Le nuove vie delle scienze della vita

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The Institute for Research in Biomedicine

- Non profit private research Institute founded in 2000 in Bellinzona
- Governed by a Foundation Council (President, Giorgio Noseda)
- 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 m^2 lab space +
animal house with BSL3

IRB 1300 m^2 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

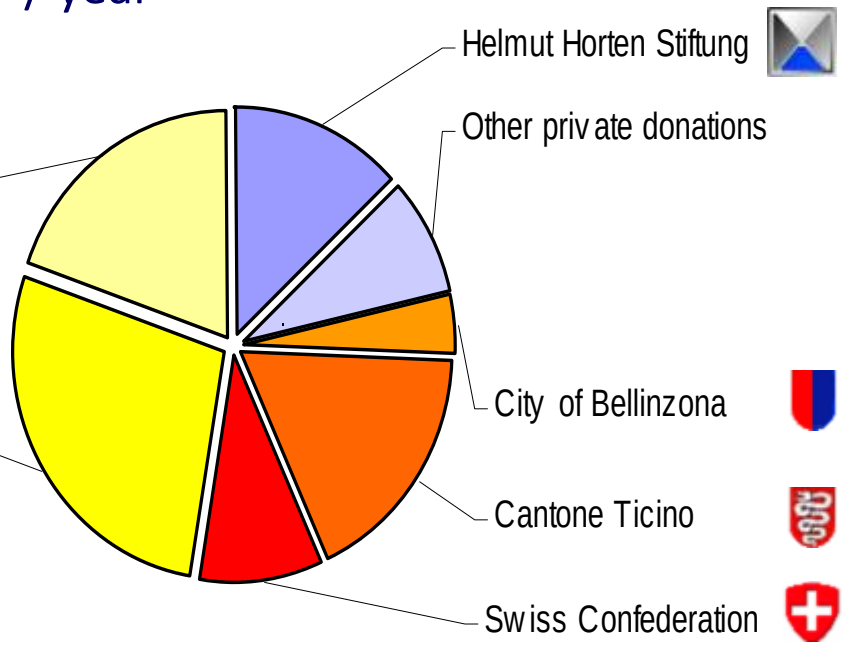
- 250 publications (IF:11.5)
- 40 PhD degrees since 2000
- 4 postdocs established independent laboratories abroad
- 4 group leaders obtained prestigious positions in other institutes or universities
- Several patents licensed in the field of antibodies

- 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



FNSNF Swiss National Science Foundation

erc

European Commission

wellcome trust

National Institutes of Health

Bill & Melinda Gates foundation

"the IRB is very cost effective"

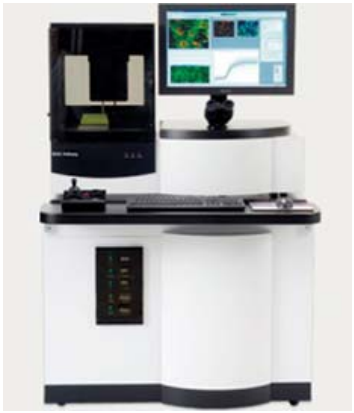
Some of the strengths of IRB

- 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

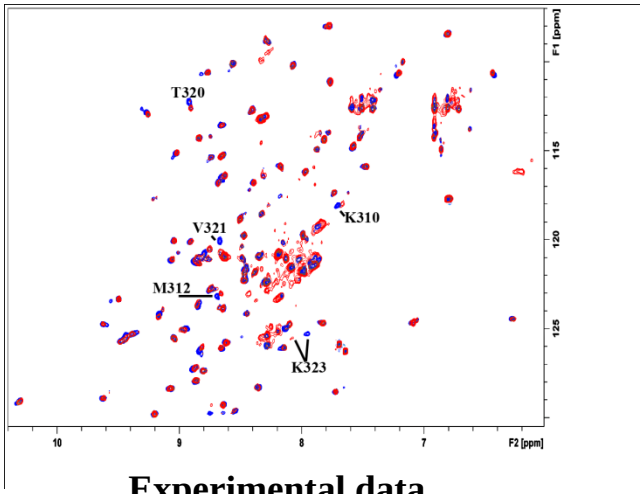
…thymic Treg cell development is a TCR-instructive process involving a niche that can be saturable at much lower clonal frequencies than is the niche for positive selection…

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

- Crystal structure
- Nuclear magnetic resonance
- Mutagenesis

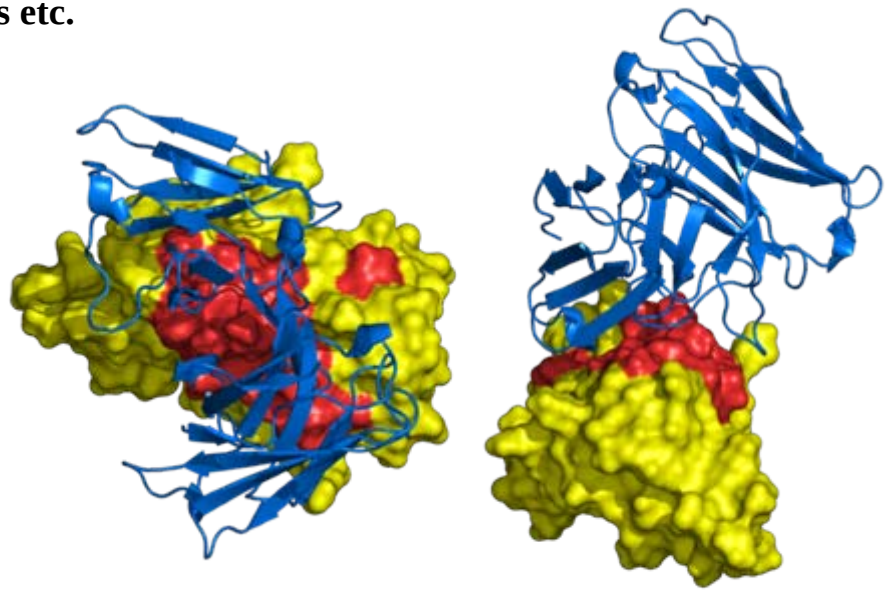
- Structure prediction
- Docking
- Molecular dynamics

Experiments in vitro, in vivo and in silico



Experimental data
NMR, escape mutants etc.

