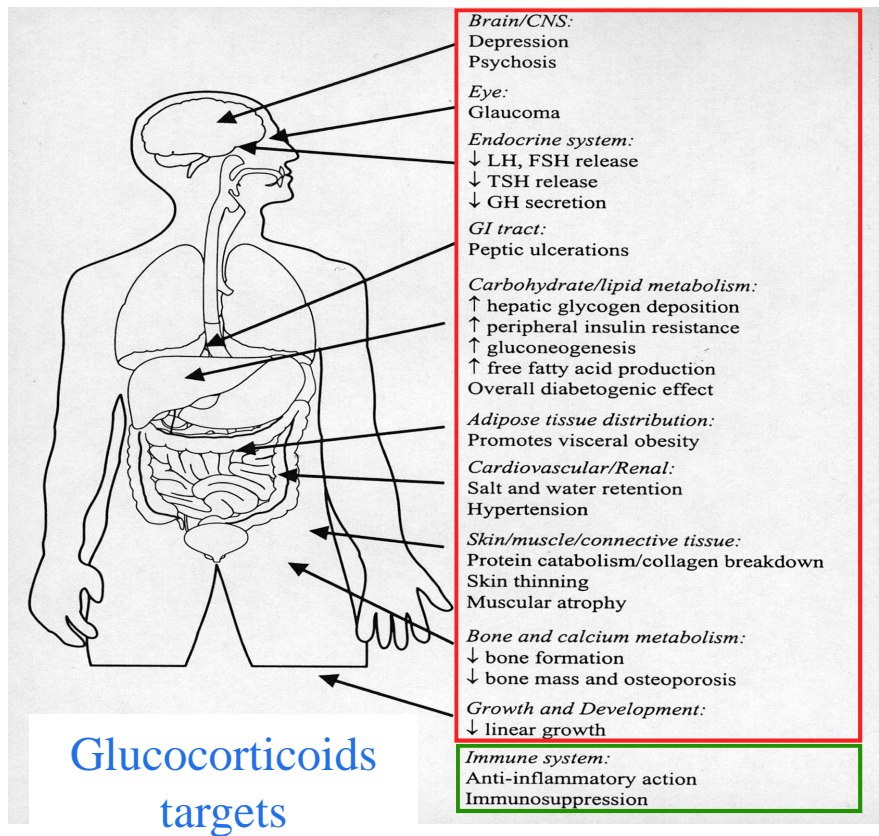
# Mieux comprendre le lupus



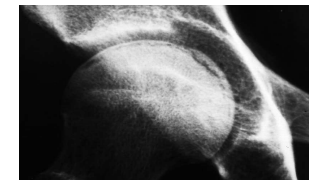
# Les traitements ciblés du lupus

Cible	Nom générique	Nom déposé	Industrie
BLyS	belimumab	Benlysta	HGS-GSK
IFN $\alpha$	kinoid IFN		Neovacs
	sifalimumab		Astra-Zeneca
IL6			Centocor
CD20	rituximab	MabThera	Roche
CD22	epratuzumab		UCB
CD28	abatacept	Orencia	BMS

# Eviter les glucocorticoïdes



Why patients  
hate them



Why physicians love them

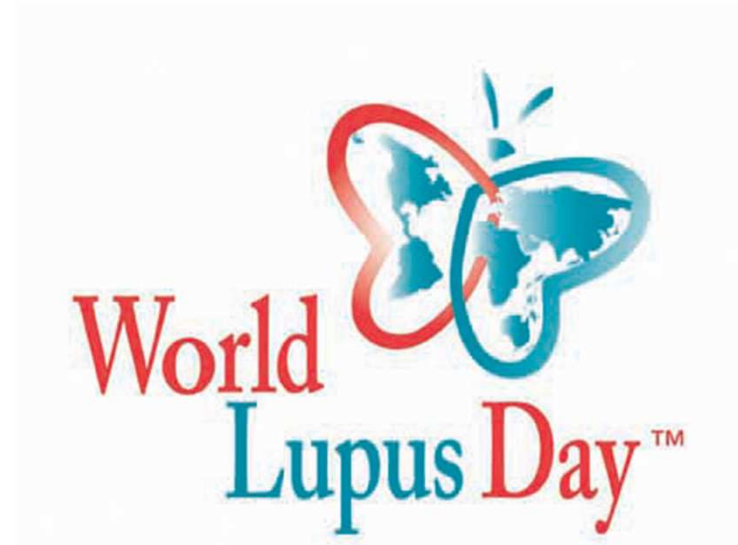
*C'est bien pour un malade de se sentir mieux;  
mais c'est mieux pour un malade de se sentir bien*  
Maxime Dougados

## Approche globale

De nouveaux acteurs

Paramédicaux

Associations de patients





# Remerciements

Marie-Christine Thomas  
Dominique Bénicourt  
Marie M'Zoughui  
Lizzy-Anne Denève  
Tiziana Masini  
Annie Lavis  
Nathalie Dessaint  
Yolande Detry  
Laurence Tedeschi  
Cyril Mougin

Marie Avaux  
Philippine Del Marmol  
Séverine Nieuwland  
Pauline Hoelinger

Isabelle Faille  
Anne-Sophie Mertens  
Bérénice Bloc  
Laurie Vekeman  
Zineb Berbit

Dominique Rachin  
Dominique Dienst  
Chantal Legrelle

Bernard Lauwerys  
Patrick Durez  
Adrien Nzeuseu Toukap  
Maria Stoenoiu  
Marie Vanthuyne  
Jean-Pierre Devogelaer  
Daniel Manicourt  
Laurent Meric de Bellefon

Geneviève Depresseux  
Valérie Badot  
Anne-Lise Maudoux  
Julie Ducreux

FNRS  
FRSM  
SRBR/KBVR  
Région Wallonne  
Biowin  
CRIV/GSK  
Merck  
Abbott  
BMS  
Roche  
Pfizer  
Neovacs  
Association LE

**UCB**  
**UCL**





# Une science clinique élégante

## Les acquis

Clinimétrie rigoureuse

Imagerie performante

Mécanismes élucidés

Traitements ciblés

## Les défis

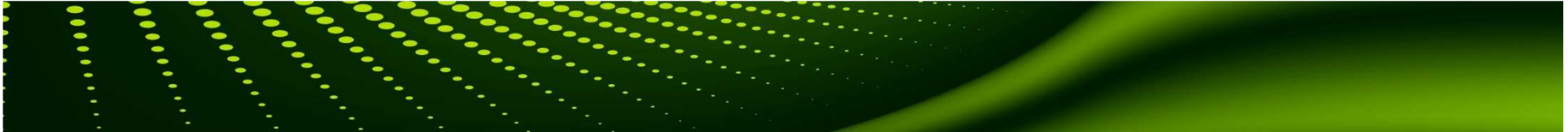
Mieux prédire

Guérir

Prévenir

*Dans la vie, rien n'est à craindre;  
tout est à comprendre*

Marie Curie



# Témoignage

*Madame Sabrina Della Riva*



# Vers un diagnostic et des traitements plus performants

*Professeur Bernard Lauwerys*

Faculté de médecine et médecine dentaire  
Institut de recherche expérimentale et clinique  
Pôle de Pathologies rhumatismales



