BIOLOGICAL SCIENCES’ BASIC RESEARCH AND BIOTECHNOLOGY IN ARGENTINA
Long tradition of excellence on scientific developments and training of high qualified human resources
HOWARD HUGHES GRANTS

43 Argentine Scholars since 1985
Total amount = u$s 16.396.330
R&D INVESTMENT IN ARGENTINA

**R&D investment**
Millions of dollars and as percentage of GDP

<table>
<thead>
<tr>
<th>Year</th>
<th>R&amp;D Investment (Millions of US$)</th>
<th>R&amp;D/GDP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>666</td>
<td>0.44%</td>
</tr>
<tr>
<td>2005</td>
<td>838</td>
<td>0.46%</td>
</tr>
<tr>
<td>2006</td>
<td>1,053</td>
<td>0.49%</td>
</tr>
<tr>
<td>2007</td>
<td>1,325</td>
<td>0.51%</td>
</tr>
<tr>
<td>2008</td>
<td>1,711</td>
<td>0.52%</td>
</tr>
<tr>
<td>2009</td>
<td>1,828</td>
<td>0.60%</td>
</tr>
<tr>
<td>2010</td>
<td>2,277</td>
<td>0.62%</td>
</tr>
<tr>
<td>2011</td>
<td>2,885</td>
<td>0.65%</td>
</tr>
</tbody>
</table>
R&D ARGENTINE PERSONNEL EVOLUTION

Total R&D Personnel FTE

Total R&D Personnel

Year
2003
2004
2005
2006
2007
2008
2009
2010
2011

Number
39.393
42.454
45.361
49.359
53.187
56.987
59.683
65.761
69.693

Number
55.635
59.150
62.543
67.856
73.558
79.391
83.211
92.201
98.445
ARGENTINE DISTINGUISHED SCIENTISTS
ARGENTINE DISTINGUISHED SCIENTISTS

HUGO LUJÁN

- Ph.D. in Biochemistry
- National Council for Science and Technology (CONICET) Principal Investigator
- Catholic University of Córdoba Full Teacher (Department of Biochemistry)
- Senior Fellow at the Guggenheim Foundation

PUBLICATIONS
- 44 Publications (as author and co-author)
- 4 Books & Book’s Chapters

PATENTS
- Vaccine against *Giardia Lambia* for human and veterinarian health treatments
- Oral vaccine production platform
- *Giardia* antigen for oral medicine supply

AWARDS
- NIH Inventor Award, 1995/97/99
- Council for S&T of Córdoba, 1999
- School of Medicine, 2000
- National Council for S&T of Argentina, 2000/02/05
- Argentine Society for Protozoology and Parasitic Diseases, 2001

Research focus: *Giardia Lambia* treatment
RESEARCH PROJECTS, PAPERS AND PATENTS

RESEARCH PROJECTS FINANCED BY ANPCyT

   “Cellular differentiation mechanism in Giardia lamblia”

   “Cellular differentiation mechanism in Giardia lamblia and other intestinal protozoan”

   “Cellular differentiation mechanism in one of the most primitive eukaryote cells, the intestinal protozoan Giardia lamblia”

   “Vaccine development against intestinal protozoan Giardia lamblia, based on manipulation of antigenic variation”

   “Molecular mechanisms of protein trafficking in the primitive eukaryote Giardia lamblia”.

   “Molecular mechanisms of antigenic variation in the intestinal parasite Giardia lamblia”.

   “Development of oral vaccines based on variant-surface proteins of the intestinal parasite Giardia lamblia”.

   “Molecular mechanisms of protein intracellular traffic during growth and differentiation of primitive eukaryote Giardia lamblia”.
REMARKABLE PAPERS

1. **CHARACTERIZATION OF SNARES DETERMINES THE ABSENCE OF A TYPICAL GOLGI APPARATUS IN THE ANCIENT EUKARYOTE GIARDIA LAMBLIA.**


2. **ANTIGENIC VARIATION IN GIARDIA LAMBLIA IS REGULATED BY RNA INTERFERENCE.**


3. **DISRUPTION OF ANTIGENIC VARIATION PROVES CRUCIAL FOR EFFECTIVE PARASITE VACCINE.**

Rivero, F.D., Saura, A. Prucca, C.G., Carranza, P.G., Torri, A., and Lujan, H.D.
PATENTS

1. MODIFIED PROTOZOAN EXPRESSING AT LEAST TWO VARIABLE SURFACE PROTEINS (VSP), A VACCINE COMPRISING IT AND PROCEDURES, USES, AND METHODS THEREOF.

