

Le nuove vie delle scienze della vita

Antonio Lanzavecchia

Institute for Research in Biomedicine, Bellinzona
Institute of Microbiology, ETH Zurich



The Institute for Research in Biomedicine

- Non profit private research Institute founded in 2000 in Bellinzona
- Governed by a Foundation Council (President, Giorgio Nosedà)
- Since 2010 is affiliated to the Università della Svizzera Italiana (USI)
- Mission: study host defense mechanisms with emphasis on the human system



New-IRB
in 2015?

IRBis 500 m² lab space +
animal house with BSL3

IRB 1300 m² lab space,
cell sorting facility

Other links on site:
IOSI, Institute of Oncology
ICM, Istitute of Microbiology





8 group leaders, 14 postdocs, 29 PhD students, 15 technicians,
7 administration/support

- 250 publications (IF:11.5)
- 40 PhD degrees since 2000
- 4 postdocs established independent laboratories abroad
- 4 group leaders obtained prestigious positions in other institutes or universities
- Several patents licensed in the field of antibodies

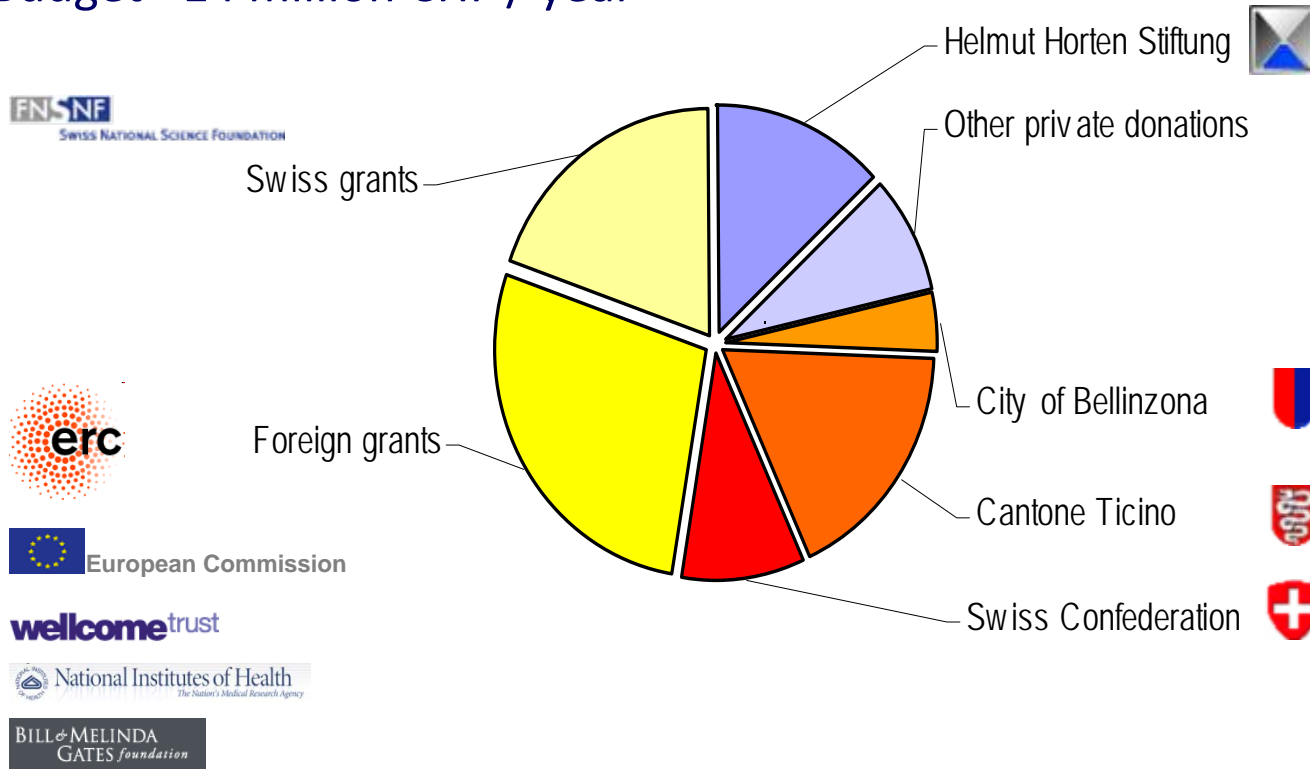


- Immunological memory
- Therapeutic antibodies
- New vaccination strategies
- Inflammation
- Cell migration
- Degenerative diseases
- Gene regulation
- Protein engineering
- Emerging infectious diseases

Organism ↔ cells ↔ molecules

An effective mixture of private, public and competitive funding

Budget ~14 million CHF / year



“the IRB is very cost effective”

Some of the strengths of IRB

- Postgraduate and Postdoctoral teaching
- Cutting edge training in life sciences
- International environment
- Expertise in human immunology
- Expertise in vaccinology and infectious diseases
- Core facilities for biomedical research

Some of the core facilities



Cell sorting



High throughput cellular screens



Imaging



DNA sequencing

Current trends in biomedical sciences

- “Big science” (HIV, cancer...)
- Top down approach (Gates, EU...)
- Emphasis on vaccine science
- Translational research
- Human vs animal studies
- High throughput approaches (equipment...)
- Discovery-driven science (genome)

Progress in DNA sequencing

Sequencing the human genome:

In 2000	International consortium, years
In 2010	~1000 USD, 2 days
In 3 years	~25 USD

“we are drowning in a sea of data, yet thirsting for knowledge”

Sydney Brenner

Interdisciplinary work



...thymic Treg cell development is a TCR-instructive process involving a niche that can be saturable at much lower clonal frequencies than is the niche for positive selection...