Computational Docking
CSCS, Manno



Luca Varani

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

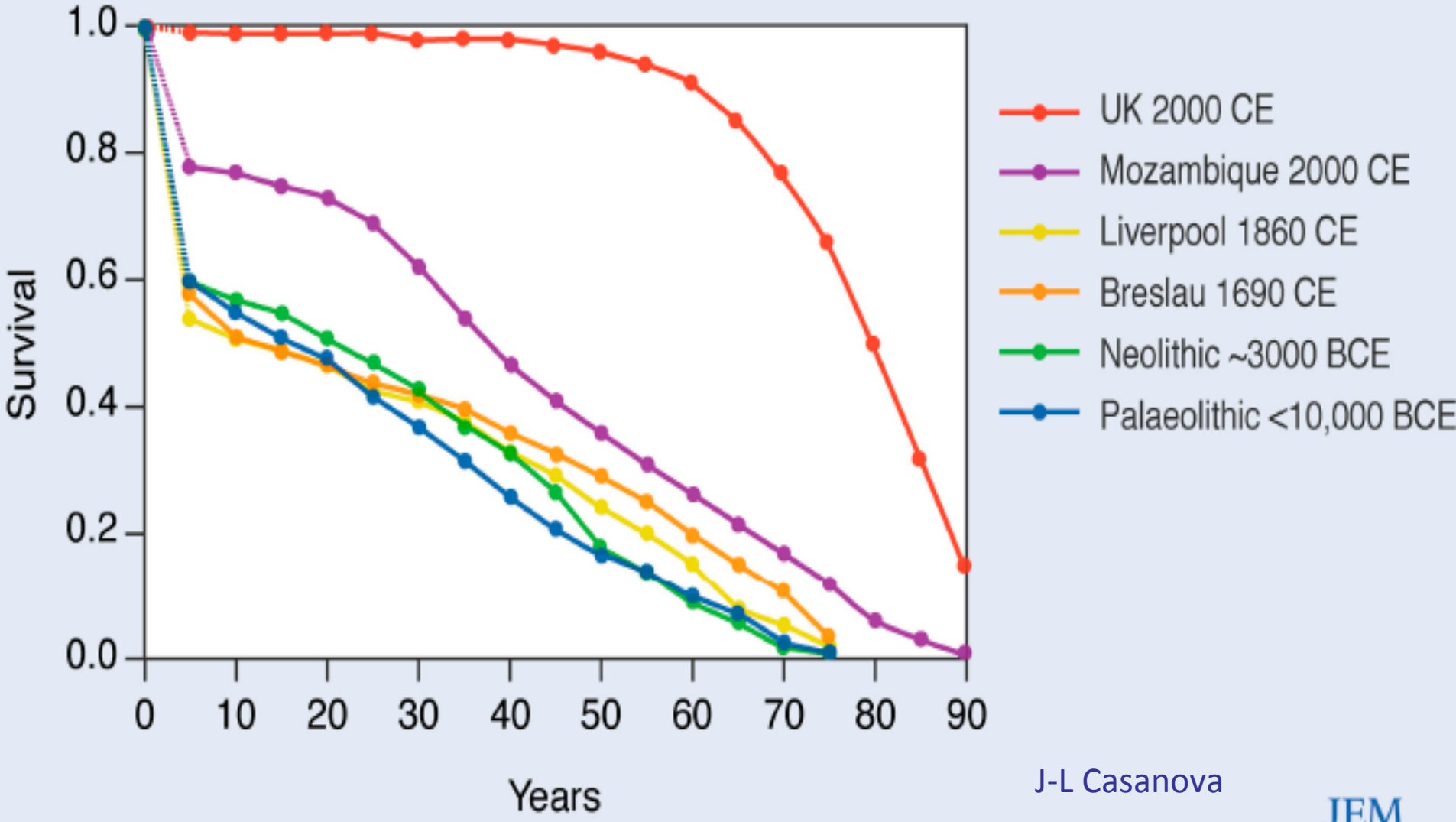
One of the biggest challenges is teaching scientists with such a diverse background how to speak with each other

