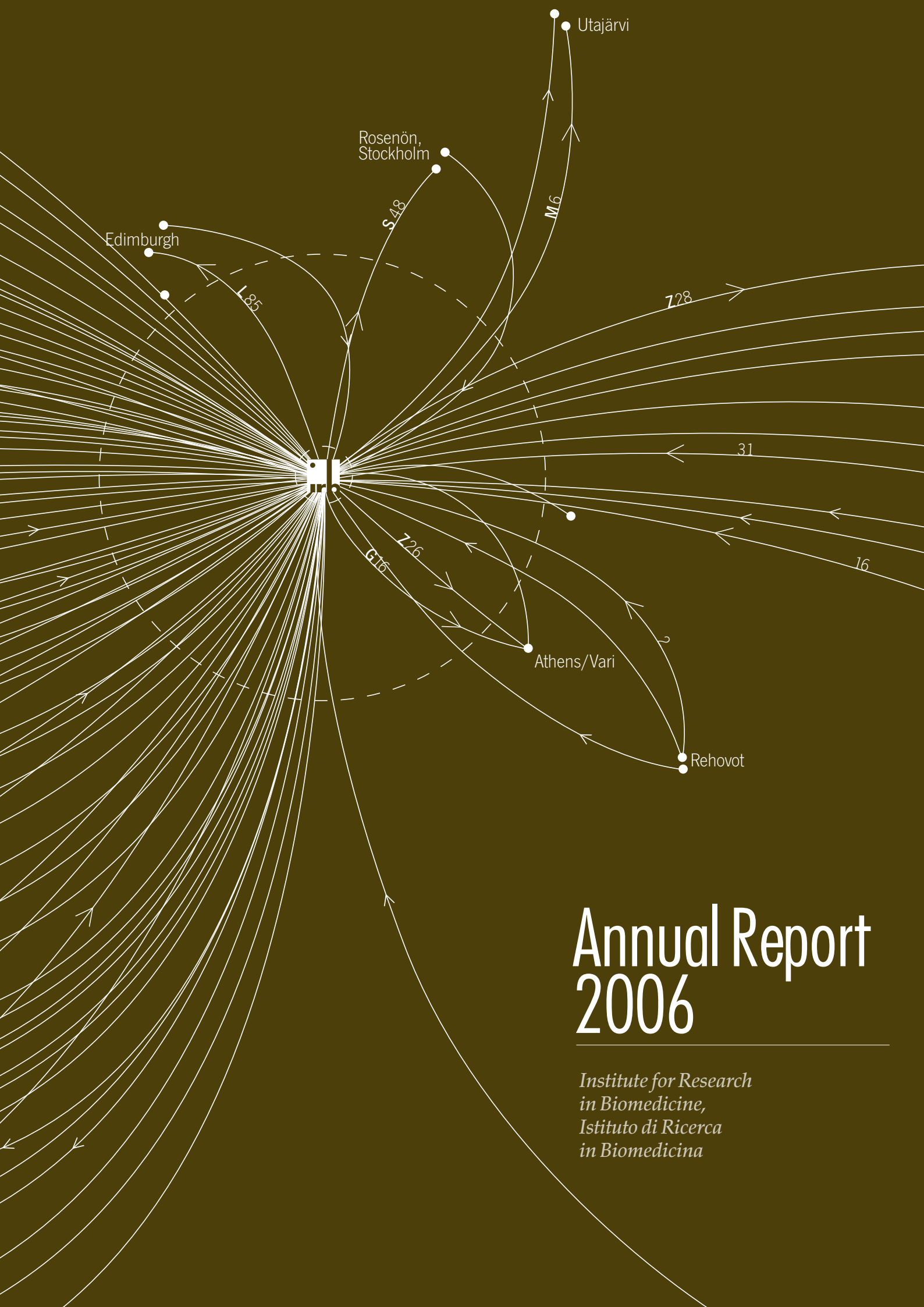