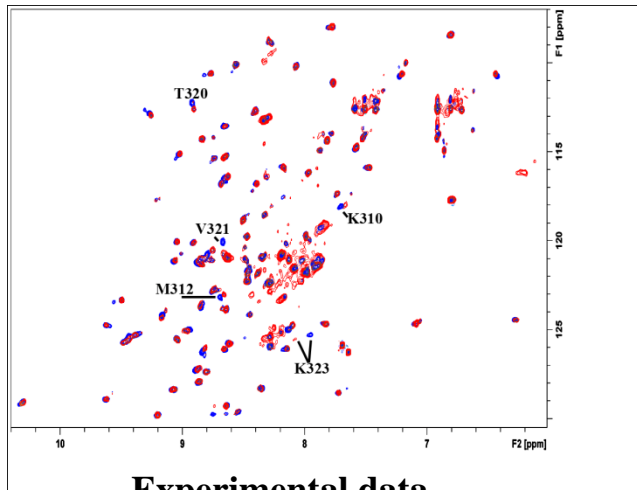
- Crystal structure
- Nuclear magnetic resonance
- Mutagenesis



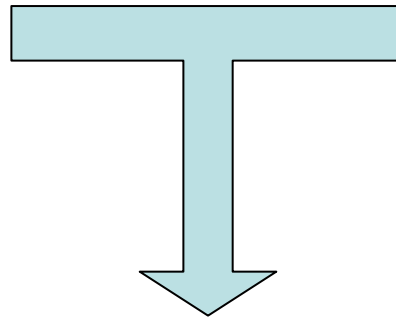
$$f(x) = a_0 + \sum_{n=1}^{\infty} \left(a_n \cos \frac{n\pi x}{L} + b_n \sin \frac{n\pi x}{L} \right)$$

- Structure prediction
- Docking
- Molecular dynamics

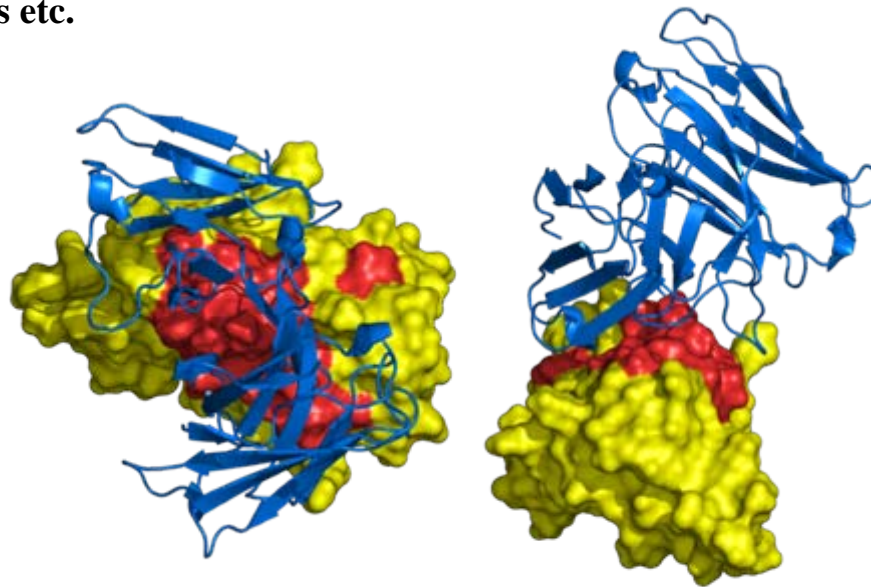
Experiments in vitro, in vivo and in silico



Experimental data
NMR, escape mutants etc.



Computational Docking
CSCS, Manno



A new breed of scientists

Biologists need help to deal with huge datasets and devise algorithms for computer simulations of biological processes