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



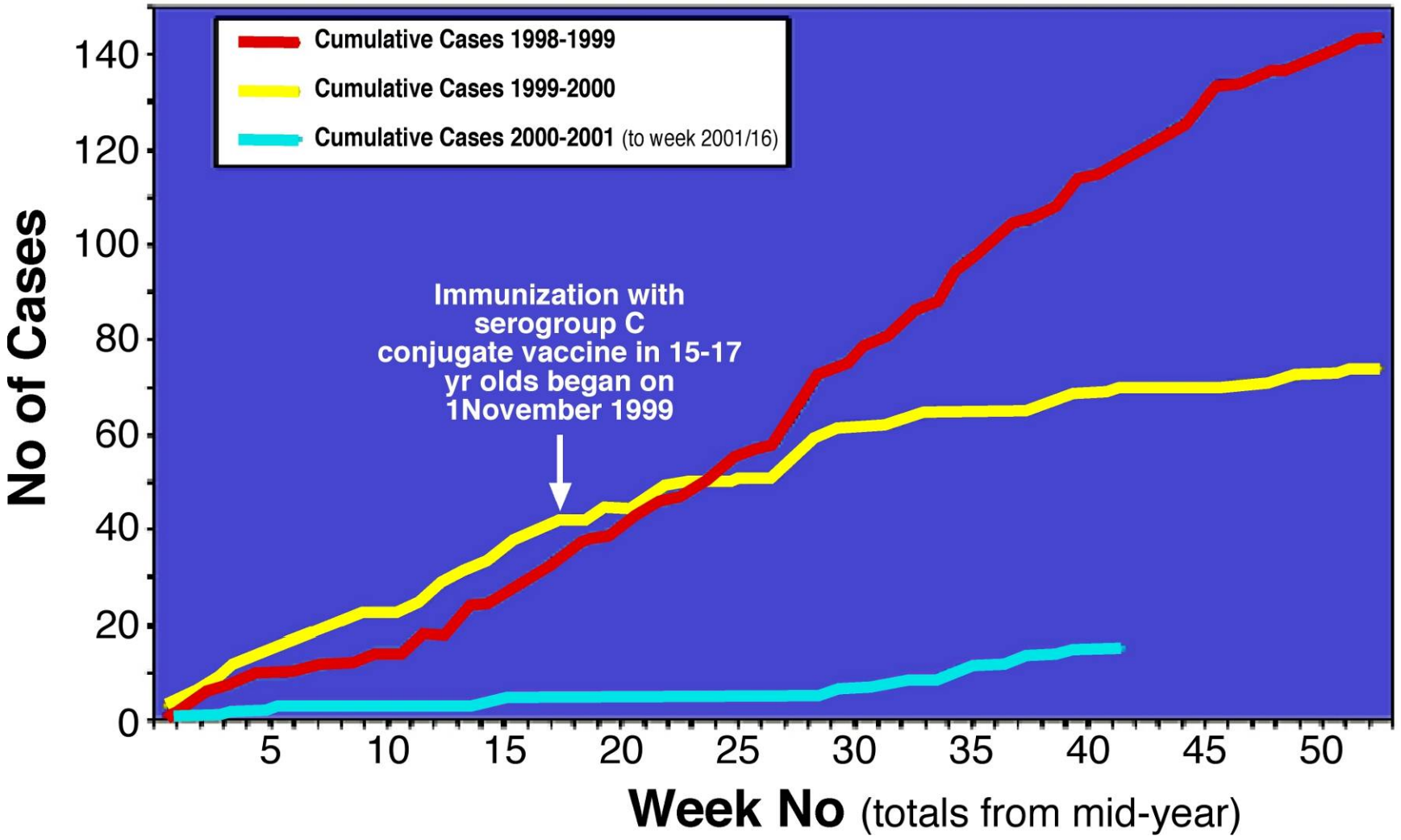
J-L Casanova

JEM

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%
H. influenzae	20000 (1992)	242	98.79%
Tetanus	1560 (1923)	26	98.44%

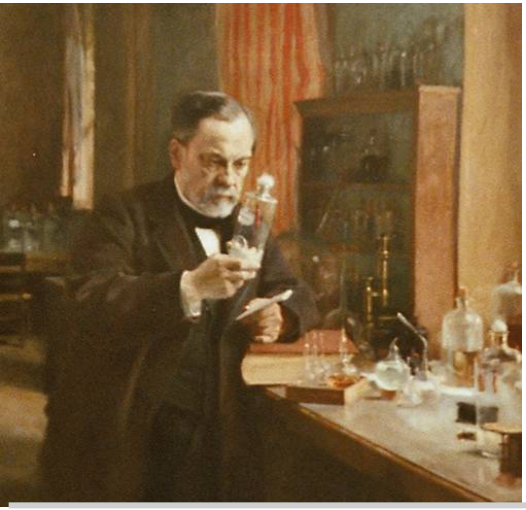
Eradication of meningococcus C by a new vaccine