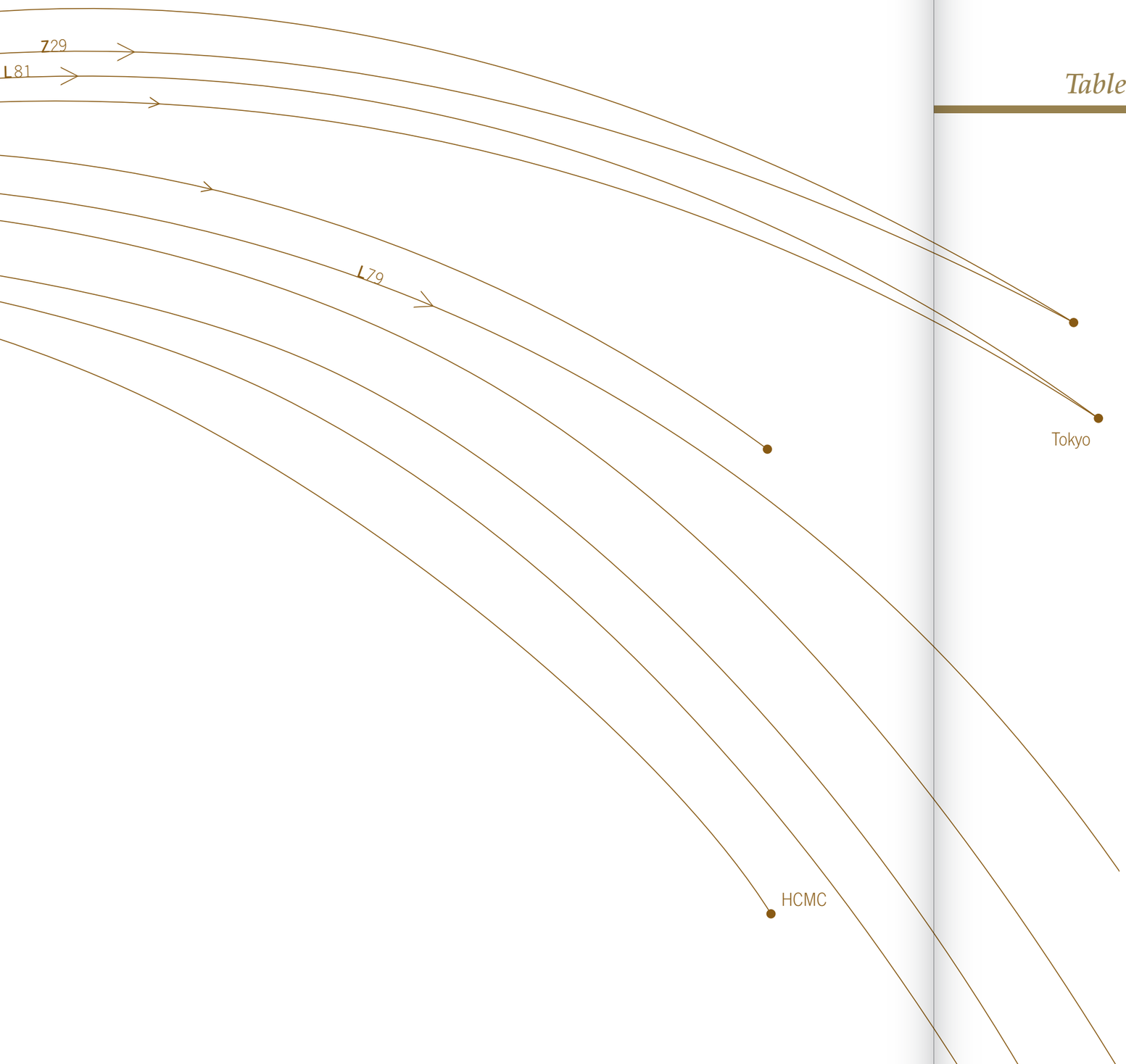