Non-biological scientists need to be shown what is most relevant

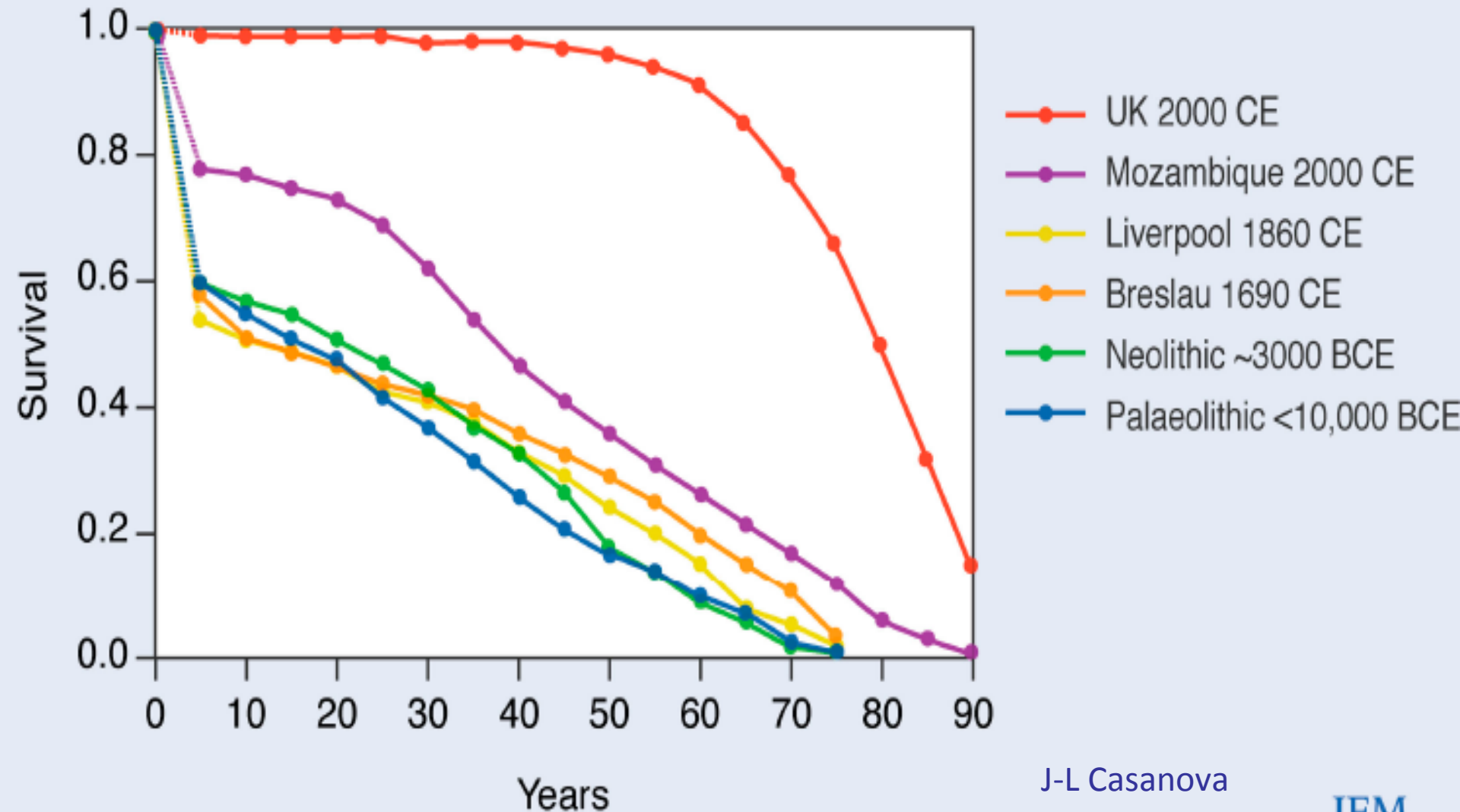
One of the biggest challenges is teaching scientists with such a diverse background how to speak with each other

We need a new breed of scientists exposed to both biological and computational training in their education

Can USI become one of the training grounds where this new breed of scientists is formed?