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

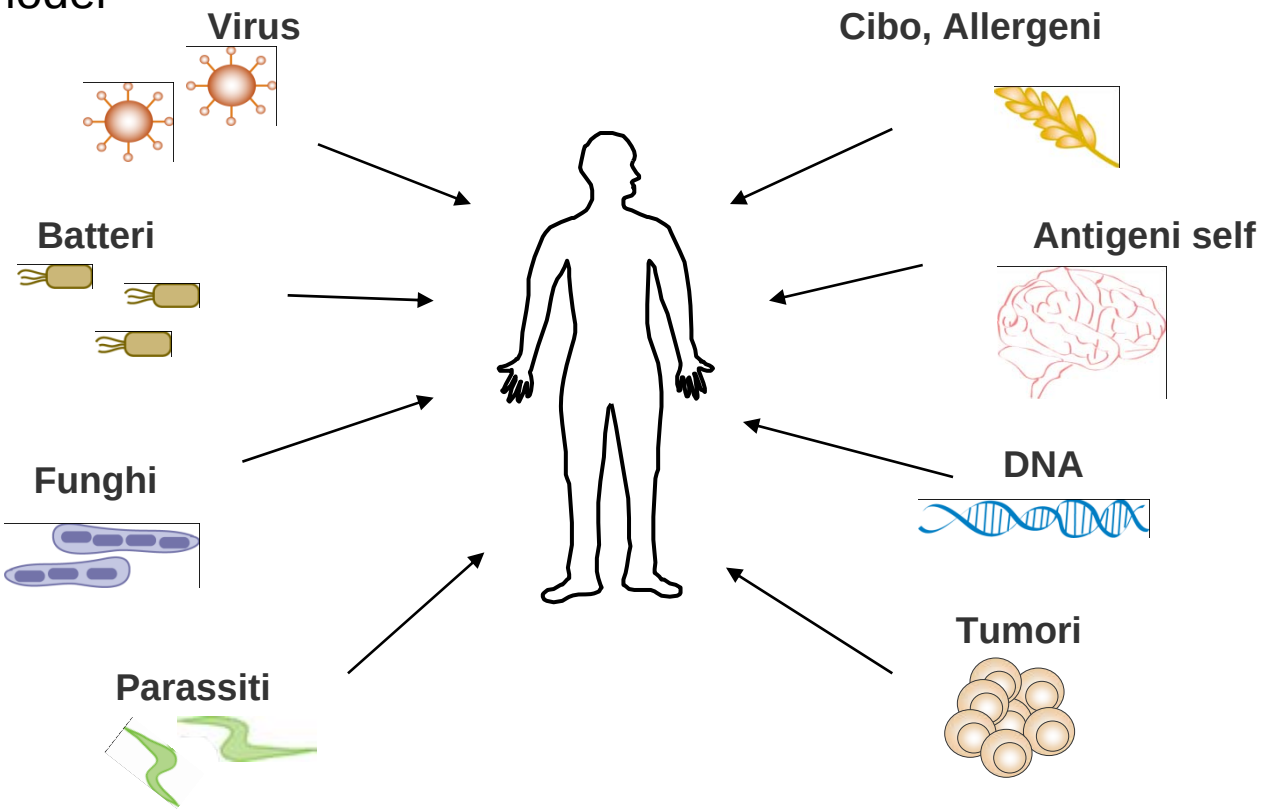
New tools for vaccine development

- 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

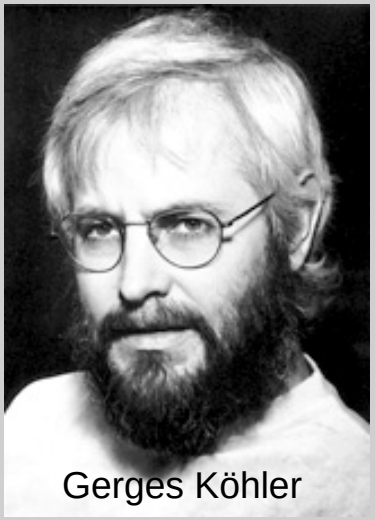
The animal model



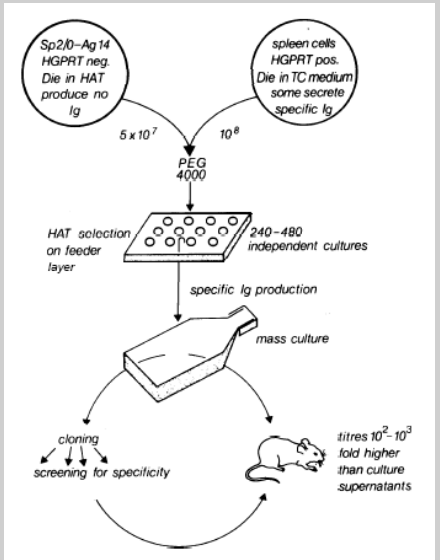
At the IRB we study the human immune response