2. PHARMACEUTICAL COMPOSITIONS COMPRISING A POLYPEPTIDE COMPRISING AT LEAST ONE CXXC MOTIF AND HETEROLOGOUS ANTIGENS AND USES THEREOF

3. PROTOZOAN VARIANT-SPECIFIC SURFACE PROTEINS (VSP) AS CARRIERS FOR ORAL DRUG DELIVERY
ARGENTINE DISTINGUISHED SCIENTISTS

GABRIEL RABINOVICH

- Ph.D. in Biochemistry
- National Council for Science and Technology (CONICET) Principal Investigator
- Immunology Full Professor at the University of Buenos Aires
- Associate Professor at many foreign Universities such as Maryland University, Harvard Medical School, Miami University

PUBLICATIONS
- 155 papers published in specialized magazines
- Invited to review more than 120 articles
- 11 book’s chapters

PATENTS
- 6 international patents granted
- 1 Argentine patent granted

AWARDS
- Mizutani Foundation for Glycosciences Award, 2005
- John Simon Guggenheim Memorial Foundation Award, 2006
- Elaine R. Shepard Memorial Investigator Award, Cancer Research Institute, 2006
- Third World Academy of Sciences (TWAS) Prize in Medical Sciences, 2011
- National Academy of Sciences’s Member, 2011
- Bernardo Houssay Award in Medicine, 2005/2011
- Trade Camera Ten Outstanding Young Persons Award, 2005
- Best scientist in medical research Award 2010
- National Academy of Medicine and Baron Foundation Award in Medical Sciences, 2012

Research focus: Cancer’s immunology
**RESEARCH PROJECTS, PAPERS AND PATENTS**

**RESEARCH PROJECTS FINANCED BY ANPCyT**

**1. PICT 2003; 05-13787 FONCYT**

**2. PICT 2006; 603 FONCYT**
Director: Gabriel Rabinovich. Programación 2008-2010. Título: "Impacto de la interacción entre proteínas glicanos en la inmunoección y escape tumoral: implicancia en estrategias de Inmunoterapia"

**3. PICT BICENTENARIO TIPO V PARA GRUPOS CONSOLIDADOS NACIONALMENTE Y RECONOCIDOS INTERNACIONALMENTE. PICT 2010-870.**

**4. PICT 2012; 2440. FONCYT**
Director: Gabriel Rabinovich. Programación 2013-2016. “Circuitos regulatorios mediados por lectinas y glicanos en la resistencia a terapias anti-angiogénicas”
REMARKABLE PAPERS

1. **Targeted inhibition of galectin-1 gene expression in tumor cells results in heightened T-cell-mediated rejection: a potential mechanism of tumor-immune privilege**

Natalia Rubinstein, Mariano Alvarez, Norberto Zwirner, Marta Toscano, Juan M. Ilarregui, Alicia Bravo, José Mordoh, Leonardo Fainboim, Osvaldo Podhajcer & Gabriel Rabinovich


2. **Differential glycosylation of TH1, TH2 and TH17 effector cells selectively regulates susceptibility to cell death**

Marta A. Toscano, Germán A. Bianco, Juan M. Ilarregui, Diego Croci, Jorge Correale, Joseph Hernandez, Norberto W. Zwirner, Francoise Poirier, Eleanor Riley, Linda G. Baum & Gabriel Rabinovich

Nature Immunology (2007) 8:825 – 834

3. **Tolerogenic signals delivered by dendritic cells to T cells via a galectin-1-driven immunoregulatory circuit involving IL-27- and IL-10**

Juan M. Ilarregui, Diego O. Croci, Germán A. Bianco, Marta Toscano, Mariana Salatino, Mónica Vermeulen, Jorge Geffner & Gabriel A. Rabinovich

4. **Galectin-1 deactivates classically-activated microglia and protects from inflammation-induced neurodegeneration**

Sarah C. Starossom, Ivan D. Mascanfroni, Jaime Imitola, Li Cao, Khadir Raddassi, Silvia F. Hernandez, Ribal Bassil, Diego O. Croci, Juan P. Cerliani, Delphine Delacour, Yue Wang, Wassim Elyaman, Samia J. Khoury & Gabriel A. Rabinovich

5. **Disrupting galectin-1 interactions with N-glycans suppresses hypoxia-driven angiogenesis and tumorigenesis in Kaposi’s sarcoma**