Vaccines, antibodies and biotechnology

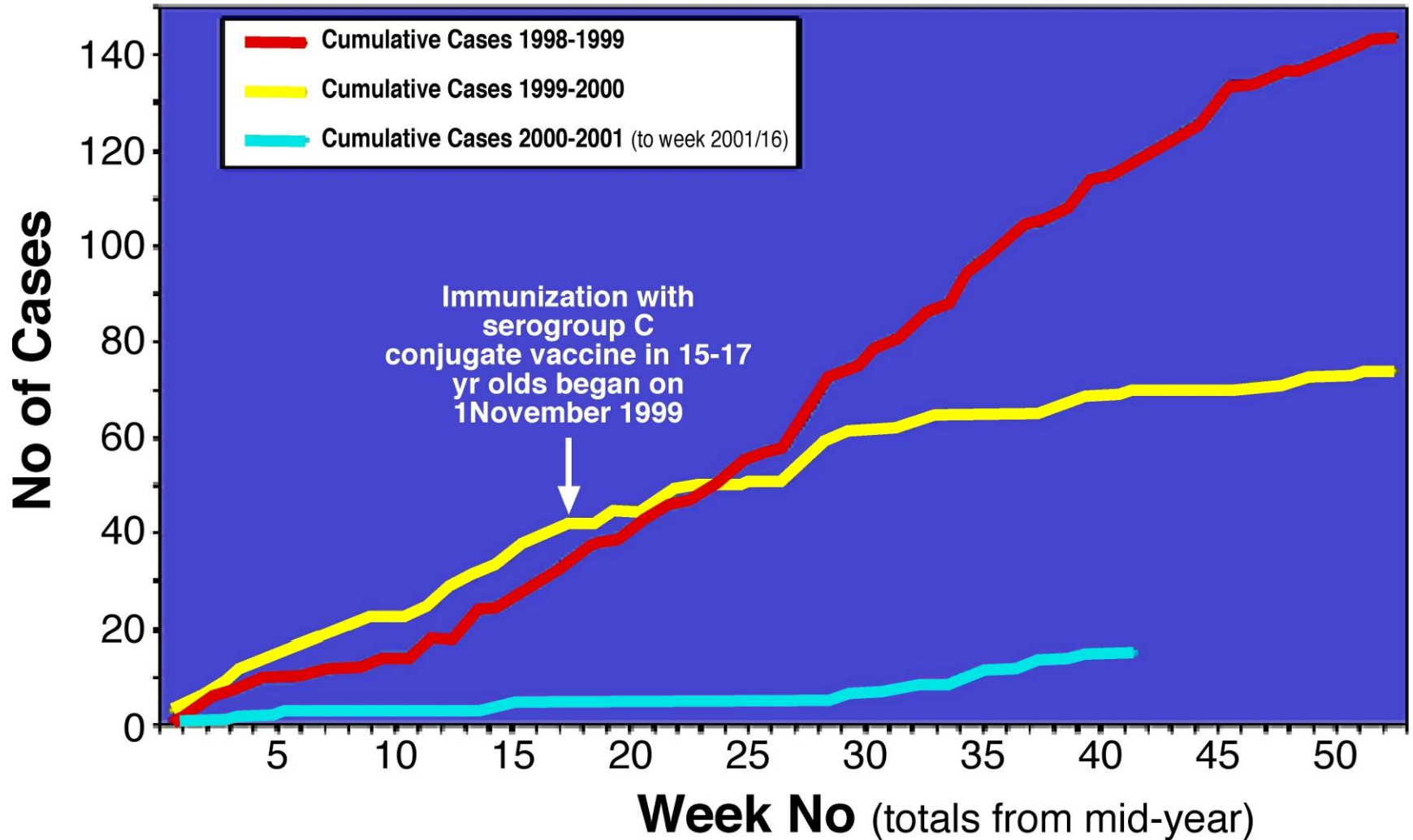
Life expectancy and medical progress



Vaccination campaigns eradicated lethal diseases

	N° of cases (year)	N° cases in 2001	Decrease
Smallpox	48,164 (1901-1904)	0	100%
Polio	21,269 (1952)	0	100%
Diphtheria	206939 (1921)	2	99.99%
Measles	894134 (1941)	96	99.99%
Rubeola	57686 (1969)	19	99.78%
Mumps	152209 (1968)	216	99.86%
Pertussis	265269 (1934)	4788	98.20%
<i>H. influenzae</i>	20000 (1992)	242	98.79%
Tetanus	1560 (1923)	26	98.44%

Eradication of meningococcus C by a new vaccine



Unique aspects of vaccines

- 
- Intangible value
 - Individual vs. society
 - Safety and efficacy
 - Compliance

Many vaccines were developed without a precise knowledge of the underlying mechanisms



The method of Pasteur:

1. Isolate
2. Inactivate
3. Inject

New challenges and new areas

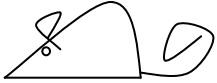
- Influenza
- HIV
- HCV
- Malaria
- Tb
- Emerging viruses
- ...
- Tumors
- Autoimmune diseases
- Neurodegenerative diseases

New tools for vaccine development

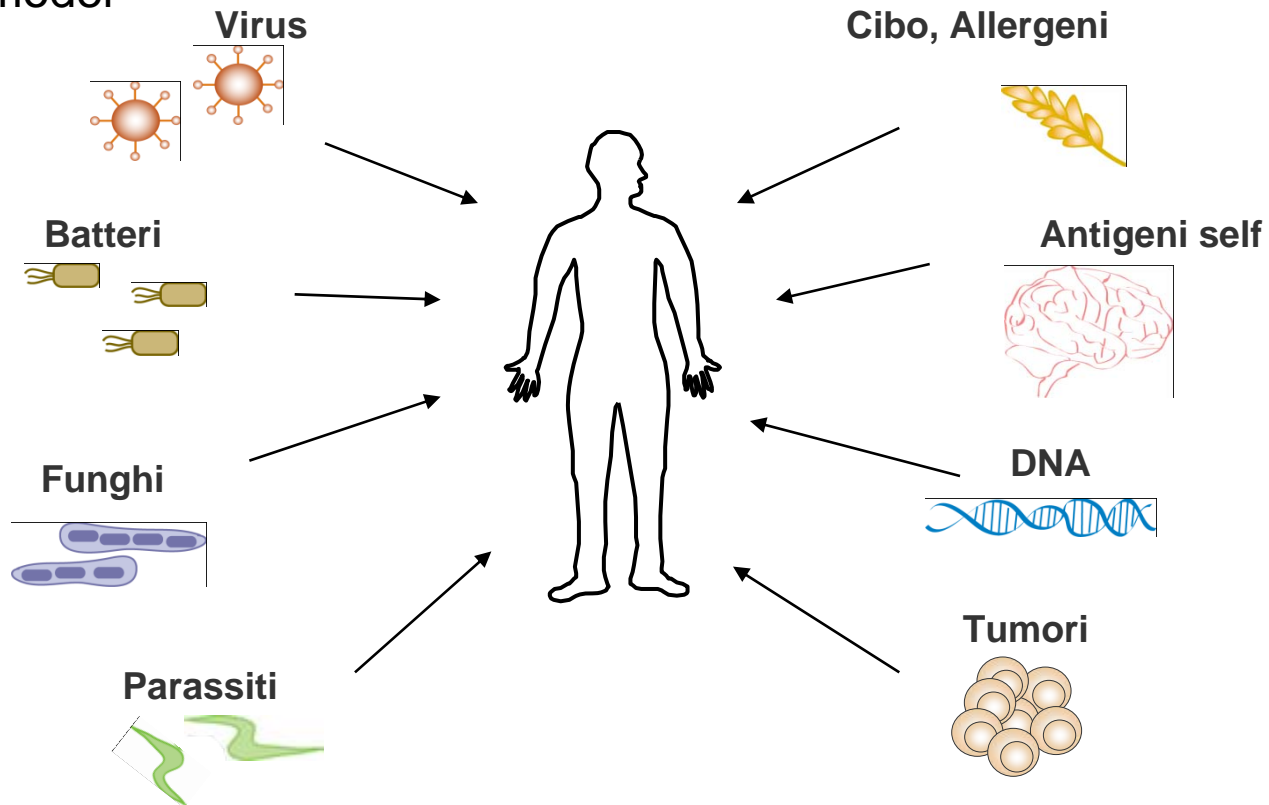
- Temperature sensitive mutants
- Viral deletion mutants
- Reassortment
- Codon deoptimization
- Replicating vectors
- Virus-like particles (Gardasil)
- DNA plasmids
- Fusion proteins
- Nanoparticles
- Vaccines for noninfectious diseases
- Therapeutic vaccines
- Antigen targeting
- Dendritic cells
- Adjuvants
- Monoclonal antibodies
- Analytic vaccinology