From serotherapy to monoclonal antibodies

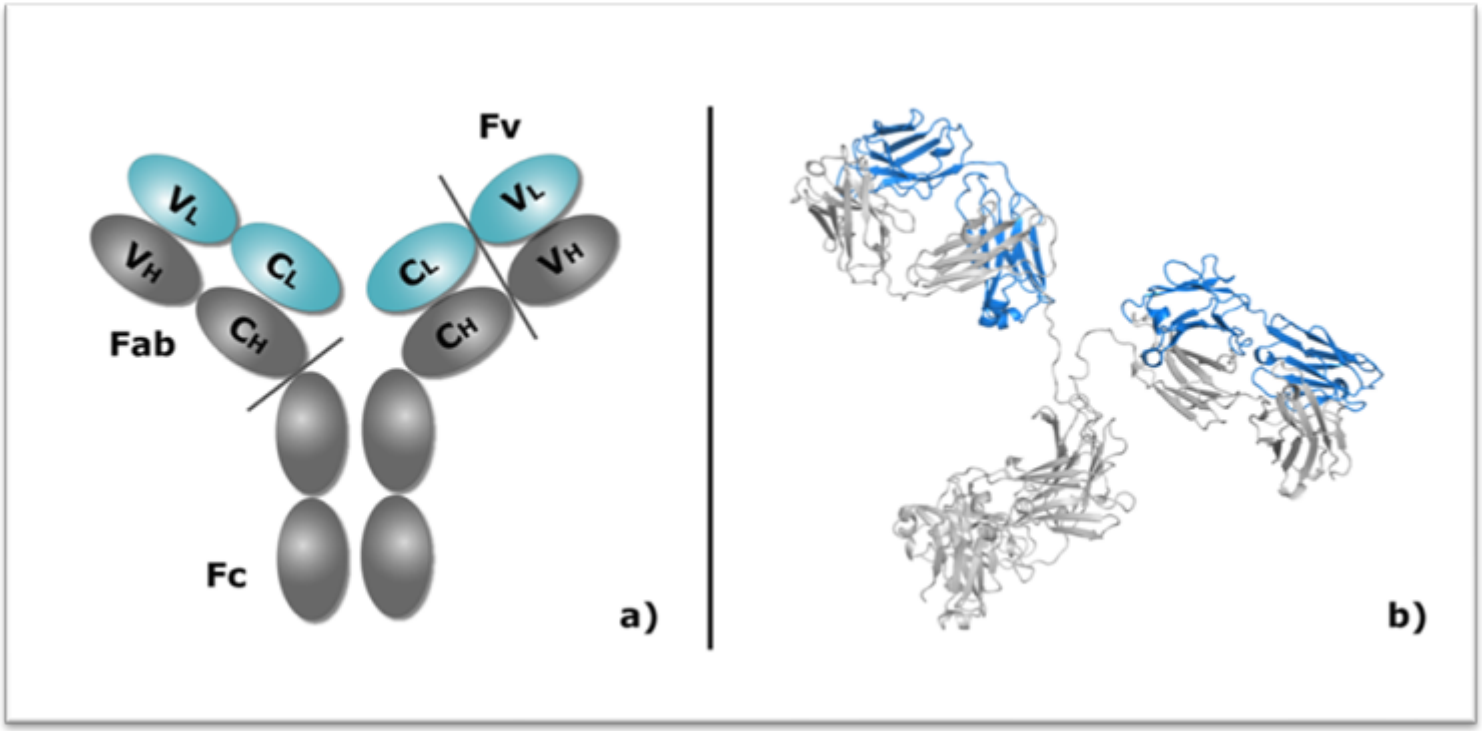

Emil von Behring


Gerges Köhler


Cesar Milstein



Antibodies as drugs



1. **Specificity**
2. **Safety**
3. **Long half life**

Monoclonal antibodies on the market

$ >$1 B sales in 2008

Transplantation
OKT3, Zenapax
Simulect

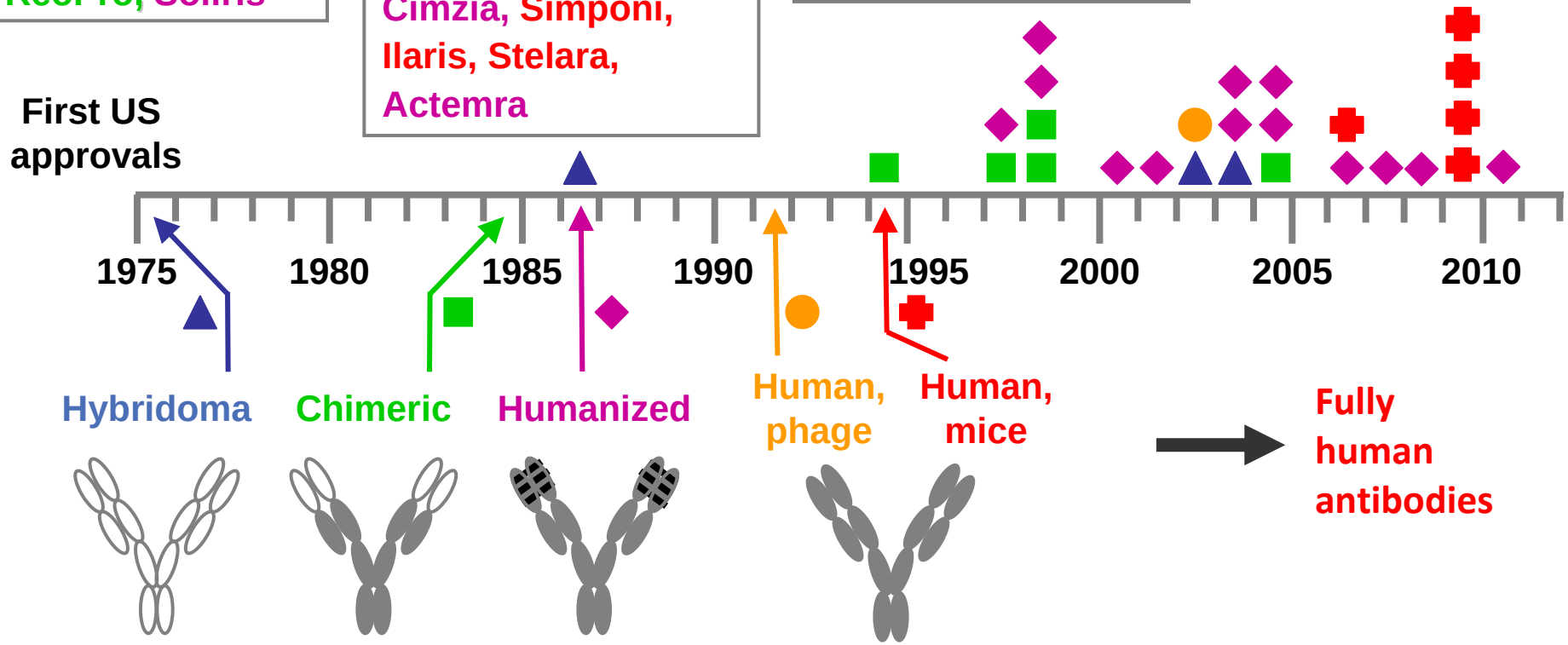
Cardiovascular Disease
ReoPro, Soliris

Inflammation and Autoimmunity
Remicade $
Humira $
Xolair, Raptiva
Tysabri, Rituxan $
Cimzia, Simponi,
Ilaris, Stelara,
Actemra

Oncology
Rituxan $
Herceptin $
Mylotarg Campath
Zevalin, Erbitux $
Bexxar, Avastin$
Vectibix, Arzerra