# **Challenge**

---

**Traitements des maladies réfractaires :**

**Agents biologiques**

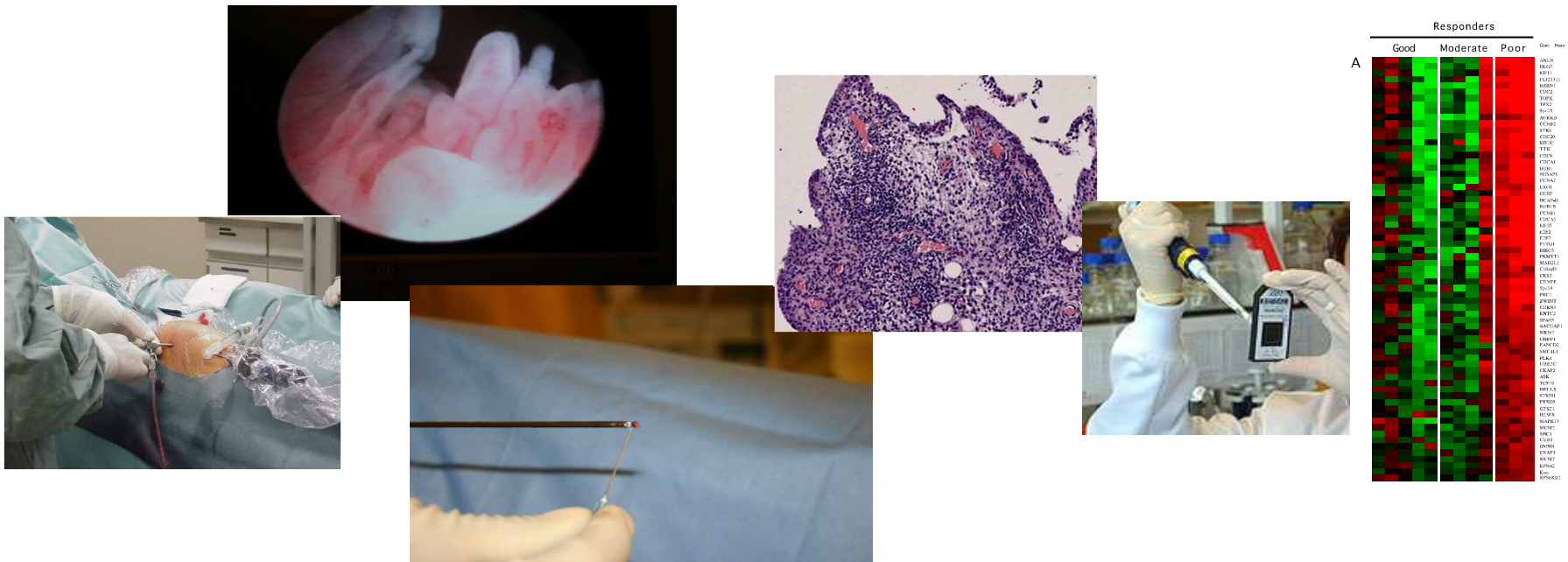
**Evaluation des patients:**

**Examen clinique, radiographies, tests sanguins**

# Challenge



# Plonger au cœur des maladies grâce aux nouvelles technologies





# **Nos thèmes de recherche**

---

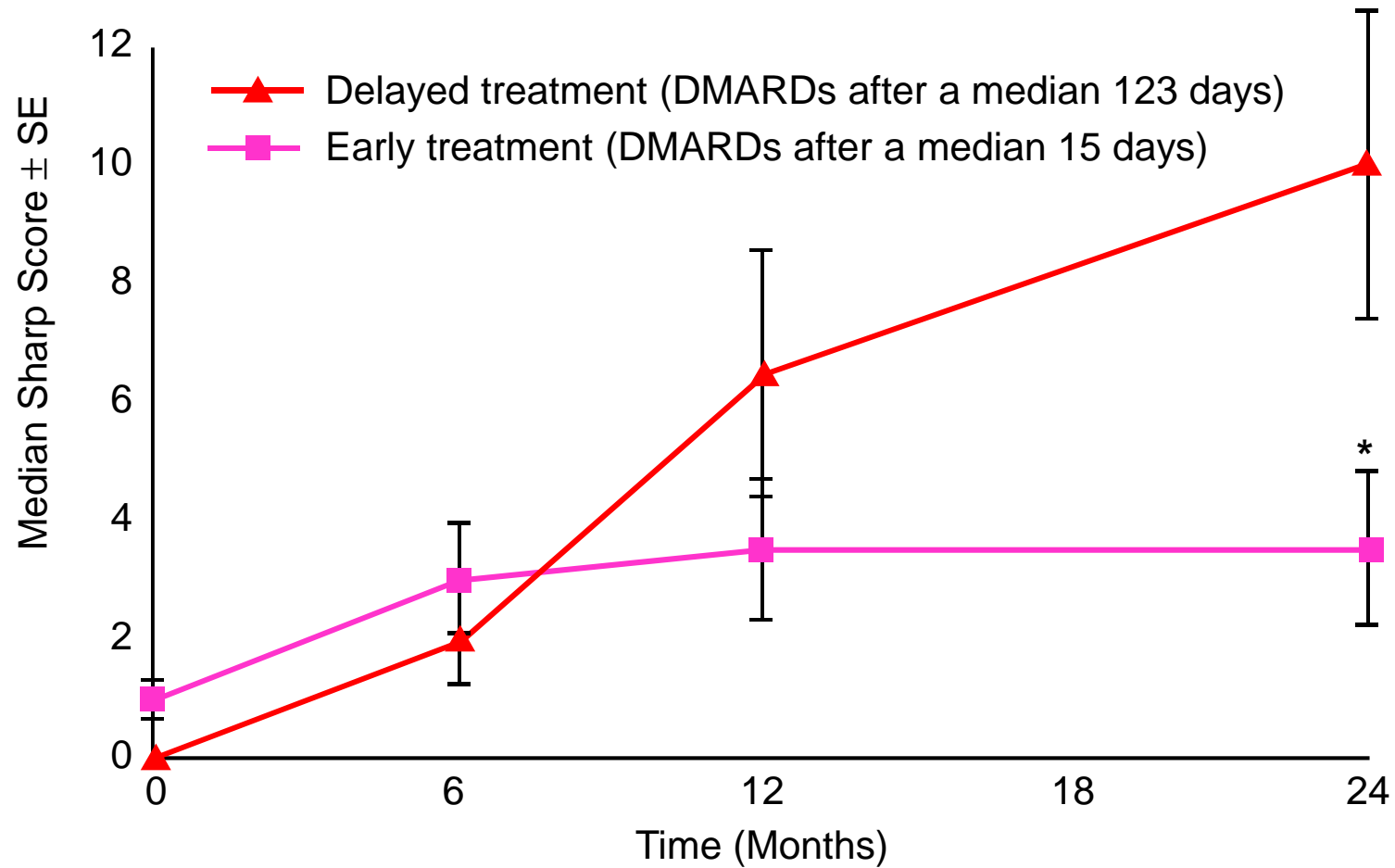
**Diagnostic précoce de la polyarthrite rhumatoïde**

**Evaluation de la sévérité de l'arthrite et des besoins thérapeutiques**

**Prédiction des réponses thérapeutiques**

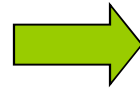
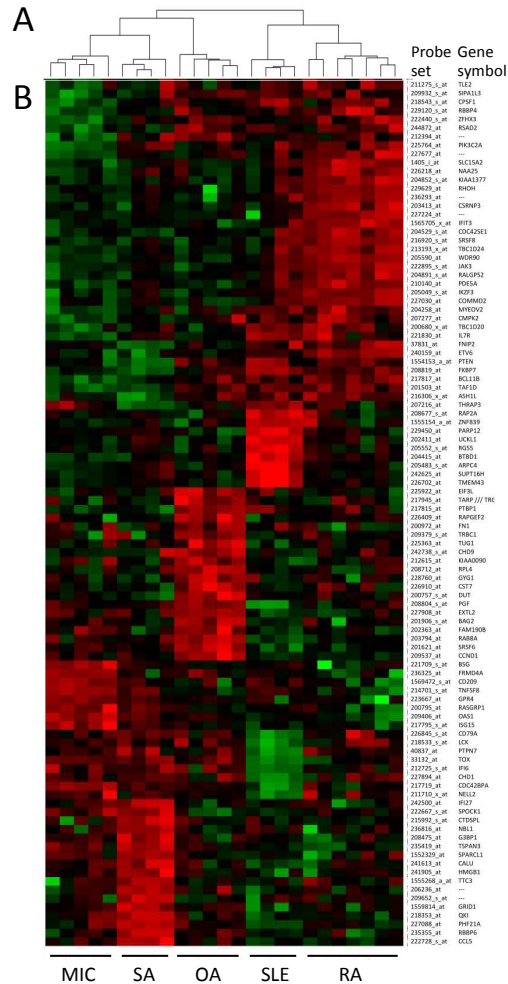
**Individualisation des décisions diagnostiques et thérapeutiques**