- 
- Poxviruses
 - Adenoviruses
 - AAV
 - VSV
 - Alphaviruses
 - Cytomegalovirus
 - Lentiviruses
 - VEE
 - BCG
 - *Listeria*
 - *Salmonella*

A new trend: from Mice to Man

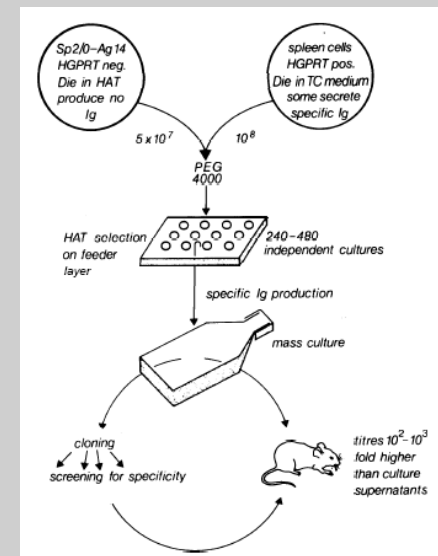
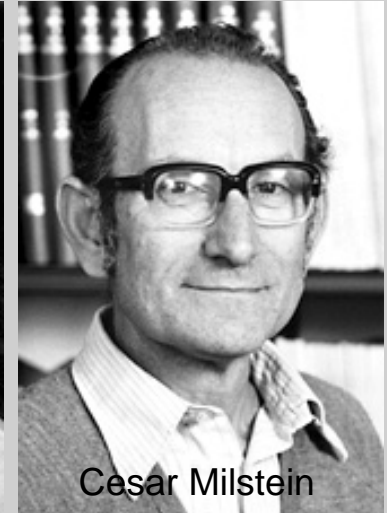