Diego O. Croci, Mariana Salatino, Natalia Rubinstein, Juan P. Cerliani, Lucas Cavallin, Howard J. Leung, Jing Ouyang, Juan M. Ilarregui, Marta A. Toscano, Carolina Domaica, María C. Croci, Enrique Mesri, Adriana Albini & Gabriel A. Rabinovich

6. **A pivotal role for galectin-1 in feto-maternal tolerance**

Sandra M. Blois, Juan M. Ilarregui, Mareike Tometten, Mariana García, Arif Suphi Orsal, Rosalia Cordo-Russo, Marta A Toscano, Germán Bianco, Bori Handjiski, Irene Tirado, Udo R. Markert, Francoise Poirier, Julia Szekeres-Bartho & Petra C Arck*, Gabriel Rabinovich*
1. COMPOSITIONS, KITS, AND METHODS FOR THE DIAGNOSIS, PROGNOSIS AND MONITORING OF IMMUNE DISORDERS BY MEANS OF GALECTIN-GLYCAN INTERACTIONS

Date: July 9th 2009

2. COMPOSITIONS, KITS AND METHODS FOR THE DIAGNOSIS, PROGNOSIS, MONITORING, TREATMENT AND MODULATION OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS AND HYPOXIA-ASSOCIATED ANGIogenesis disorders USING GALECTIN-1

International Application № PCT/US10/056547

3. "METHODS OF PREPARING A THERAPEUTIC FORMULATION COMPRISING GALECTIN-INDUCED TOLEROGENIC DENDRITIC CELLS"

Date: June 11th 2008.
ARGENTINE DISTINGUISHED SCIENTISTS

RAQUEL CHAN

• Ph. D in Molecular Biology
• Full Investigator at the Litoral Agrobiotechnology Institute, National Council of Science and Technology (CONICET)

PUBLICATIONS
• More than 63 papers published in specialized magazines
• 5 book’s chapters

AWARDS
• Argentine Excellency Institute, Human Excellency Award, 2006
• Argentine National Senat, Personality of the year, 2010
• Santa Fe Congress Award, 2012

PATENTS
• 7 invention patents granted. Most of them on stress tolerance in plants
• Hahb -10 and 11 gene

Research focus: Crop drought resistance
VEGETAL BIOTECHNOLOGY MAIN DEVELOPMENTS

• HAHB – 4 Gene
• Development of tolerant seeds to water and saline stress
• Productivity increase from 10% to 100%
• Crops: soybean, wheat, alfalfa and corn
• Patent and Royalties: National Council for Science and Technology (CONICET) and National University of Litoral (UNL)
• Licenced for 20 years to: BIOCERES
• Commercialization starting in 2014
Total investment in basic research grants in Life Sciences 2003-2012:

$486M (aprox. U$S 100M)

This amount could be recovered by the revenues of a single patent.
More than one third of all the patents obtained by the CONICET (168) were the outcome of basic research grants from the ANPCyT.
IBYME
Instituto de Biología y Medicina Experimental

Institute of Biology and Experimental Medicine
R&D

• Monoclonal antibodies for treatment of infectious diseases and cancer
• Glycan-protein interactions in chronic inflammatory diseases, autoimmunity and tumoral scope
• Antimicrobial peptides and proteins
• Recombinant yeast for optimization of protein expression
• Breast cancer and the role of progestagens and growth factors
IIBBA
Instituto de Investigaciones Bioquímicas de Buenos Aires

Biochemical Research Institute of Buenos Aires
R&D

- Structure-based protein engineering
- Regenerative and protective therapies of the Central Nervous System
- Development of commercial transgenic plants tolerant to biotic and abiotic stresses
- Development of induced Pluripotent Stem Cells (iPSC) for the treatment of human diseases
- Genomic cutting edge technology for gene sequencing and analysis
- High throughput screening of antiviral drugs
- Gene Therapy for cancer treatment
IAL
Instituto de Agrobiotecnología del Litoral
Litoral Institute of Agrobiotechnology
R&D

- Genetic modified crops of technological interest
- Development of tolerant plants to adverse environmental conditions
- Production of microbial pesticides
- Development of chemical and biological tools for applications in biorefineries
IBR
Instituto de Biología Molecular y Celular de Rosario
Rosario Institute of Molecular and Cellular Biology
R&D