# Diagnostic précoce





# Diagnostic précoce de l'arthrite



**Puce de basse densité**

**Utiliser les signatures moléculaires délivre un diagnostic 'correct' dans 90% des cas**

**Vers un diagnostic moléculaire de l'arthrite ?**



# **Prédiction des réponses thérapeutiques**

---

**Profil de réponse au traitement dans la polyarthrite  
rhumatoïde**

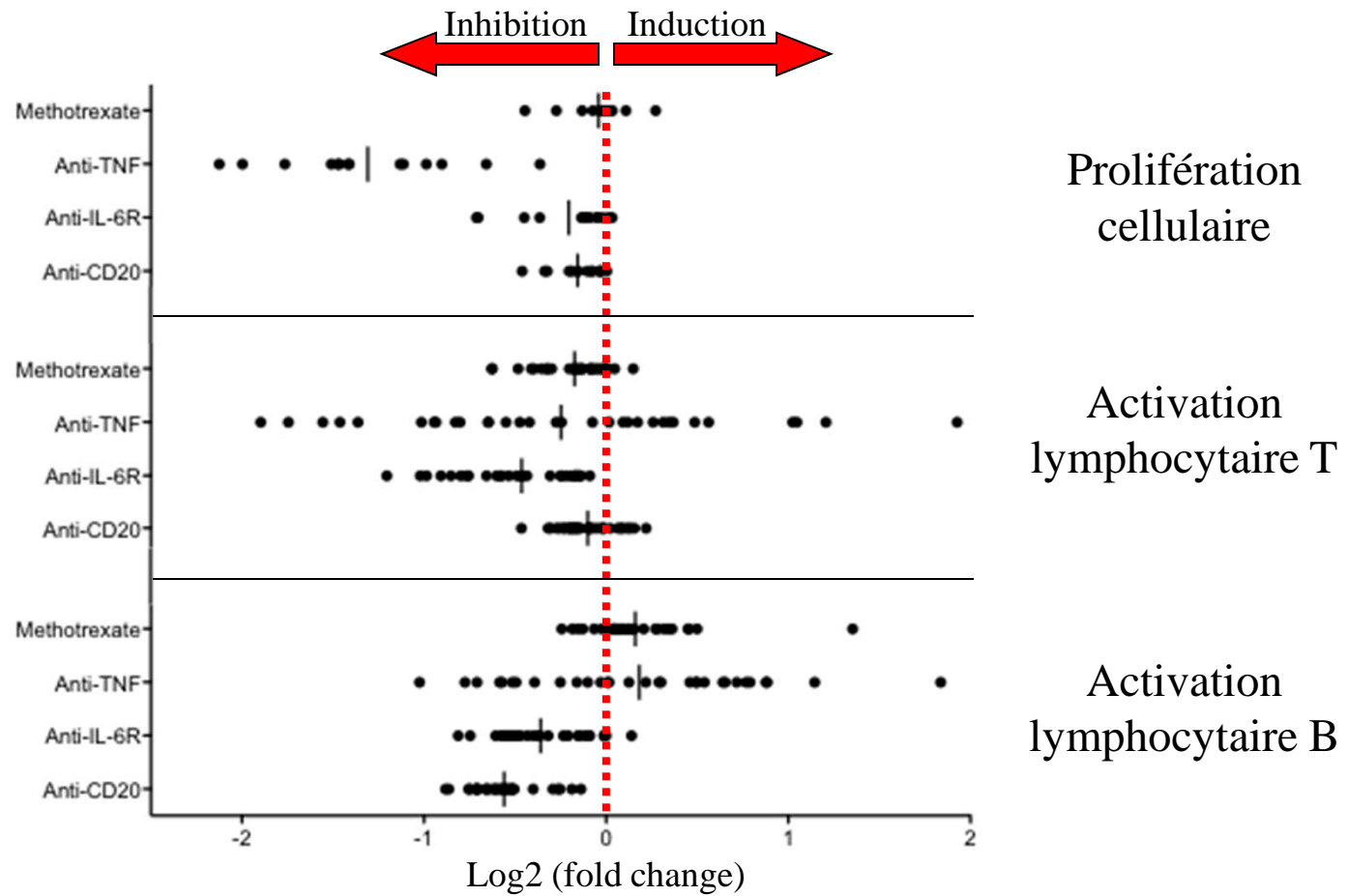
**Bonne réponse : 30%**

**Réponse modérée : 40%**

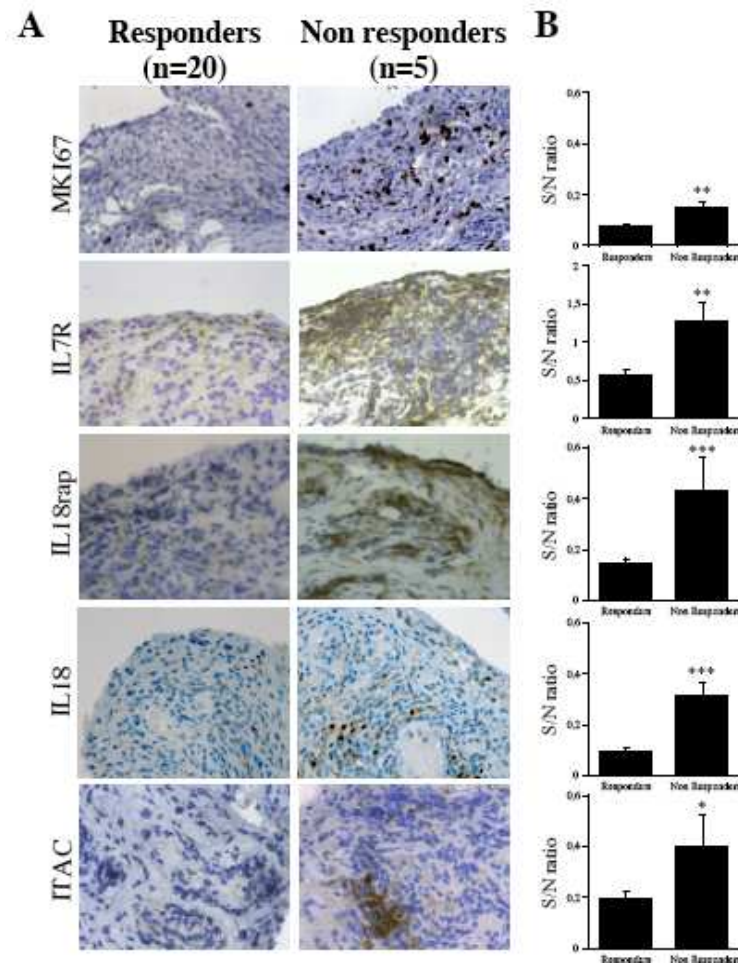
**Pas de réponse : 30%**

**Peut-on prédire la réponse avant l'instauration du  
traitement ?**

# Effets des traitements



# Prédiction des réponses thérapeutiques



**Gènes prédisant  
l'absence de réponse  
aux agents bloquant  
le TNF**

**Ces gènes font du  
sens !**

**Induits par TNF $\alpha$ ,  
IL1 $\beta$  +/- IL17**

# Prédiction des réponses thérapeutiques

**CYTOKINE:**  
rHu IFN-alpha

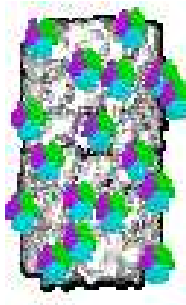


**KLH**

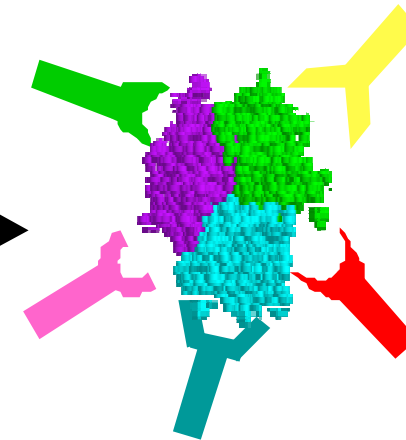
(carrier protein)

Inactivation  
&  
Conjugation

**KINO ID:**  
IFN-K



IM ADMINISTRATION  
Emulsion Adjuvant



**Self polyclonal anti-IFN-alpha antibodies**

**Target multiple epitopes**

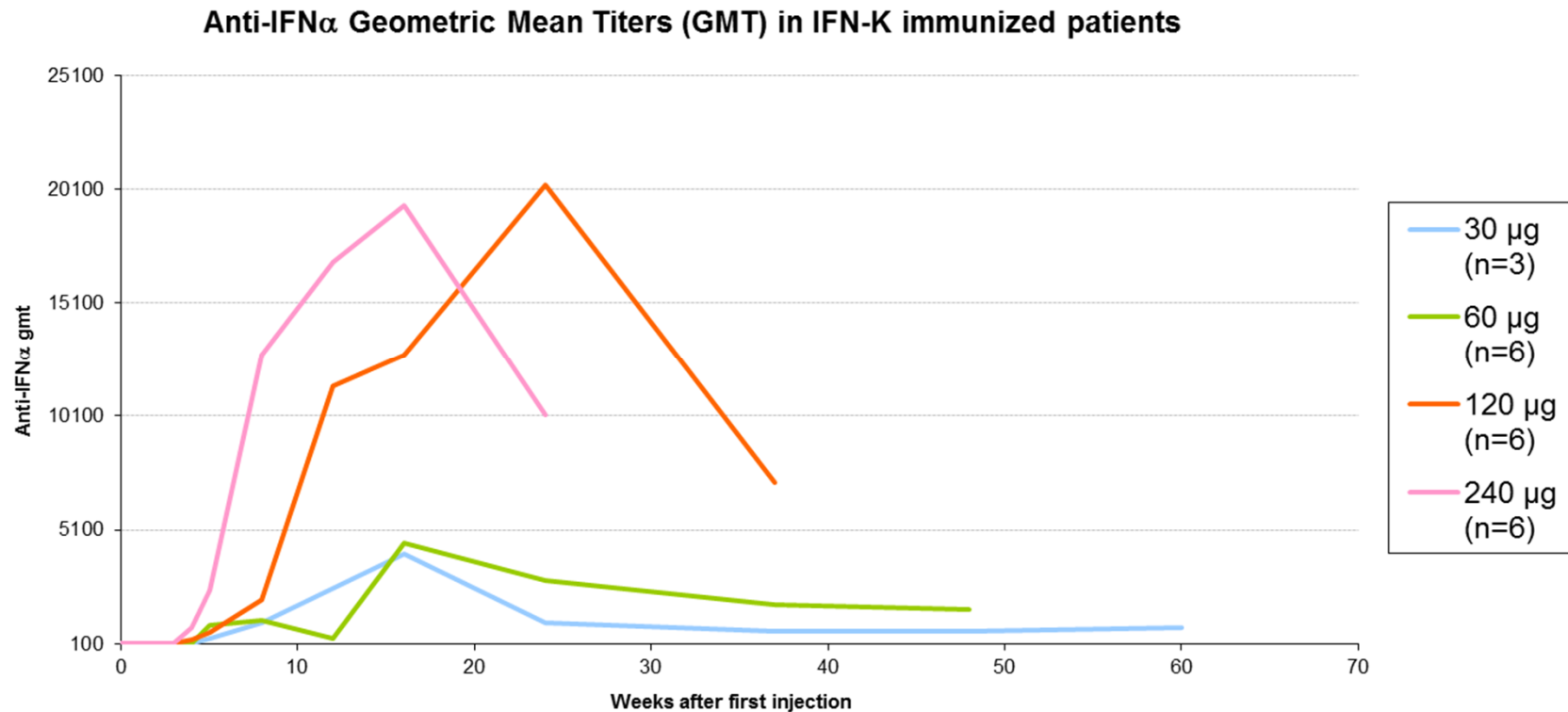
**Neutralization of 13 IFN-alpha subtypes**