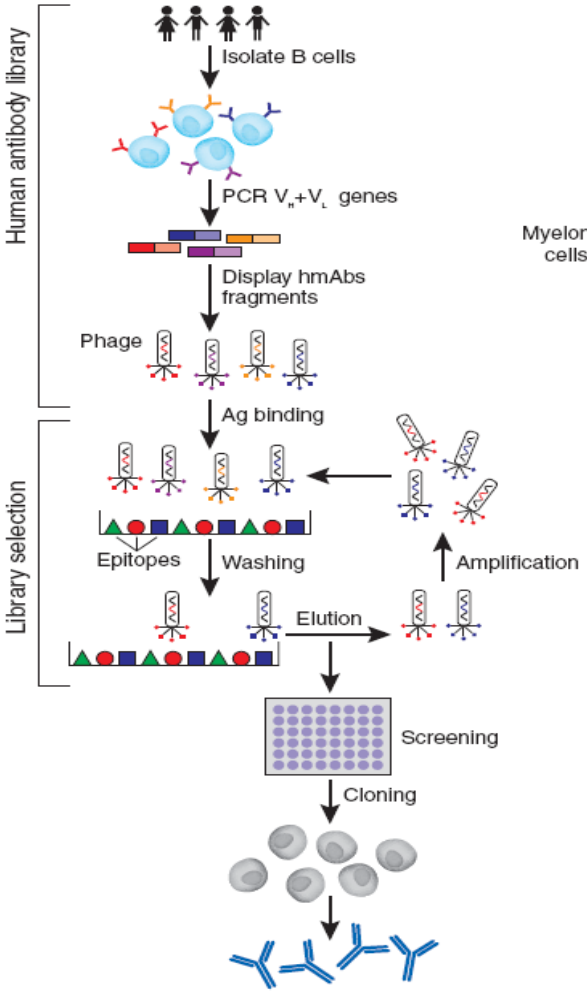
Infectious Disease
Synagis $

Ophthalmology
Lucentis $

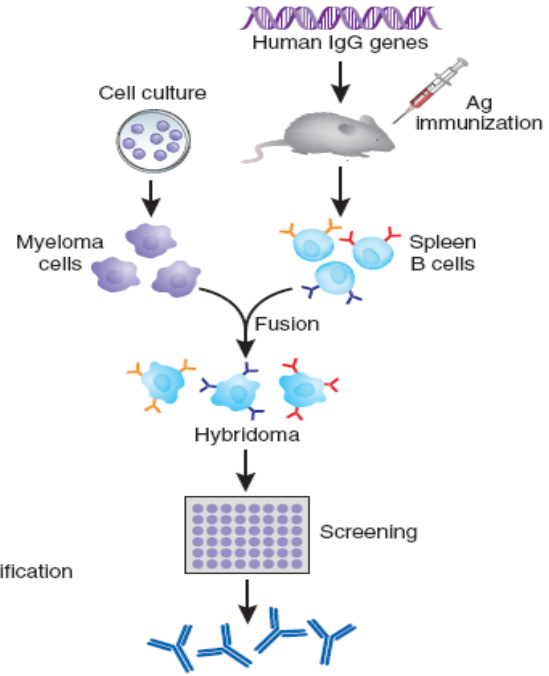


Human antibody techniques

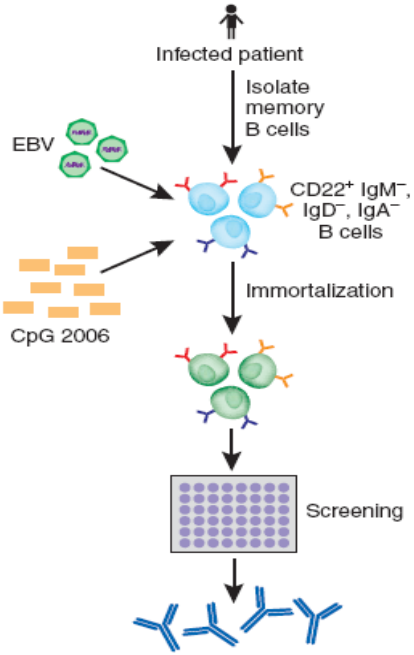
In vitro selection



Hu-Mouse immunization



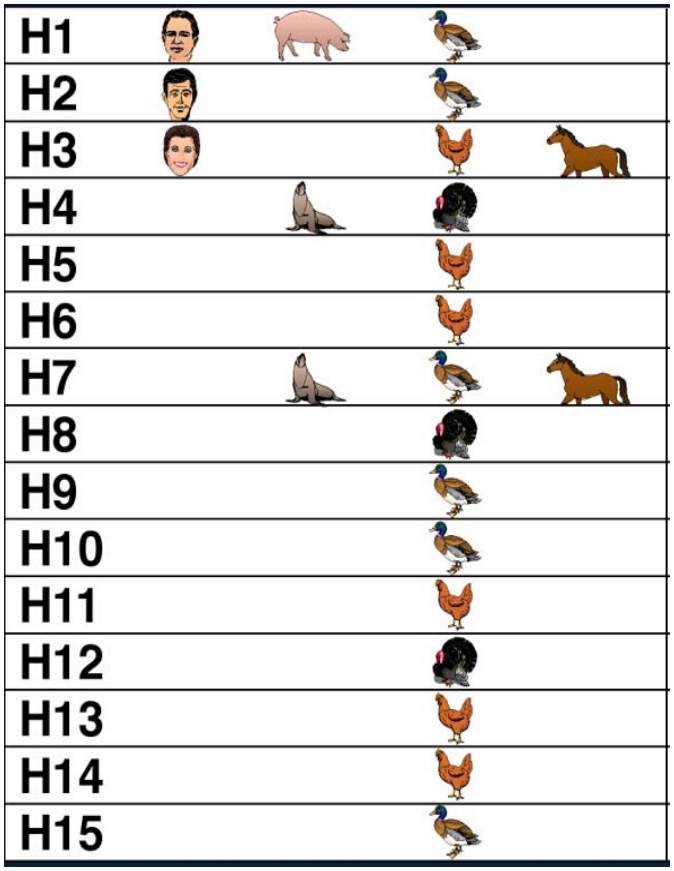
Ex vivo human (IRB)