Annual Report 2006

Institute for Research in Biomedicine, Istituto di Ricerca in Biomedicina



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Professor Giorgio Noseda, President of the Foundation Council

When we formed the Foundation for the Institute for Research in Biomedicine in 1997 our objective was to create the ideal conditions for the establishment of a world-class research institute in Ticino. The overwhelming success of the IRB in its first six years attests to our having reached that ambitious goal. Scientific and academic productivity of the IRB are well documented in 159 publications and 17 PhD thesis granted to our students. The growth of the annual budget from 3.8 million Fr. in 2000 to more than **11.3 million Fr**. in 2006 is due to both the trust demonstrated by our public and private sponsors as well as by the increasing ability of our researchers to attract competitive grants.

Preparing the ground for success is not the same as managing success however. The year 2006 saw an important strategic transition begin for the Foundation Council. No longer the"new kid on the block", the IRB now successfully competes head to head with the leading research institutions worldwide. Remaining competitive at this level the Foundation and the Institute must offer ideal conditions, which include solidity, predictability, management excellence, as well as an increased involvement in the academic landscape of Switzerland to provide recognition of the excellence of our researchers.

In 2006 we prepared our renewed requests to the Cantonal and Federal governments for increased future funding. We solidified our connections with Swiss Universities and in particular opened discussions with the Swiss polytechnic institutes. In December of 2006 the IRB, together with the EPFL, the CHUV (University of Lausanne) and the Ludwig Institute for Cancer Research formed the Swiss Institute for Vaccine Research. These four institutes will pursue a coordinated program for research on vaccines. Funds provided by the Bill and Melinda Gates Foundation to individual researchers will be matched by the Confederation to accelerate this program.

Since 2000 the institute has grown to **77** people; **8** group leaders, **21** researchers, **33** students, **8** technicians and an administrative staff of **7**. This growth has put intense pressure on our lab space and infrastructure. To ease this pressure, in June of 2006 we expanded our facilities through the transformation of a local building into a state of the art laboratory and animal facility.

Joining the IRB as tenants in this new building will be Humabs, a young U.S. based biotechnology company that has recently opened a swiss office in Ticino. Humabs has licensed IRB technology, developed by Prof. Antonio Lanzavecchia, for the production of monoclonal antibodies. The Foundation believes strongly in the importance of academic and industrial alliances to foster important and effective research programs without compromising independence.

While the Foundation takes stock of the past six years we also look forward with renewed enthusiasm to the challenges that lie ahead. We will transition ourselves to be in the best position possible to achieve our ambitions and the ambitions of our scientists.

Giorgio Noseda, MD
President Foundation Council

Professor Antonio Lanzavecchia, Director of the Institute for Research in Biomedicine

This report provides an overview of the activity at the Institute for Research in Biomedicine (IRB).

In 2006 two research groups have been recruited. Markus Manz, after completing the qualification in hematology and oncology at the University of Tubingen, has expanded his research program on stem cell biology, hematopoietic differentiation, and blood cell maligancies. Jeremy Luban, on sabbatical from the Columbia University since 2005, has joined the institute as a group leader in August 2006. His research on the innate mechanisms of resistance to HIV-1 will strengthen the IRB program in this important field. In addition, his laboratory is undertaking the challenging task of tracking viral transport inside infected cells using a novel microscopy approach.

Scientists that have left the IRB in this period have found positions in leading institutions in Switzerland, Germany, Italy, USA, Canada, UK, Japan and Singapore.

The IRB continues to play an important role in education by training graduate students through collaborations with Swiss Universities, in particular Basel, Bern, Fribourg, Lausanne and Zurich and participates in an international PhD program with the Vita-Salute San Raffaele University in Milan, Italy. The students furthermore benefit from an intensive lecture series held by renowned scientist from all over the world, organized with the generous support of the Gustav & Ruth Jacob Foundation. In turn, the IRB greatly profits from the curiosity and ambitious work of our young scientists. At present 30 graduate students are enrolled at the IRB and since beginging in 2002, 17 students have successfully completed their training.