**Specific to IFN-alpha: no cross-neutralisation IFN-beta, -gamma**

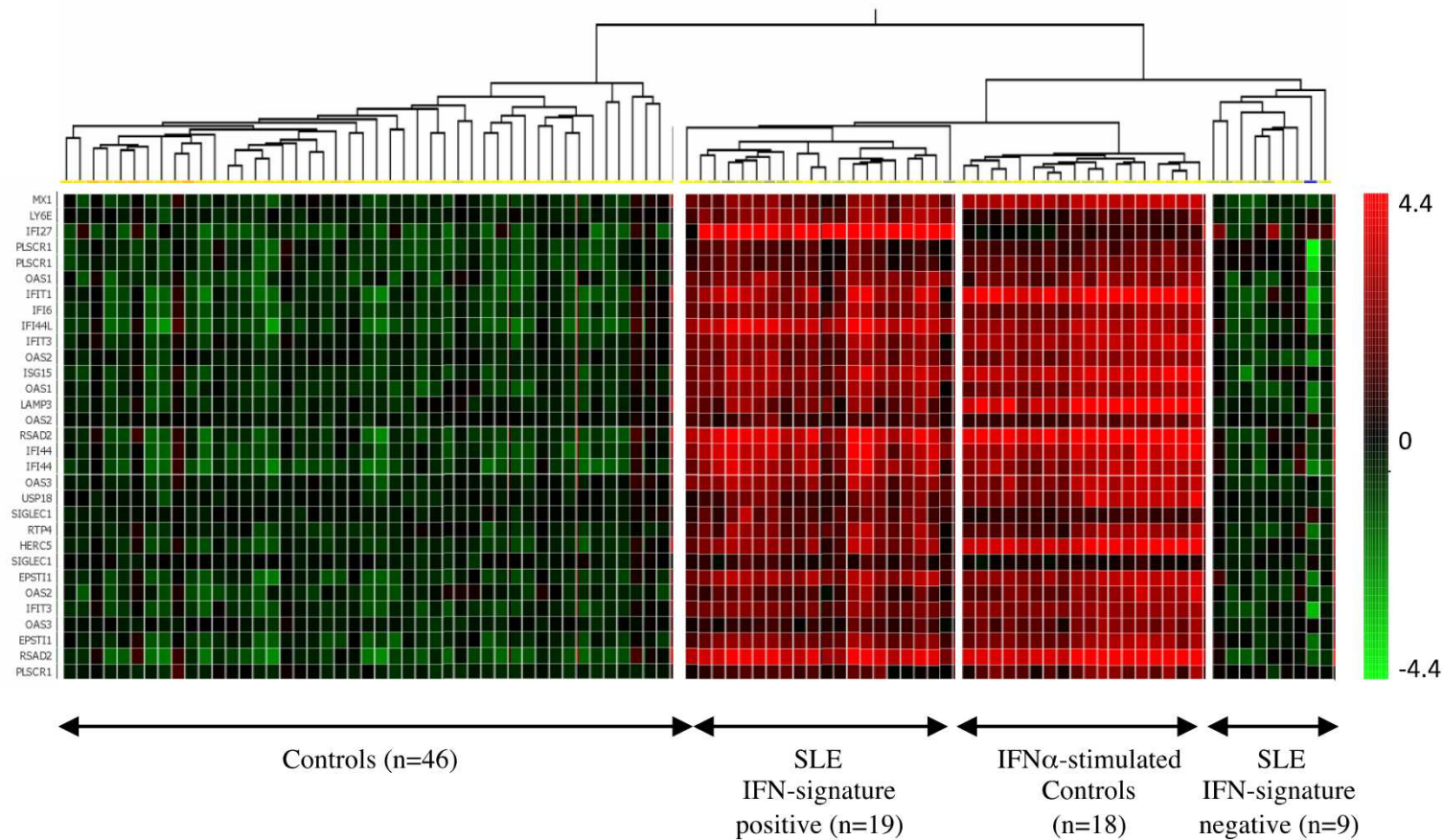
**No blocking anti-Ab antibodies (ADA)**

**Broad and sustained efficacy**

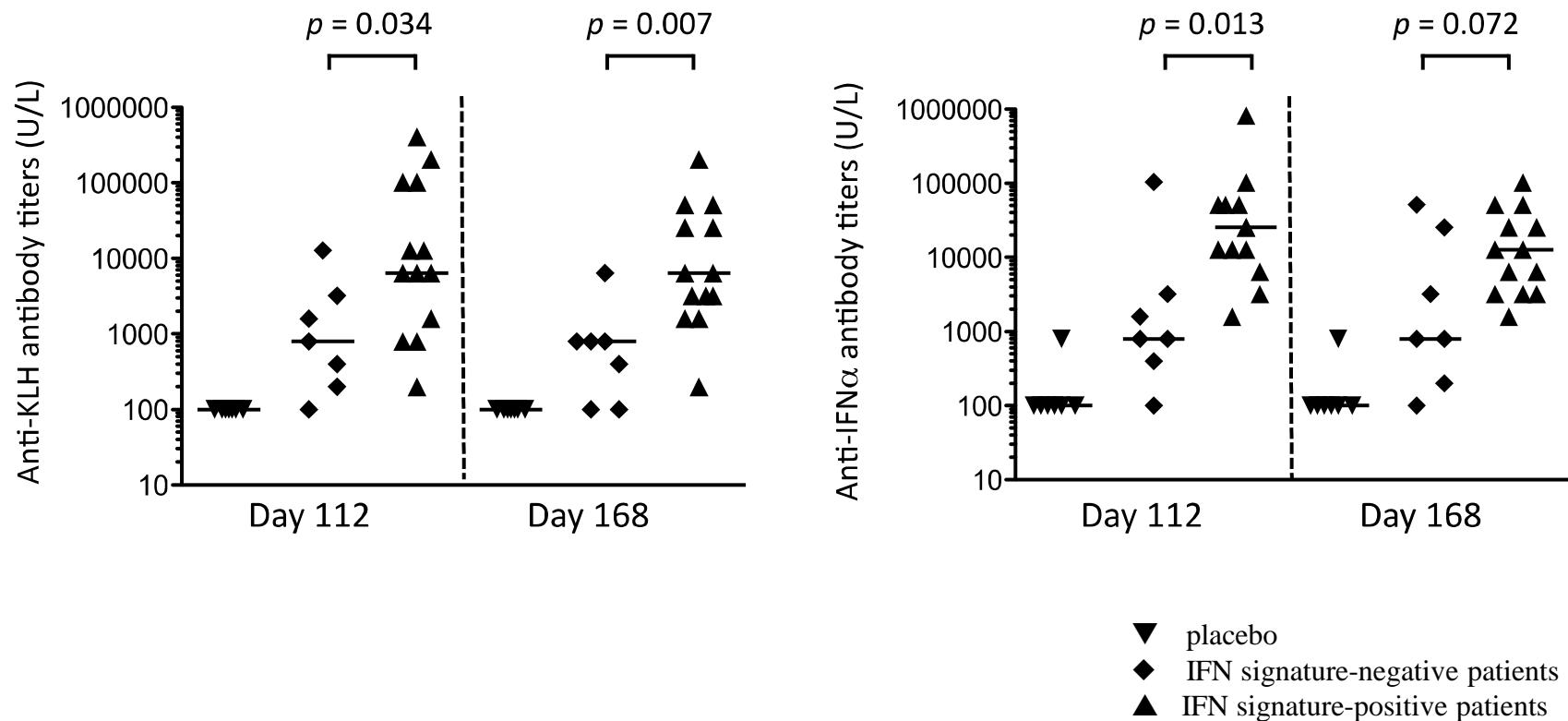
# Prédiction des réponses thérapeutiques



# Prédiction des réponses thérapeutiques



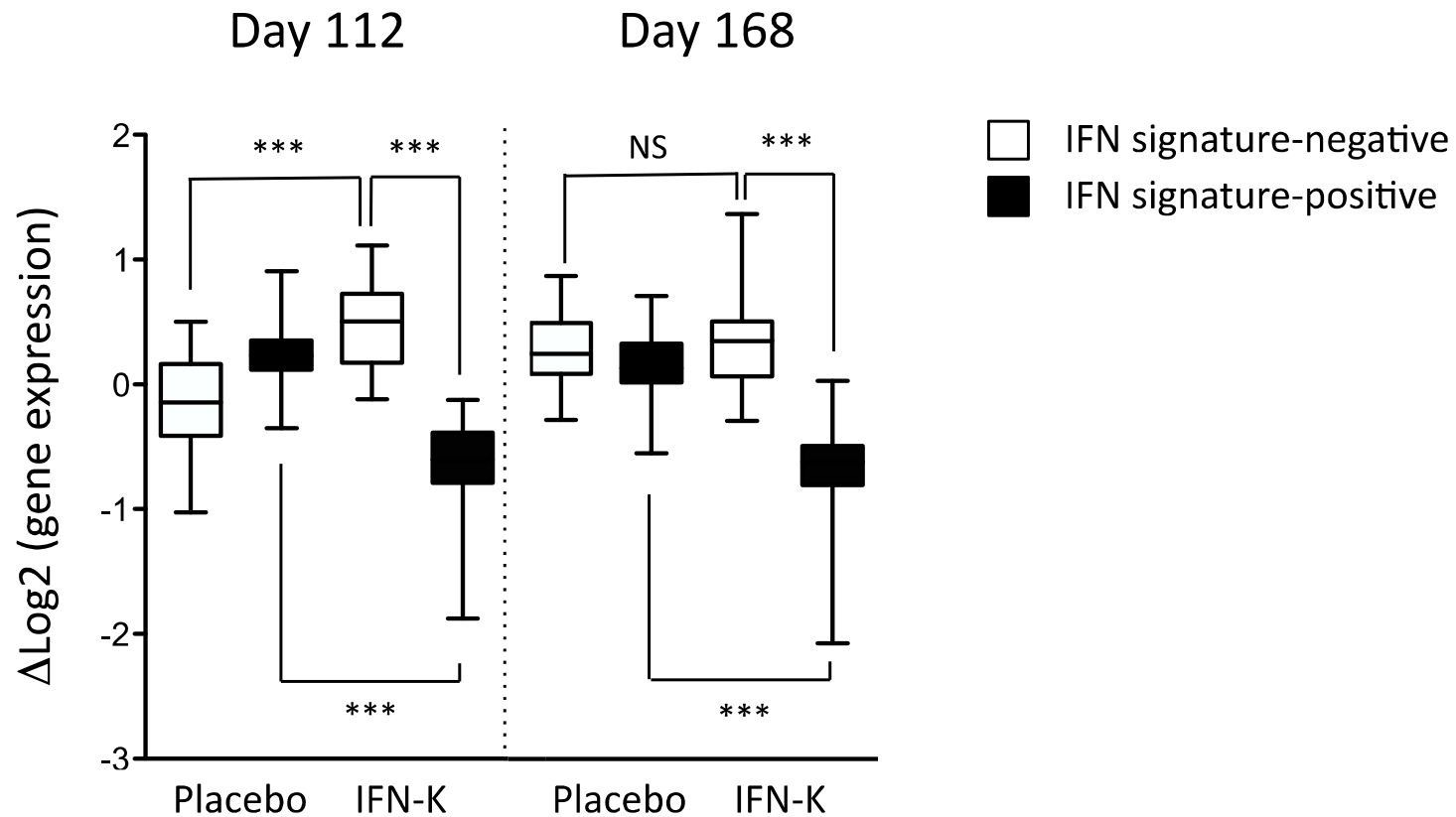
# Prédiction des réponses thérapeutiques