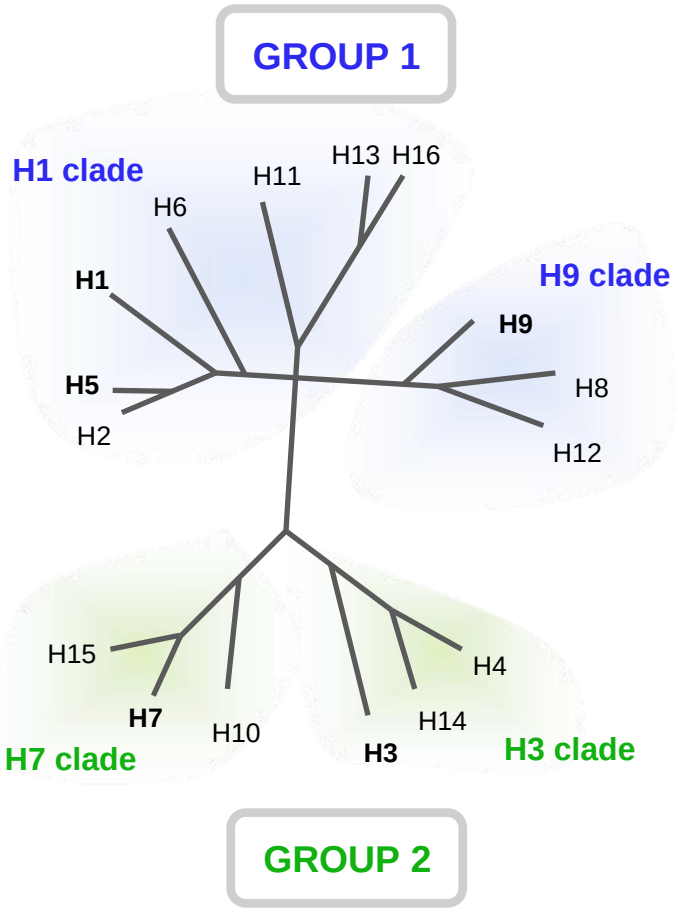


Marasco, Nature Biotechnology. 2007

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

Influenza A virus subtypes

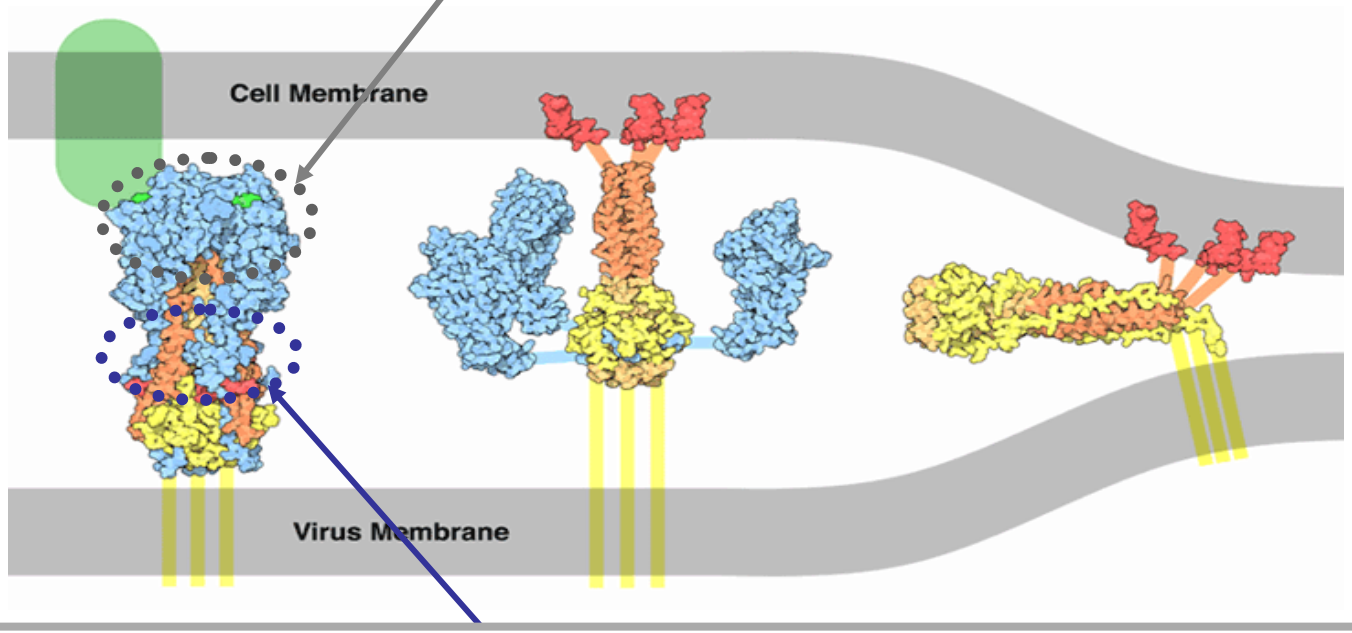




Are there antibodies that neutralize multiple influenza virus subtypes?