Research at the IRB has increasingly focused on the study of host defense mechanisms in the human system. IRB researchers have developed coherent programs that have the potential to be translated into novel therapies.

Manz and colleagues have shown that mice reconstituted with a human hemato-lymphoid system can be successfully infected with viruses that target human cells but normally do not infect animals. This work provides, for the first time, a small animal model for long-lasting HIV infection and is supported by the Bill & Melinda Gates Foundation Grand Challenges in Global Health program. The need to advance the study of the human immune system is illustrated by the finding by Sallusto and colleagues that the development of a particular type of inflammatory effector cells, called Th17, is differentially regulated in humans as compared to mice. A very dynamic program stems from the development of a proprietary method to clone human memory B cells which has been licensed to an american startup company, Humabs LLC, that is establishing its laboratories in Bellinzona. Using this proprietary method broadly neutralizing antibodies have been isolated against viruses such as SARS, Dengue, H5N1, Cytomegalovirus and HIV-1. These antibodies can be used not only to confer immediate protection by passive administration to virus-exposed or infected individuals, but also as tools to identify the antigens that elicit neutralizing antibodies, a process that has been defined as "analytic vaccinology". Another example of how basic research can open new therapeutic avenues comes from Molinari's laboratory where they have shown in a model system that an antibody can inhibit the formation of Alzheimer lesions in vivo.

The translational programs above stem directly from strong basic research, which remains the mission of the IRB. The scientific impact of this research rests on the **159** IRB publications which deal with molecular aspects of protein trafficking and quality control, cell signaling migration and differentiation, and with immune effector mechanisms in normal and pathological conditions.

IRB scientists have established an effective network of collaborations with leading institutions in Europe, America and Asia.

The IRB is a Founding member of the Swiss Vaccine Research Institute (SVRI) together with the CHUV, the EPFL and the Ludwig Institute in Lausanne.

The aim of the SVRI is to boost vaccine research and development via creation of common platforms and recruitment of young talents. Effective collaborations have been established with the Institute of Oncology of Italian Swizerland (IOSI) in the field of transcriptional profiling and in the study of the effect of irradiation on adoptive immunotherapy. Markus Manz has taken clinical responsibilities at the IOSI, a move that is expected to facilitate translational research in the field of haemato-oncology.

The urgent need to expand laboratory space, core facilities, and the animal house has been partially met by the rapid refurbishment of a new building called IRBis located a few hundred meters from the main site, and by establishing a cutting edge imaging facility, generously supported by private donations and the Confederation. We are grateful to the City of Bellinzona for hosting us in these two buildings and for sharing our vision of the future.

After six years of activity I am confident to say that the IRB has fulfilled the initial expectations and has become an internationally visible centre for basic and translational research. This fact is witnessed by the success in obtaining grants not only from the Swiss National Science Foundation and the European Union, but also from foreign agencies among which are the Bill & Melinda Gates Foundation, the Wellcome Trust, and the US National Institute of Health.

The Institute is especially fortunate in receiving core funding from its main sponsors, the Helmut Horten Foundation, the Cantone Ticino and the Swiss Confederation. Our gratitude also goes to the many individuals who support us through donations and fellowships. We believe that the progress and achievements of the Institute will reward their dedication to the advancement of science.

Antonio Lanzavecchia, MD
Director

Cultivating Discovery

The IRB seeks to provide the ideal conditions for the creation of new knowledge.

IRB scientists participate in the virtuous cycle of discovery by asking important questions, learning what is known, building new knowledge and sharing their discoveries.

Advancing Discovery

Teaching

Discovery

The cowbell is rung to call students to a seminar

The IRB is a dynamic teaching institute with 30 full time graduate students from Swiss and international universities.

Focusing
Discovery

IRB research programs explore how the human body defends itself.

The cafeteria is in the heart of the building, an open space where students and scientists gather and exchange ideas.