SLE patients with positive IFN signature produce 10x more anti-KLH and IFN-binding Ab in response to kinoid



# Prédiction des réponses thérapeutiques





# **Challenge**

---

**Les technologies actuelles permettent d'obtenir une caractérisation fine de situations individuelles de patients souffrant de pathologies rhumatismales**

**Traduction clinique: démarche diagnostique classique → diagnostic moléculaire**

**Collaborations cliniciens – scientifiques – statisticiens  
/ multicentriques**



# **Chaire UCB-UCL**

---

**Validation de marqueurs diagnostiques et  
théranostiques permettant d'optimiser les soins  
prodigués aux patients souffrant de rhumatismes  
inflammatoires**

**Mise au point d'un microdamier de basse densité  
permettant de prédire sur base individuelle la  
réponse aux traitements**



# Remerciements

---

**J Ducreux, V Badot, AL Maudoux, A De Groof, I Gutierrez-Roelens**

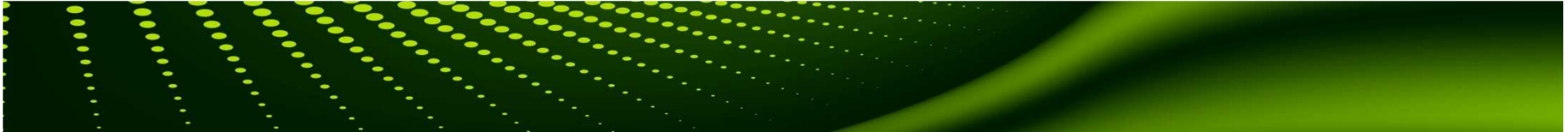
**FA Houssiau, P Durez, A Nzeusseu Toukap, JP Devogelaer, D Manicourt, M Stoenoiu, L Méric de Bellefond, I Faille, G Depresseux**

**B Van den Eynde, P Coulie, C Galand, P Dupont, T Helleputte, D Hernandez-Lobato**



**Merci pour votre attention !**

---



# ***Monsieur Didier Malherbe***

UCB - Vice President Public Affairs  
UCB Belgium - Administrateur délégué



# UCB's vision



## Focusing on severe diseases in Immunology and the Central Nervous System

### UCB: A patient-centric biopharma leader

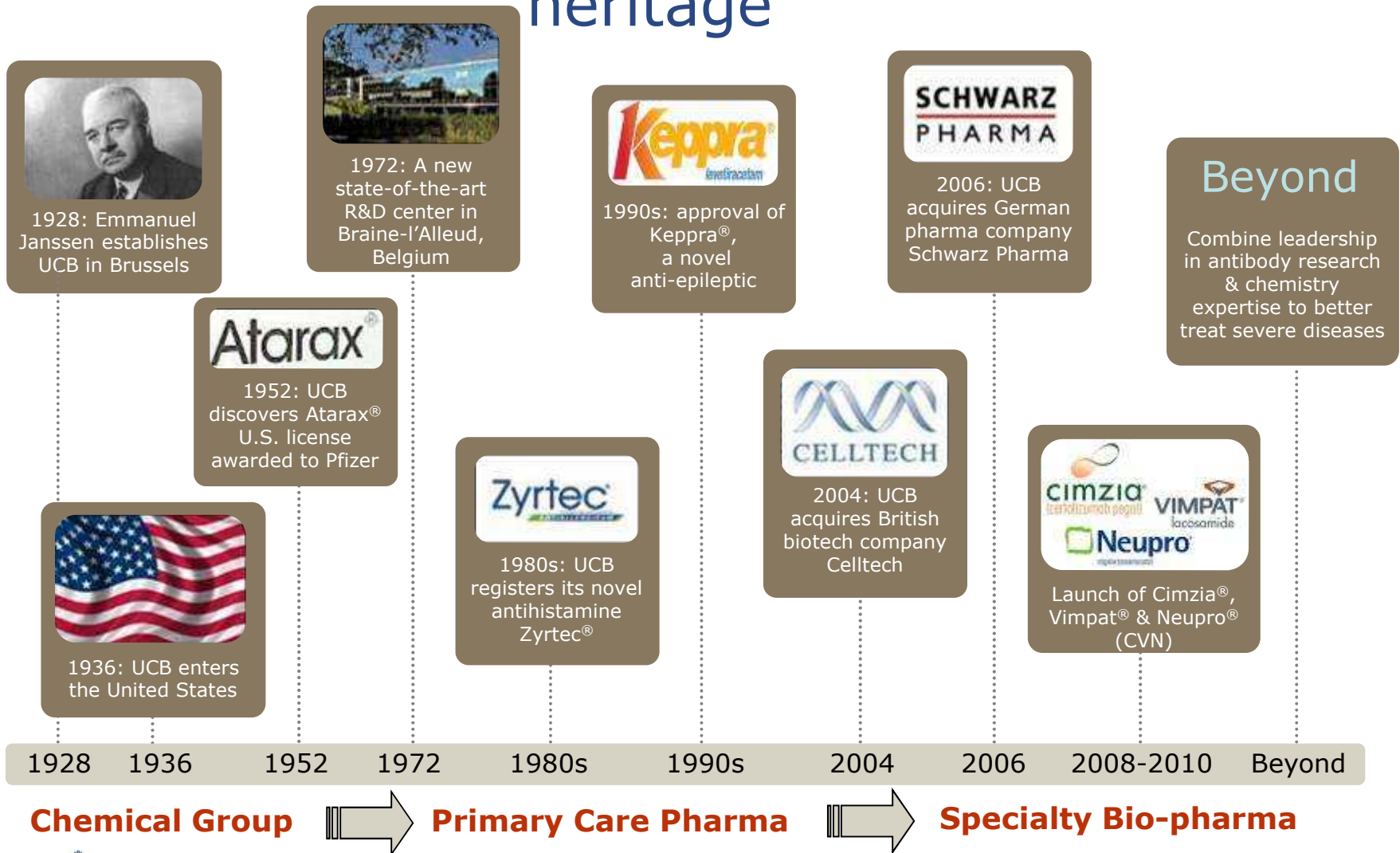
- 2011 revenue: **€3.2 billion**
- More than **8 500** employees globally
- Operations in more than **40** countries
- R&D Spend: **24%** of revenue
- Listed on **Euronext**



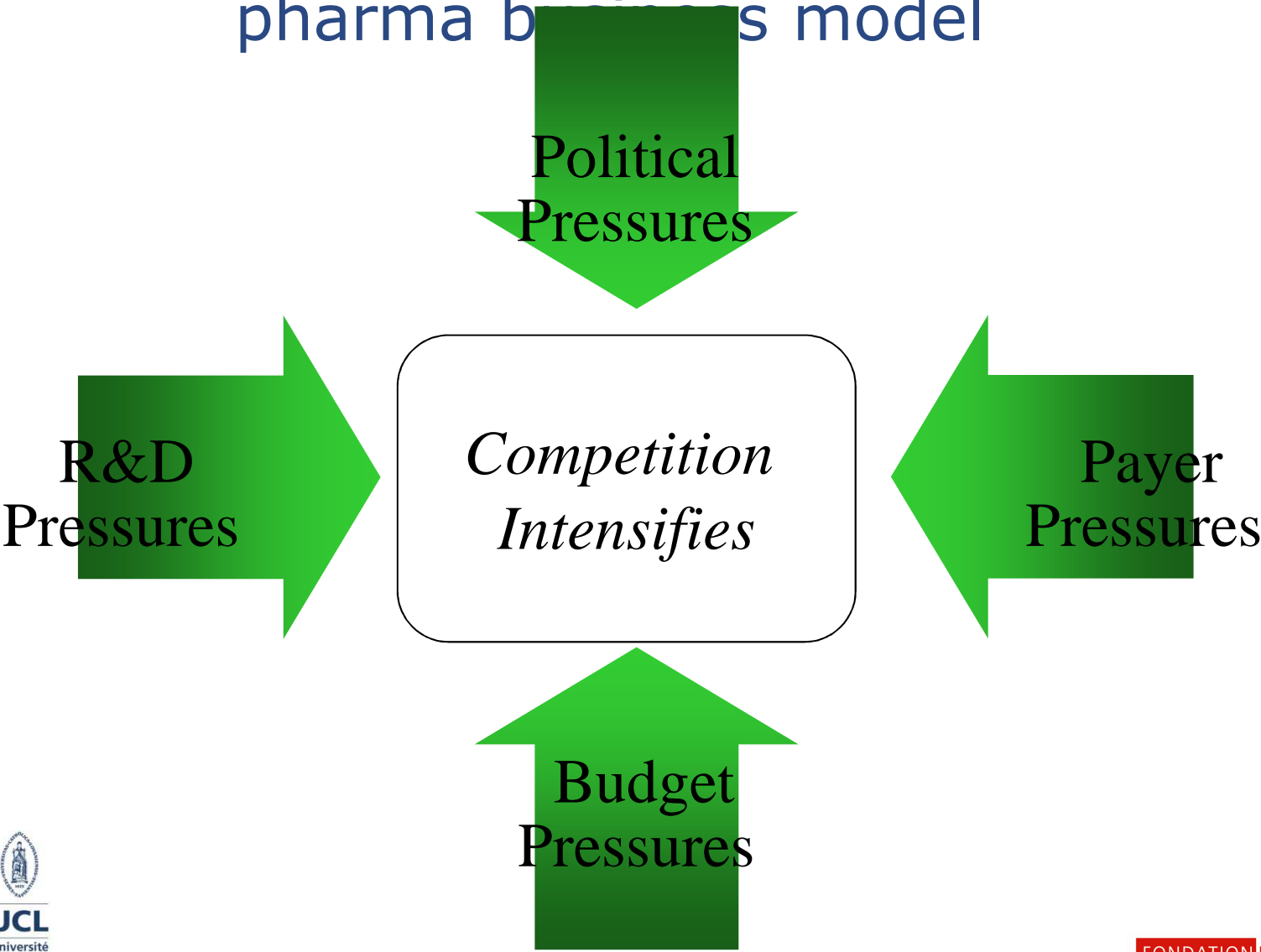
Stephanie, living with rheumatoid arthritis