- Drug development for Chagas disease
- Development of biotechnological tools for diagnosis and monitoring of human viral diseases
- Genetic engineering development and bioprocessing technology
- Breakthrough of antibiotic resistance mechanisms
- Genetic diagnosis of human diseases
CIDIE
Centro de Investigación y Desarrollo en Inmunología y Enfermedades Infecciosas
Research and Development Center on Immunology and Infectious Diseases
CIDIE
Centro de Investigación y Desarrollo en Inmunología y Enfermedades Infecciosas
Research and Development Center on Immunology and Infectious Diseases

R&D

• Research and development of monoclonal antibodies, recombinant proteins and viral particles for diagnosis and treatment of diseases

• Protozoan Variant-Specific surface proteins as carriers for oral or mucosal drug delivery

• Production of a novel diagnostic kit for a fast and simple detection of enteric pathogens
IIB-INTECH
Instituto de Investigaciones Biotecnológicas
Biotechnology Research Institute
• Reproductive biotechnology and animal breeding
• Genetic engineering and bioprocessing technology
• Bioinformatic optimization of epitopes for antibodies production
• Development of diagnostic kit for Chagas disease
• Development of novel diagnostic techniques for infectious diseases
• Development of veterinary vaccines
CERELA
Centro de Referencia en Lactobacilos
Lactobacilli
Reference Centre
R&D

- Development of new lactic ferments and probiotics applied to food, veterinary and pharmaceutical industry
- Basic and applied studies of lactic bacteria of biotechnological interest
- Identification, typification, differentiation and sequencing of bacterial strains
RESEARCH INSTITUTES

PROIMI
Planta Piloto de Procesos Industriales Microbiológicos
Pilot Plant of Microbiological Industrial Processes
RESEARCH INSTITUTES

PROIMI
Planta Piloto de Procesos Industriales Microbiológicos · Pilot Plant of Microbiological Industrial Processes

R&D

• Biomolecules and biomaterials for biotechnological applications
• Biological control of agronomic pests
• Optimization of microbial bioprocess
• Design and optimization of the process of biomass production
• Biochemical and molecular identification of bacteria
Comparative proteomics and immunoproteomics for the identification of new vaccine candidates for *B. pertussis*

Identification of the mechanisms involved in the cellular duplication and resistance of *B. pertussis*

Production of industrial enzymes and microbial soil inoculants

Control and production of Brucelosis vaccine

Antigen production for vaccine formulation against *B. pertussis*
RESEARCH INSTITUTES

INGEBI
Instituto de Investigaciones en Ingeniería Genética y Biología Molecular
Genetic Engineering and Molecular Biology Research Institute

R&D

• Tobacco and potato transgenic plants resistant to viral, bacterial and fungal diseases
• Detection of gene mutations related to human diseases
• Epitope production of bovine rotavirus and human papilloma virus in tobacco plants
• Molecular and immunological markers for diagnosis, prognosis, monitoring and treatment of Chagas disease
• Non viral vectors for cancer gene therapy
ICT-MILSTEIN
Instituto de Ciencia y Tecnología
Dr. César Milstein
Dr. César Milstein Institute of Science and Technology
R&D

- Development of new generation vaccines for Aftosa fever
- Use of a platform of vegetal production for the development of vaccines against the viral bovine diarrhea
- Development of an inactivated vaccine against Hepatitis A
- Development of nanoantibodies
- Development of universal influenza vaccines
- Development of molecular and bioinformatic methods for the characterization and diagnosis of Aftosa fever virus
BIOTECHNOLOGY COMPANIES IN ARGENTINA
BIOTECHNOLOGY MAIN INSTITUTIONS

• 50 partners (national and international enterprises)
• Promotes Latinamerican Biotechnology Integration
• Suitable vehicle for scientific knowledge communication

• 21 Companies (Pharma, diagnostics, plant and animal biotechnology, biofuels, forestry, etc.)
• Promotes development of the sector and public-private partnership.
According to Bisang – Stubrin (2013) there are around 240 biotechnological enterprises in Argentina.
LEADING BIO COMPANIES

HIGH QUALITY BIOPHARMACEUTICALS

- Therapeutic proteins pipeline

- Transgenic animals, gene therapy and biodiversity technological platforms:
  - Angiogenesis and muscle regeneration using the vascular endothelial growth factor
  - White Genome Project: isolate, identify and characterize Antarctic bacterial strains for sequencing of the complete genome (*Bizonia Argentinensis* bacteria)
High level expression of bioactive recombinant human growth hormone in the milk of a cloned transgenic cow (J. Biotechnology, 2006)

Daniel Salamone1,2, Lino Barañao3, Claudio Santos1, Jorge Artuso1, Carlos Werning1, Leonardo Bussmann6, Aida Prync1, Cesar Carbonetto1, Susana Dabsys1, Carlos Munar5, Guillermo Berra4, Ignacio Berra, Roberto Salaberry1, Nahuel Fernández1, Mariana Papouchado, Marcelo Foti5, Norberto Judewicz1, Ignacio Mujica5, Luciana Muñoz, Silvana Mannocci1, Silvina Fenández Alvarez1, Eliseo González, Juan Zimmermann, Marcelo Criscuolo1, Carlos Melo1.