The animal model

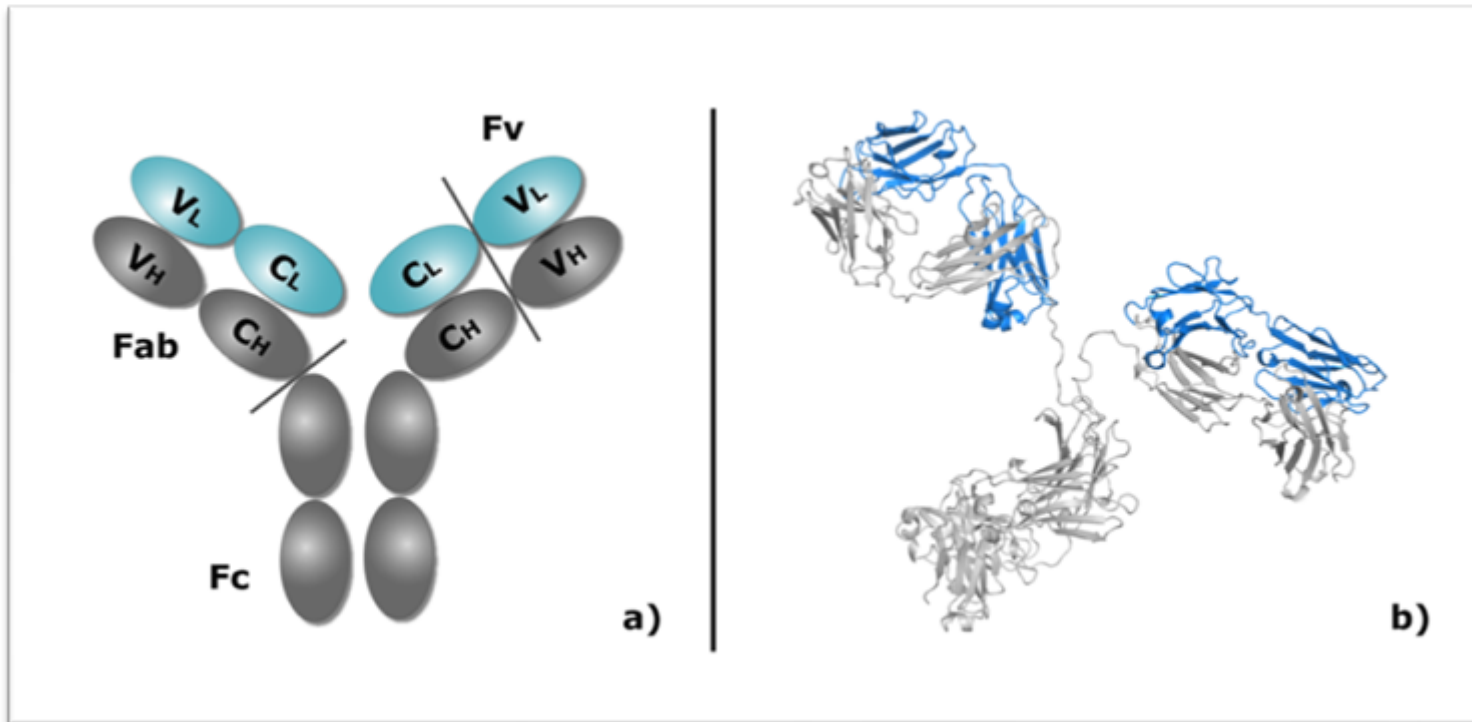


At the IRB we study the human immune response

From serotherapy to monoclonal antibodies



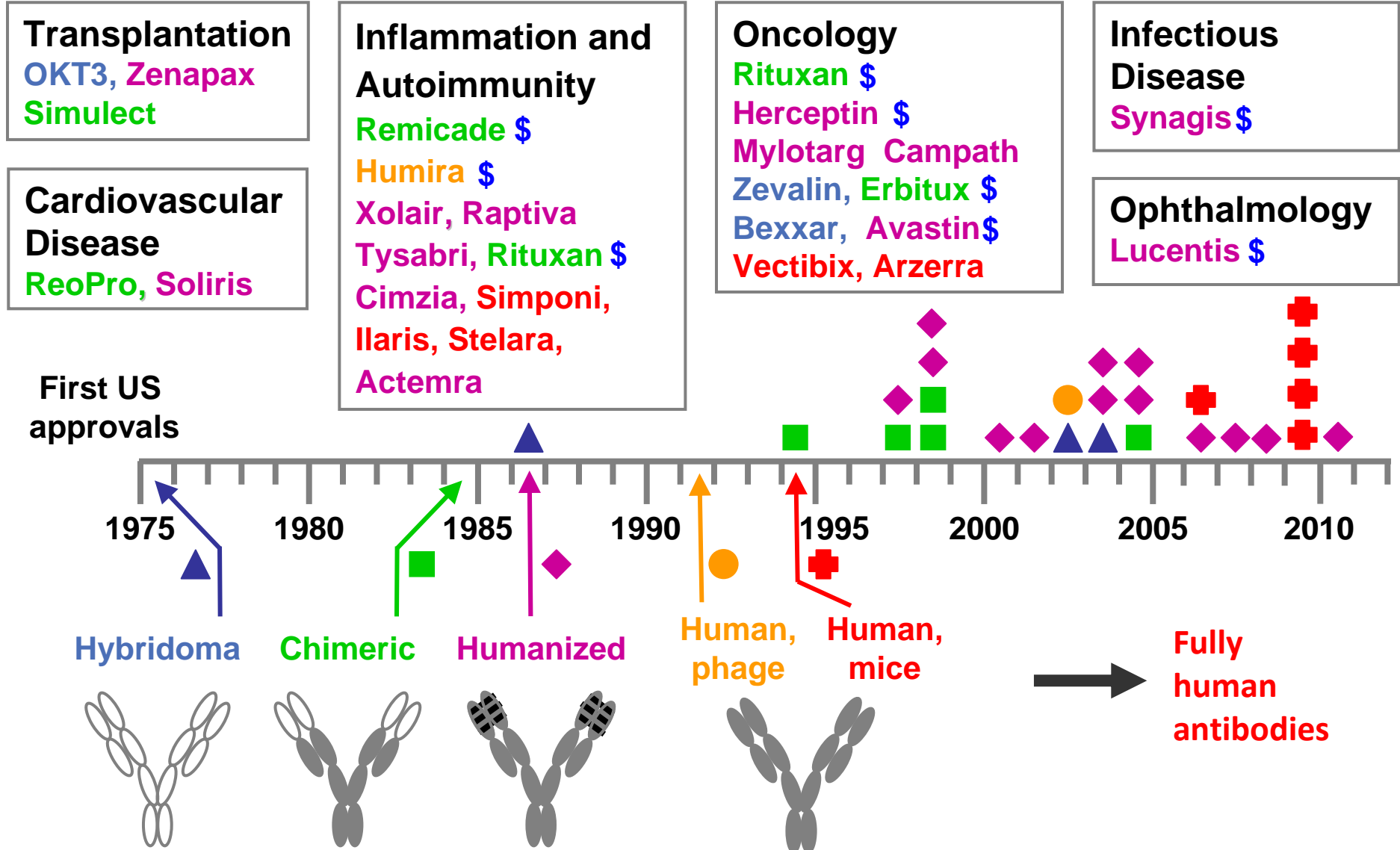
Antibodies as drugs



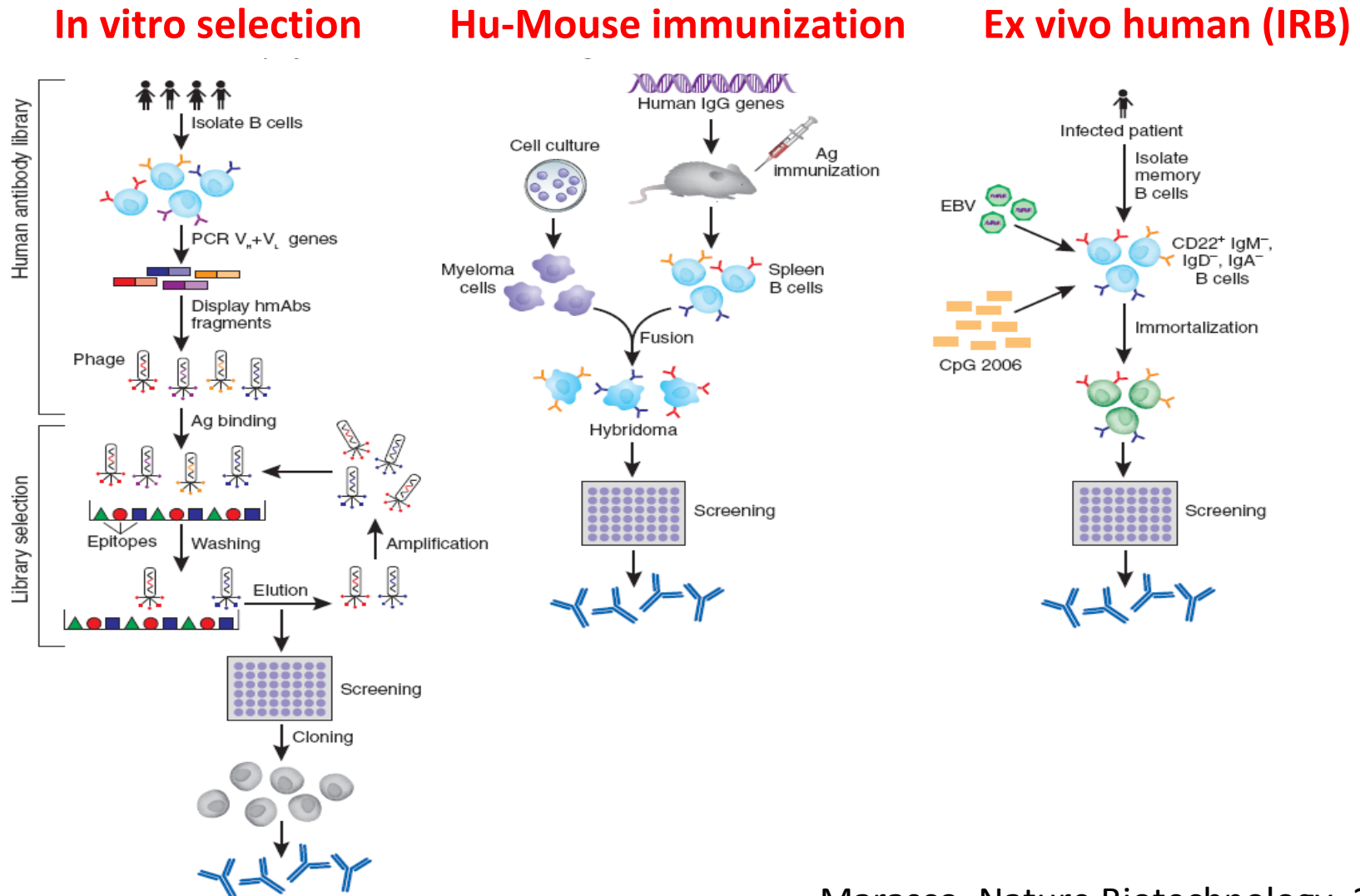
1. Specificity
2. Safety
3. Long half life

Monoclonal antibodies on the market

\$ >\$1 B sales in 2008


























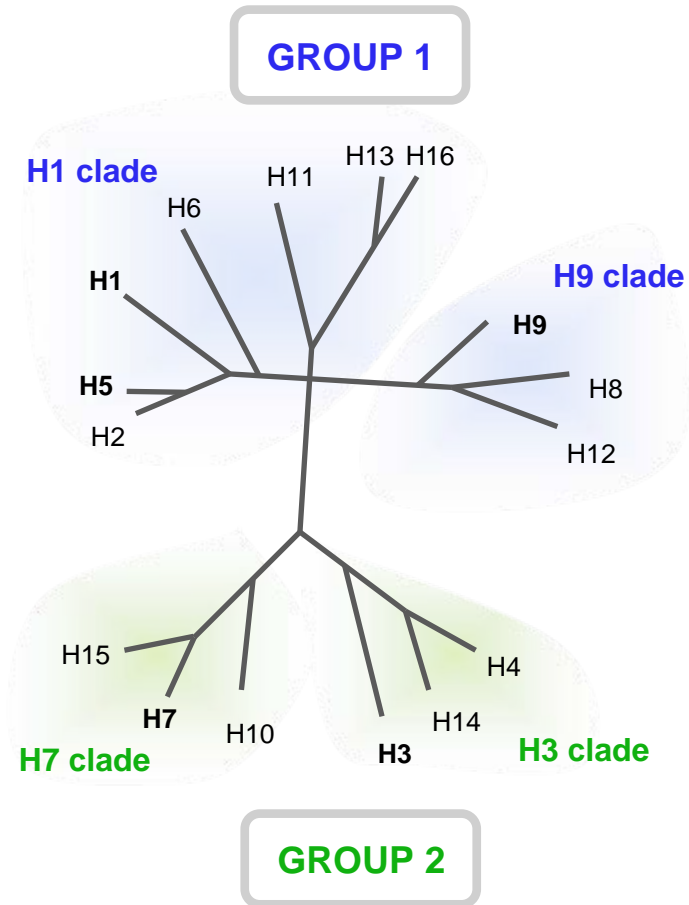
Human antibody techniques



The recurrent problem of seasonal influenza and the unpredictability of pandemic viruses

Influenza A virus subtypes

H1			
H2			
H3			 
H4			
H5			
H6			
H7			 
H8			
H9			
H10			
H11			
H12			
H13			
H14			
H15			

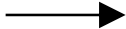
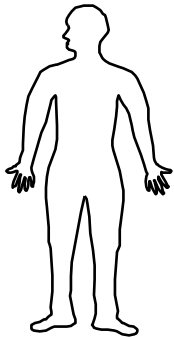


Are there antibodies that neutralize multiple influenza virus subtypes?