# UCB: reinventing itself, leveraging a solid heritage

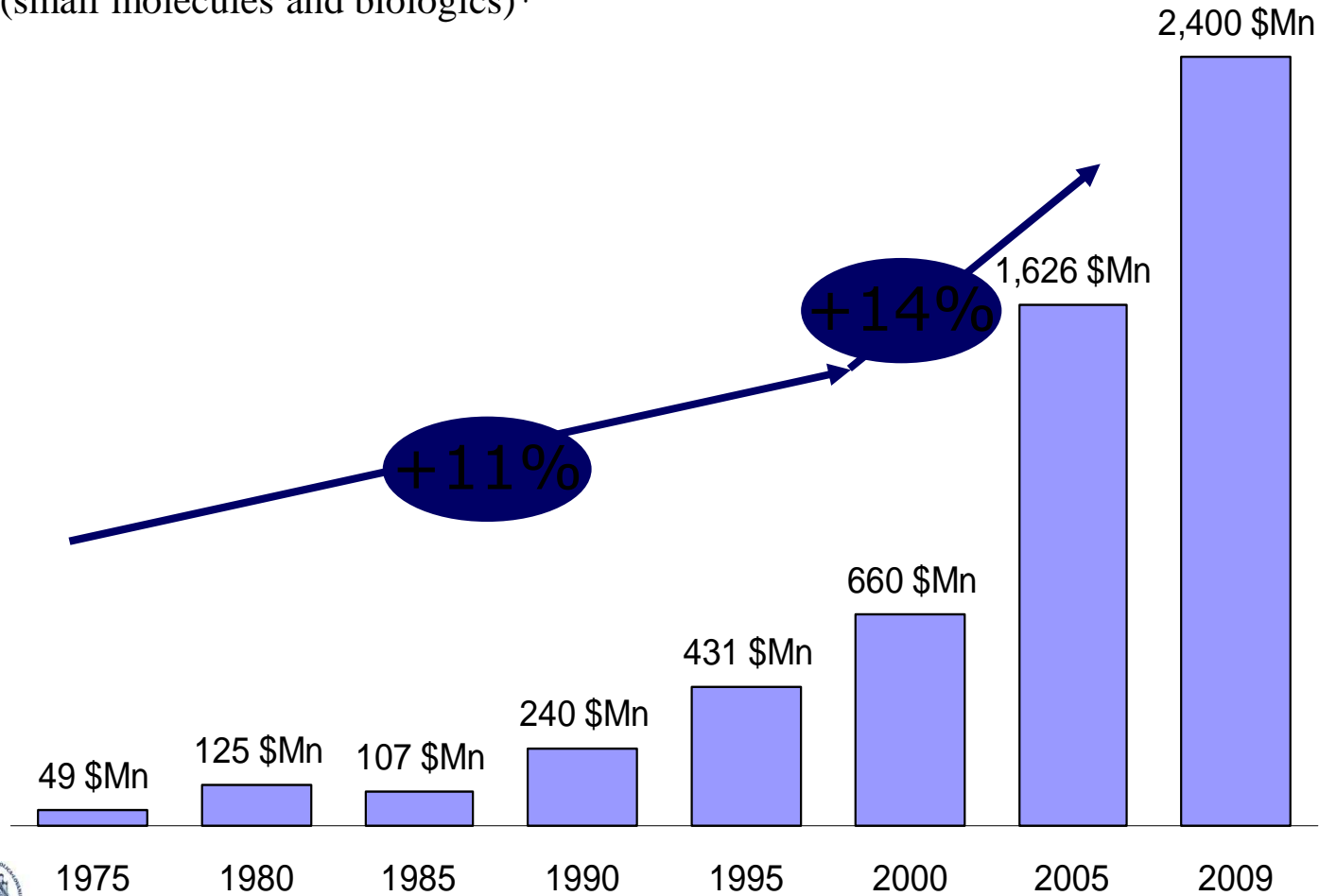


# Managing the pressures of the current pharma business model

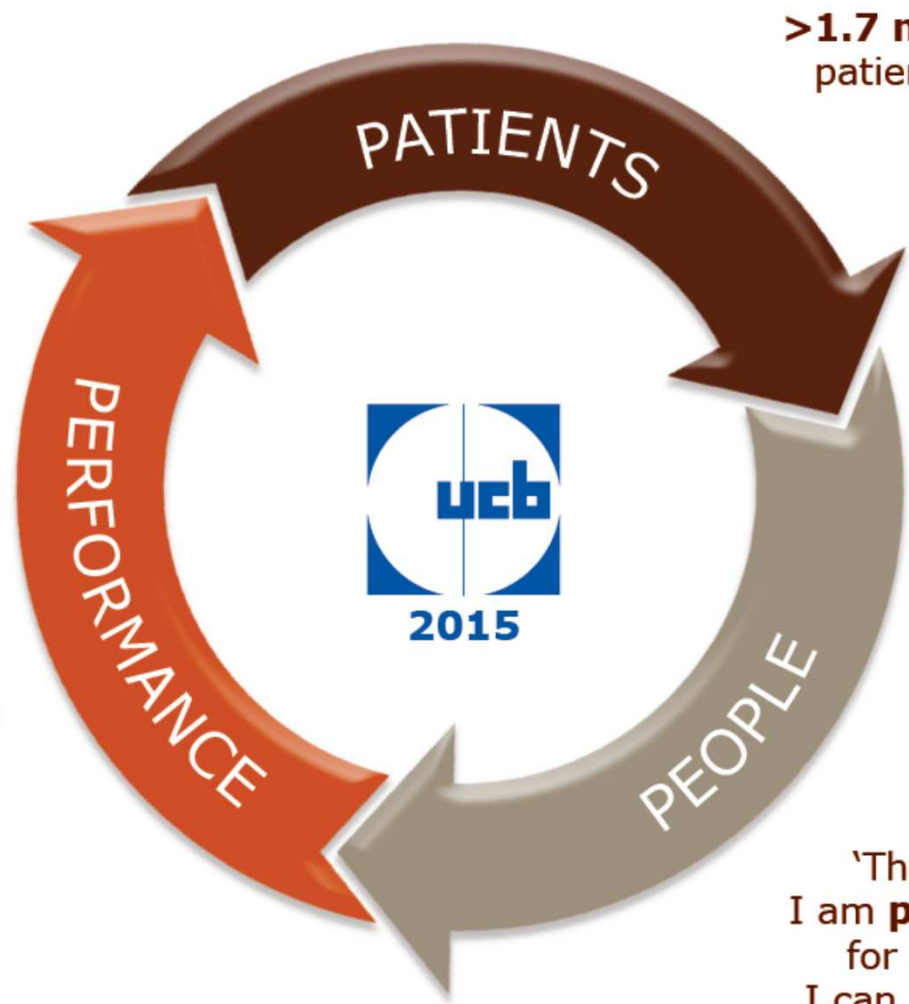


# Significantly increasing average R&D spend per NME

Average R&D spend per FDA Approval  
(small molecules and biologics)\*



\* Average R&D spend per NME defined as 5 year lagging average R&D spend divided by sum of present period NME and BLA approvals  
 Note: Biologics included only from 1986 onward, biologics approvals assumed negligible in prior periods  
 Source: McKinsey analysis, NME data from multiple publications and statistical sourcebooks Industry R&D spend data from the Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2006.



>1.7 million new patients treated

Intense revenue **growth**

'The company I am **proud** to work for and where I can have impact'



# A turning point

Launching of 3 new medicines for patients with severe diseases



Rheumatoid arthritis

- Launched in the U.S. (May 2009)
- Launched in Europe (October 2009)

Crohn's disease

- Launched in the U.S. (May 2008)



Epilepsy adjunctive therapy

- Launched in Europe (September 2008)
- Launched in the U.S. (June 2009)



Parkinson's disease & Restless legs syndrome

- Launched in Europe (June 2009)
- Launched in the U.S. (July 2012)

# Patients at the heart of all strategic decisions



Everything we do starts with a simple question:  
"How will this make a difference to the lives of  
people  
living with severe diseases?"