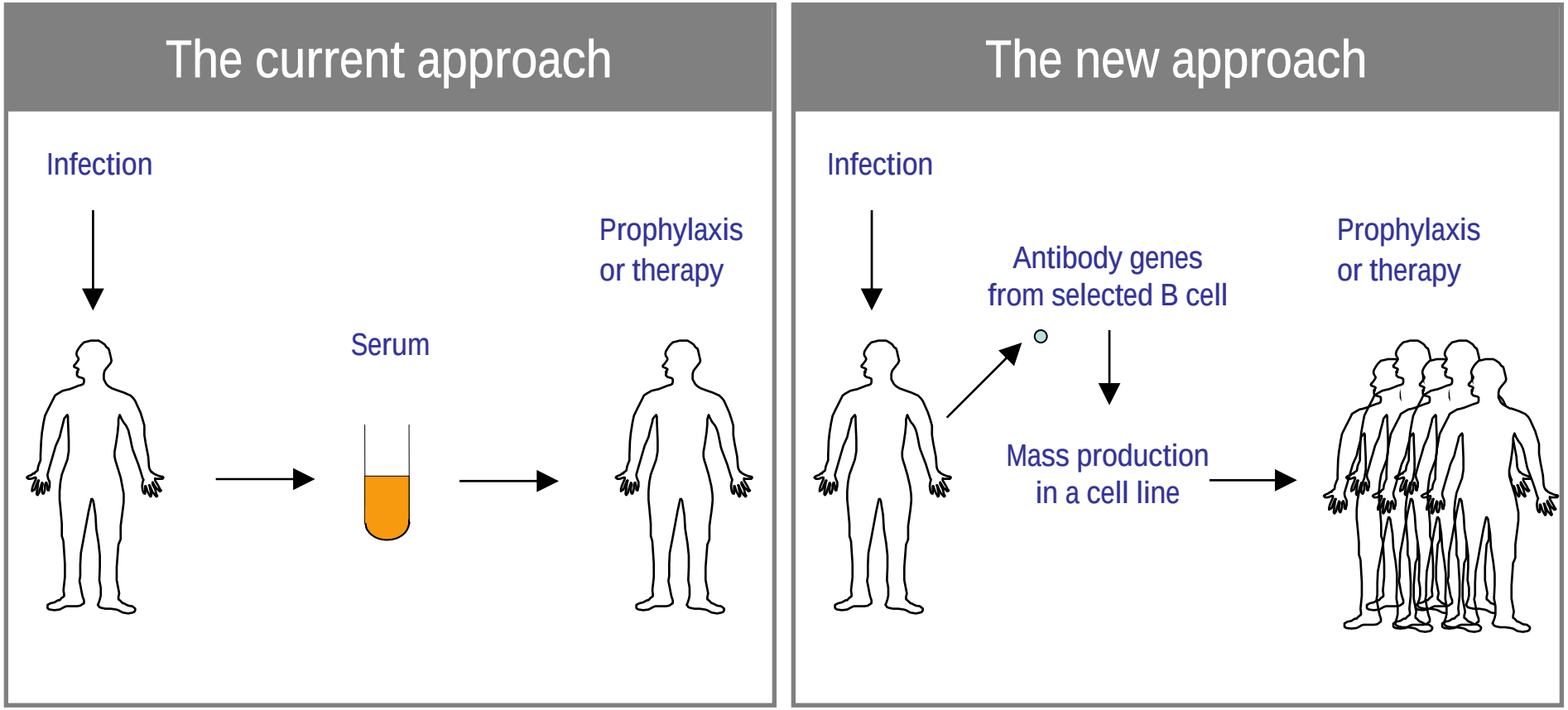
The Achille's heel of influenza virus

Classic neutralizing antibodies bind to a variable region and neutralize only a few viruses within a single subtype



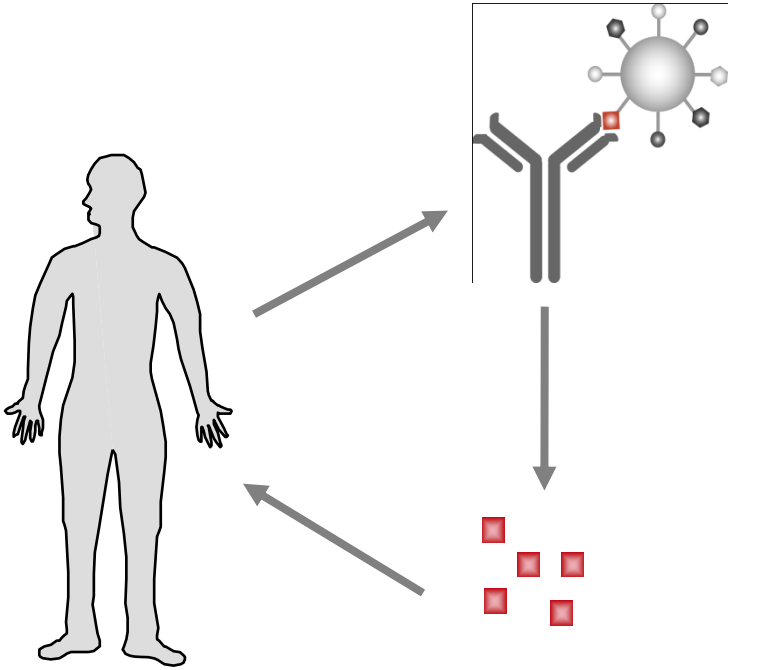
Some individuals make antibodies that bind to a conserved region. These antibodies neutralize most and in some cases all subtypes

Passive vaccination



Human monoclonal antibodies for serotherapy and analytic vaccinology

Can be used as drugs



Can be used as tools for vaccine design

Current projects:

- Influenza
- Cytomegalovirus
- Dengue
- HIV-1
- HCV
- HBV
- Malaria
- Rabies
- Ebola

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

Institute for Research in Biomedicine

L’IRB fa il bilancio dei suoi primi dieci anni