SHAPING PROTEINS

Maurizio Molinari earned his PhD in Biochemistry at the ETH-Zurich in 1995. From 1996-1997 he was a post-doc in the laboratory of Cesare Montecucco at the Dept. of Biomedicine, University of Padua, Italy and subsequently in the laboratory of Ari Helenius at the ETH-Zurich (1998-2000). Since October 2000 he is group leader at the IRB in Bellinzona.

The studies performed by Molinari's group at the IRB have made a significant contribution to the knowledge of the mechanisms devised by cells for the production of functional polypeptides and for efficient disposal of folding-defective proteins.

The knowledge acquired on the mechanisms of protein production and transport along the secretory line of mammalian cells allowed the group to set up a novel approach based on intracellular expression of specific single chain antibodies, that proved very efficient in reducing the in vivo production of amyloid -Beta (Aβ), a toxic peptide that deposits in the human brain and elicits neurodegenerative processes associated with Alzheimer's disease.

Dr. Molinari has received the Science Award 2002 from the Foundation for study of neurodegenerative diseases, the Kiwanis Club Award 2002 for Medical Science, the Friedrich-Miescher Award 2006 and the Research Award Aetas 2007.

Protein Folding and Quality Control

Cystic fibrosis, Alzheimer's disease, Parkinson's disease, Hungtington disease, Creutzfeld-Jakob's disease, diabetes mellitus. This is a very short selection of the several hundreds of *human diseases* with profoundly different traits but common aethiology[1]: *protein misfolding*. Several of these diseases are hereditary and most of them are rare, affecting less than 1 in 2000 individuals. For some of them, as an example for all neurodegenerative syndromes affecting old people, a sharp increase in frequency is expected in the next decades due to extension of the human life span.

Proteins[2] are fundamental components of all living cells and include many substances, such as enzymes, hormones, and antibodies, that are necessary for the proper functioning of an organism. They are fabricated in a specialized organelle present in all our cells and named the endoplasmic reticulum.

To be functional, proteins must acquire a specific structure in the endoplasmic reticulum in a series of tightly regulated processes defined as *protein folding*. Failure to do so, will result in the destruction of the defective protein and in the loss of its activity. The cell and the organism will eventually suffer as a consequence of the absence of this specific protein's function and this elicits a disease state.

The aim of our work is to understand how our cells fabricate the proteins. How correct protein folding is ensured, what happens if protein folding is not possible, how misfolded proteins are destroyed. We are convinced that a detailed knowledge of the processes that regulate protein production in our cells will allow intervention to alleviate symptoms, to delay disease onset and even to arrest and revert disease progression for all human pathologies caused by defects in acquisition of the functional protein shape.

[1] Aethiology:
The cause or origin of a disease or disorder as determined by medical diagnosis.

[2] Proteins:
The smallest structural unit of an organism that is capable of independent functioning, consisting of one or more nuclei, cytoplasm, and various organelles.

Laboratory

Group Leader: Maurizio Molinari, *PhD, 2000.*

Members: Verena Calanca, *Technician*, 2000 • Carmela Galli-Molinari, *Researcher, 2000* • Tatiana Soldà, *Technician, 2004* • Omar Vanoni, *PhD student, 2004* • Tito Calì, *PhD student, 2006* • Silvia Olivari, *PhD student, 2006.*

CELL MIGRATION

Signal Transduction

Cell migration[1] is essential for development and survival of multicellular organisms. Generally, single cells move along cues to reach their destination. The process requires polarization, i.e. the formation of a morphological distinct front and a rear end, of the cell along the axis of attraction. The intracellular pathways which sense the attracting signal and transduce it into remodeling of the actin cytoskeleton and the sequential activation of adhesion molecules is a central focus of our research.