# Providing solutions beyond novel medicines



Patient summits



Online support through online communities and educational websites



Patient Advocate programmes

Product design & e-health



Employee support of local patient initiatives

Patient and caregiver scholarship programmes

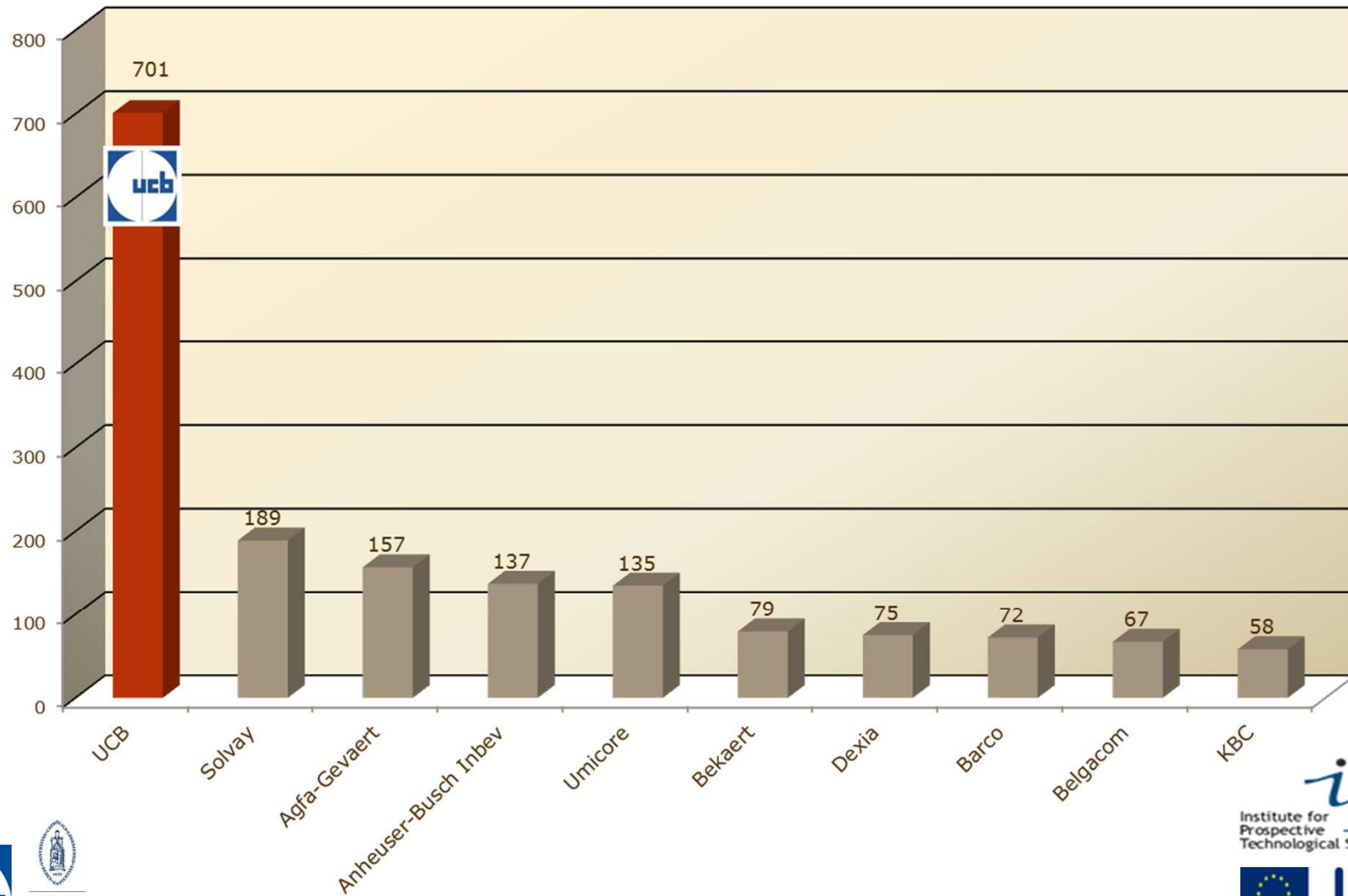


Daily support to patients



# R&D investors in Belgium

## The 2011 EU Industrial R&D Investment Scoreboard

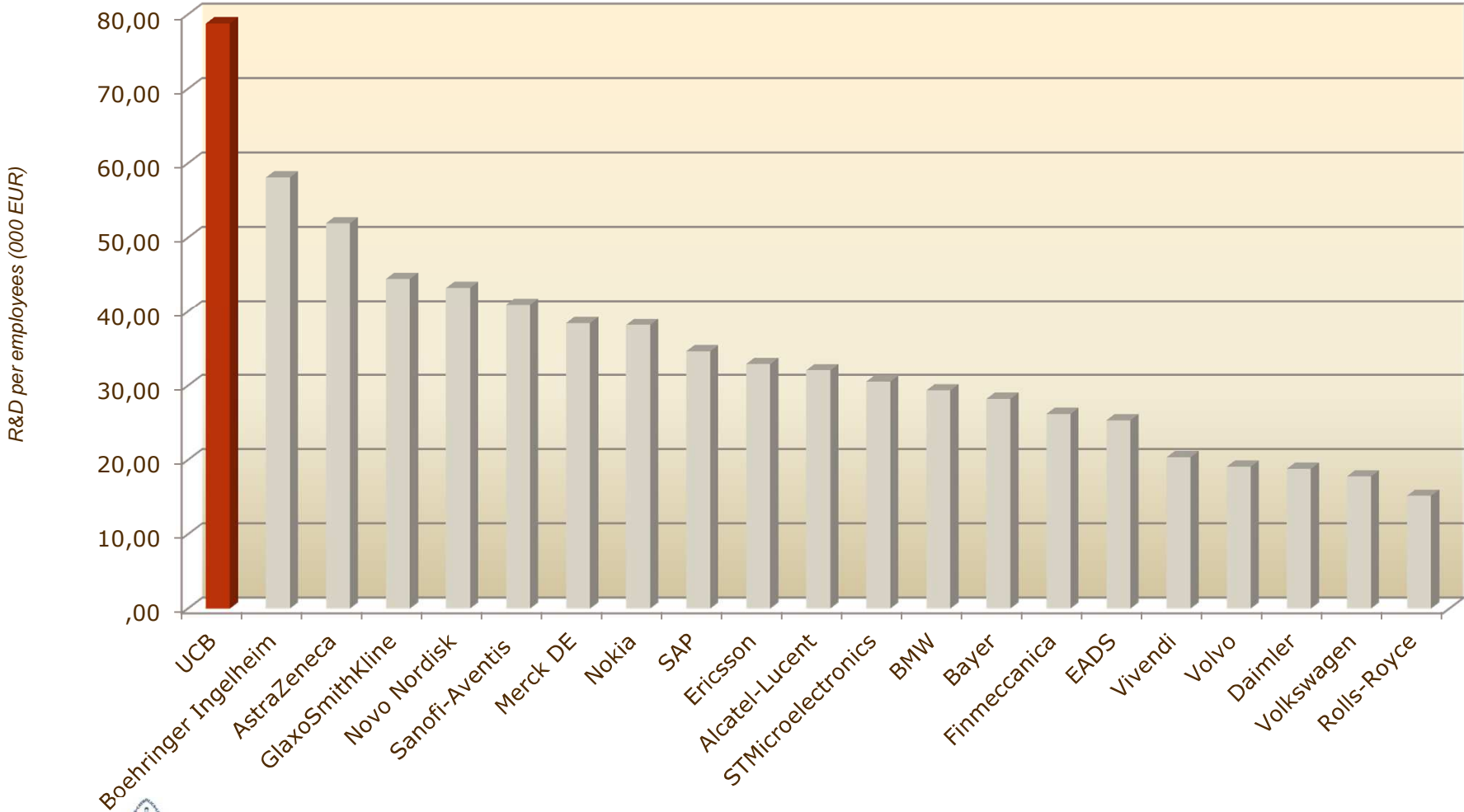


<http://iri.jrc.ec.europa.eu/reports.htm>





# An R&D leader in Europe



*Top 50 EU companies by R&D/Employees,  
the 2011 industrial R&D investment scoreboard  
European Commission, Oct 2011*

# Global presence but Belgium as main « hub »



> 140 cooperation agreements  
with most Belgian universities

KATHOLIEKE UNIVERSITEIT  
**LEUVEN**

**ULB** UNIVERSITÉ  
LIBRE  
DE BRUXELLES

**UCL**  
Université  
catholique  
de Louvain

**U** Universiteit  
Antwerpen

**UNIVERSITEIT  
GENT**

Université  
de Liège

**Vrije  
Universiteit  
Brussel**

# Cutting-edge research and science to meet unmet patient needs

- Two main **Research Centers**
- World-class expertise** in selected therapeutic areas and disease mechanisms
- Connecting science in new ways - **chemistry** (small, chemically-derived molecules) and **biology** (large antibody-based molecules), to leverage the potential of these two disciplines
- “Open innovation” model** based on strong partnerships with other biotech companies and prominent universities