1. Biosidus S.A.
2. Facultad de Agronomía, Universidad de Buenos Aires
3. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires
4. Instituto Nacional de Tecnología Agropecuaria
5. Munar y Asociados
6. Instituto de Biología y Medicina Experimental - CONICET
• **First transgenic bovine** to produce **mother’s milk**
• Artificial induction of lactancy
• Development of San Martin National University and National Institute of Agricultural Technology (INTA)
• Contribution to lactant human nutrition

• **Horses’ cloning** by embrionic aggregation technique
• Higher pregnancy rate
• Higher animal development and quality
• Animal Biotechnology Laboratory, University of Buenos Aires
LEADING BIO COMPANIES

HIGH TECH VEGETABLE BASED BIO PRODUCTS

- GMC development and production
- Vegetable based biomolecules production
- Acquisition of improved crops by genetic engineering
- In vitro seeding capacity: one million
Over one hundred pharmaceutical products and state-of-the-art biological specialties portfolio, including bacterial and viral vaccines, antibiotics, parasiticides and pharmaceutical specialties for cattle, sheep, horses, swine, and pets

First FMD Vaccine, international tender to supply U.S.A., Mexico and Canada. Supplier of all South American Countries
LEADING BIO COMPANIES

BIOTECH DEVELOPMENT AND PRODUCTION

- Worldwide recombinant proteins exporter
- Generation of Master Cell Bank and Working Cell Bank
- Development of proprietary technologies for sustained-release biopharmaceuticals
- Development of monoclonal antibodies
LEADING BIO COMPANIES

APPLIED BIOTECHNOLOGY FOR THE FOOD INDUSTRY (MEAT AND DAIRY)

• Argentinean lead producer of frozen enzymes (90% market share)
• Sustained growth in domestic sales for 7 consecutive years
• Doubled exports over the last six years (85% export share)

Consortium: Insud Group, INTI, National University of Quilmes, Oncology Institute Ángel Roffo

Pharmaceutical Dairy Project to produce somatropin (recombinant human growth hormone)

Consortium: IBYME Foundation and Biosidus
Biotechnology Consortia

Development and production of intelligent molecular nano transportation.
Consortium: National University of Litoral, Eriochem S.A. and Gemabiotech S.A.

Technological Platform Development for the production of recombinant factor VIII proteins.
Consortium: National University of Litoral, Zelltek S.A. and Gemabiotech S.A.
Bovine tuberculosis and paratuberculosis experimental vaccine’s production and evaluation.

**Consortium:** INTA Biotechnology Institute, Dr. Cesar Milstein Science and Technology Institute

Producción de vacuna para la brucelosis bovina a escala piloto.

**Consortio:** Fundación Instituto Leloir IDEHU, CONICET, Inmunova, Biogénesis Bagó, Laboratorio Azul.

Transgenic forage crop’s production for best bovine resistance to biotic and abiotic factors.

**Consortium:** INDEAR, Bioceres, Produsem, CONICET
79 KBE created between 2011 and 2013

Agriculture and livestock: 11
Energy: 3
Health: 19
Animal Health: 3
Social Development: 2
Energy: 6
Industry: 8
Infrastructure: 1
Environment: 1
Health: 7
ICT: 1
Industry: 2
Health: 4
Agriculture and livestock: 2
Energy: 2
Industry: 4
Health: 3
NEWBORN BABIES’ CHAGAS DIAGNOSIS

- Diagnosis Kits Platform’s development
- Technology application to other infectious newborn babies’ illnesses

Consortium: CONICET, Pablo Cassará Lab and Unifarma S.A.
NANOTECHNOLOGY FOR CANCER TREATMENTS

- Intelligent nanoparticles’ development for cancer diagnosis and treatment

Consortium: Fundación Instituto Leloir and Inmunova S.A.
ENZYME PRODUCTION FOR BIODIESEL

• Synthetic enzyme production through microorganism’s genetic engineering

• This product is used for pollutant elimination in biodiesel production

Consortium: CONICET and KECLON S.A.
THANK YOU.