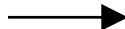
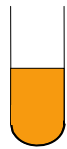
Passive vaccination

The current approach

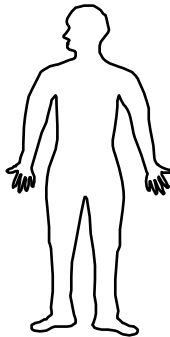
Infection



Serum

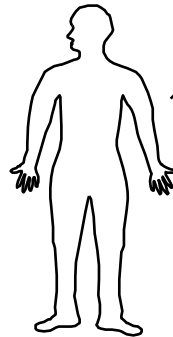


Prophylaxis
or therapy



The new approach

Infection



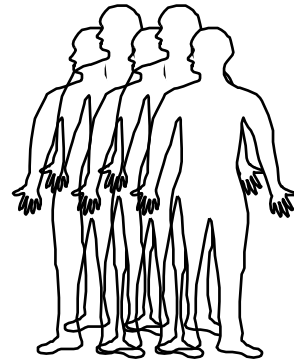
Antibody genes
from selected B cell



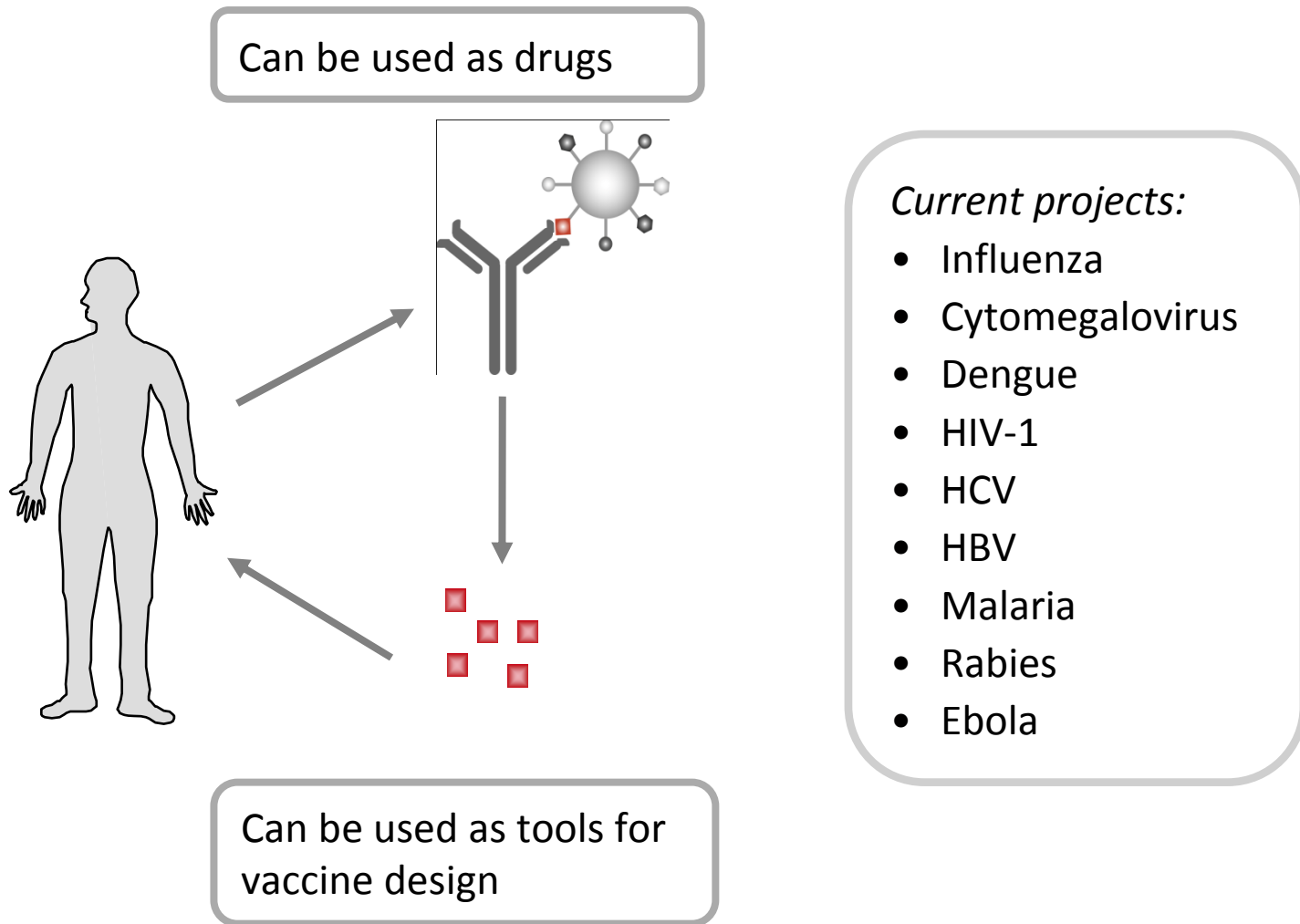
Mass production
in a cell line

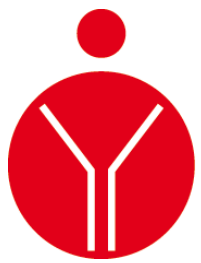


Prophylaxis
or therapy



Human monoclonal antibodies for serotherapy and analytic vaccinology





HUMABS

Humabs Biomed SA

Via Murate 5a, 6500 Bellinzona, Switzerland

- In 2004 IRB has licensed the human monoclonal antibody technologies to Humabs (William Rutter) and has established a collaboration agreement
- Humabs is a privately owned company incorporated in 2004 to develop and commercialize human monoclonal antibodies for treatment, prevention and diagnosis of infectious diseases
- In November 2010 Humabs moved from US to Ticino where is employing 8 people in the research laboratories in Bellinzona and is continuing the collaboration with IRB



L'IRB fa il bilancio dei suoi primi dieci anni