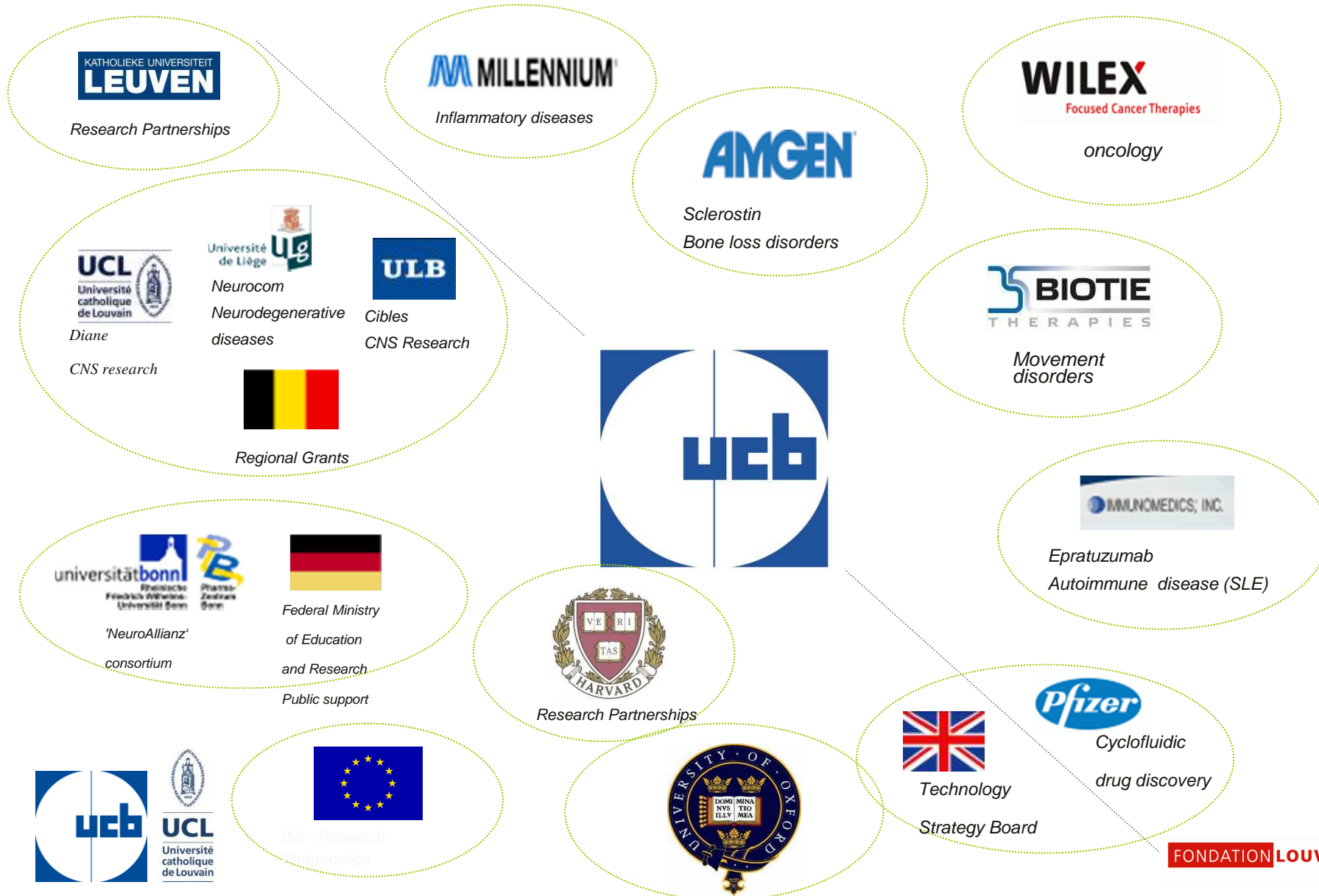
New biologics  
R&D centre -  
Slough, U.K.



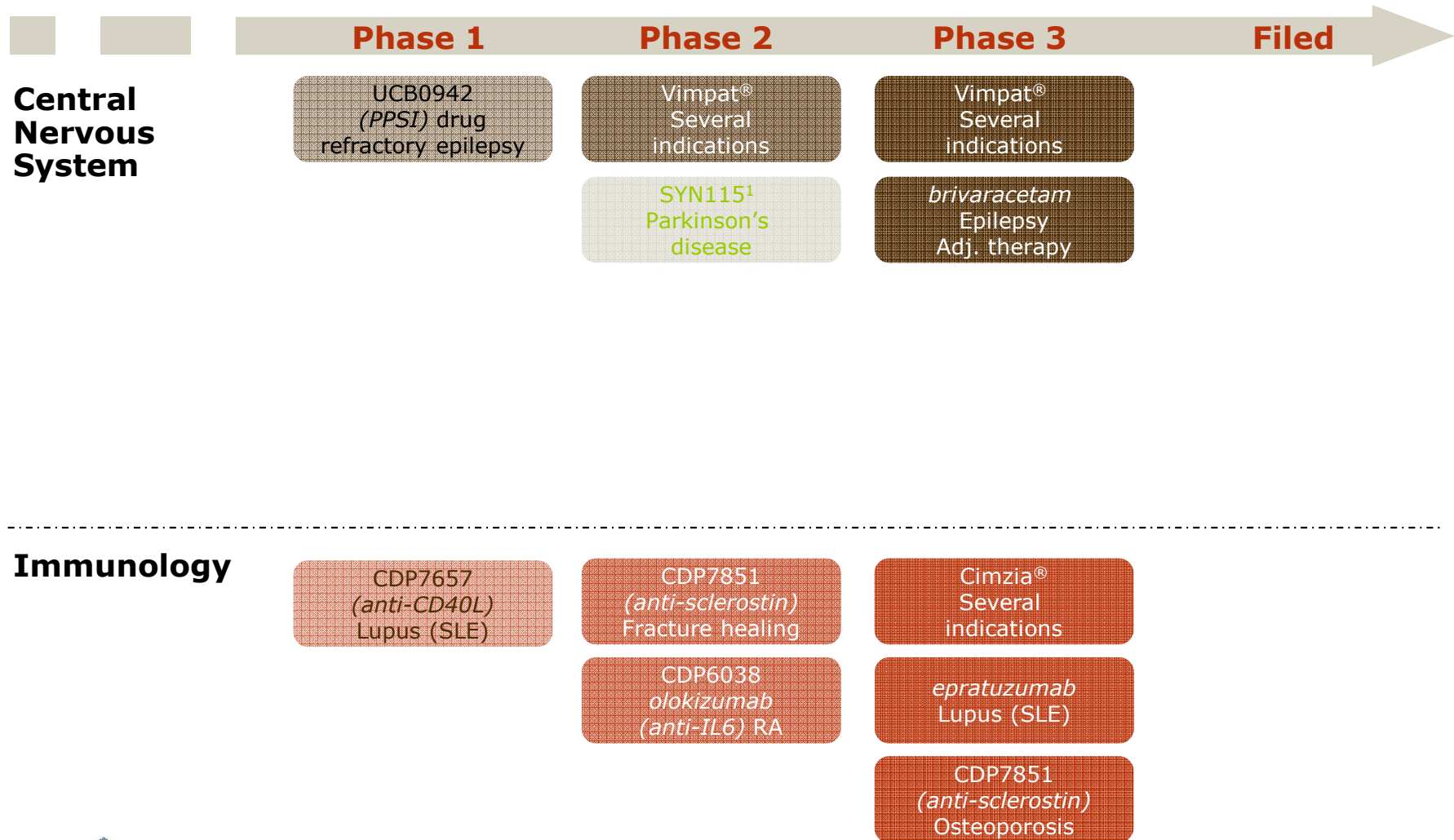
New biologics pilot plant -  
Braine-l'Alleud, Belgium

# Open innovation at UCB

## more than 400 partnerships in the world



# Strong early and late stage pipeline



# *Epratuzumab* in systemic lupus erythematosus (SLE)

Phase 3 programme on-going – first results H1 2014

- ☐ UCB holds world-wide rights for auto-immune indications
- ☐ Phase 3 programme currently recruiting
  - › Primary endpoint  
To confirm the clinical efficacy of *epratuzumab* by the % of subjects meeting treatment response criteria at Week 48 according to a combined response index build primarily around BILAG



Renee, living with lupus



## Sclerosteosis – An inherited high bone mass disorder with massive bone overgrowth throughout life



Normal

Bone deposited is:

- ☐ extremely strong
- ☐ deposited in a normal manner



Sclerosteosis

Bone Dysplasia Sclerosteosis Results from Loss of the *SOST* Gene Product, a Novel Cystine Knot-Containing Protein

Brunkow, M.E. *et al.*

*Am. J. Hum. Genet.* 68(3): 577-589, 2001

## UCB Ambassador of Belgium

1. A prominent location (Brussels, Capital of EU)
2. A unique academic and industrial network (UCL,...)
3. A highly qualified and productive workforce
4. A favorable public opinion
5. A competitive tax environment







# Since 2006 in Belgium

2007 :  
JNJ - Pilot Plant Geel  
Investment of 130 mio €



2007 :  
JNJ – Distribution Center Courcelles –  
Investment of 40 mio € +340 FTE



2007 :  
GSK Bio – Quality Control Wavre  
Investment of 150 mio €



2008 :  
Pfizer – LLN R&D Center Animal Health  
Investment of 40 mio €



2009 :  
Genzyme – Biomanufacturing - Geel  
Investment of 49 mio € +80 FTE



2009 :  
Baxter – Biosciences Lessines  
Investment of 50 mio € +120 FTE



2009 :  
UCB - BioPilot Plant Braine  
Investment of 65 mio € +100 FTE



2010 :  
Baxter – HQ – Braine L'Alleud  
+ 50 R&D FTE



2010 :  
JNJ – Distribution Center - La Louviere  
Investment of 49 mio € +110 FTE



2010 :  
GSK Bio – HQ - Wavre  
Investment of 80 mio €



2010 :  
Pfizer – Puurs + Zaventem  
Investment of 61 mio € + 190 FTE



2011 :  
Genzyme Geel  
Investment of 250 mio € + 150 FTE



# UCB: Changing the world everyday





# Conclusion

***Monsieur Benoit Cerexhe***

***Ministre de l'Économie, de l'emploi, du commerce extérieur  
et de la recherche scientifique  
de la Région de Bruxelles-Capitale***