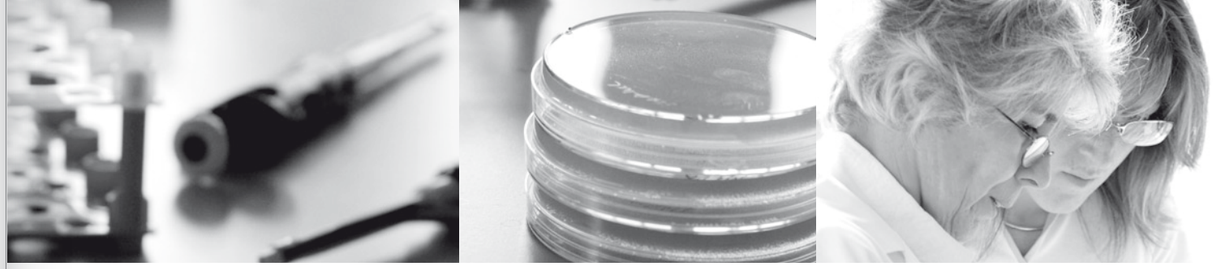
Leukocyte trafficking is largely regulated by chemokines and their respective receptor. Migration of cells expressing subsets of receptors is further controlled by spatially restricted secretion of chemokines. The mechanism is important for immune homeostasis, but is also essential for acute and chronic immune responses such as inflammation. In addition, some cancer cells appear to use the chemokine systems for metastasis.

[1] Cell migration:
Cell migration is essential in development and immunity. Cell migration occurs also under pathological conditions. Cell migration is regulated by multiple pathways. Can we specifically interfere with good and bad?

Laboratory

Group Leader: Prof. Dr. Marcus Thelen, *PhD, 2000.*

Members: Sylvia Thelen, *PhD, 2000* • Tiziana Apuzzo, *PhD student, 2006* • Ulrike Naumann, *PhD student, 2006* • Silvia Volpe, *PhD student, 2006* • Simona Infantino, *PhD student, 2003* • Elena Palmesino, *PhD student, 2002.*



Marcus Thelen obtained his PhD in 1985 from the University of Bern studying the bioenergetics of mitochondria.

He was a PostDoc at the Theodor-Kocher Institute in Bern from 1985 to 1989, later from 1989 to 1991 at the Rockefeller University in New York. In 1992 he was awarded a START fellowship from the Swiss National Science Foundation and headed a laboratory at the Theodor-Kocher Institute, University of Bern.

Since 2000 he is a group leader at the IRB. In 1994 he obtained the Venia Docendi and later in 2001 was awarded an Honorary Professor title from the University of Bern where he still is member of the Medical Faculty.

Prof. Thelen has published more than 60 papers. His research covers several aspects of biochemistry, cell biology and human immunoogy. His focus is on signal transduction in chemokine receptor mediated cell activation and migration.

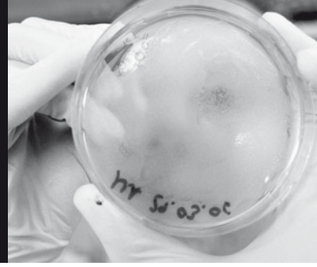
DEVELOPMENT

Fabio Grassi earned his degree in Medicine at the University of Pavia and a PhD. in Microbiology at the University of Milan. He worked at the University of Umeå in Sweden, the Institut Pasteur and Hopital Necker in Paris, the San Raffaele Scientific Institute in Milan.

He has been a Special Fellow of the Leukemia & Lymphoma Society at Harvard Medical School in Boston. He is Associate Professor of Biology at the University of Milan.

In September 2002, he joined the IRB as head of the T Cell Development lab.

His research is focused on molecular as well as cell biology of T cell differentiation in the thymus, signal transduction of the T cell in secondary lymphoid organs and in T cell mediated inflammatory conditions.



T Cell Development

The experiments performed in the lab are principally focused on the characterization of signal transduction pathways at different developmental stages of the murine T cell[1]. A first aim is to define signaling microdomains, which are involved in transducing the signal by the pre-T cell receptor (pre-TCR) and promote T cell as well as thymus development. A second aim pursued in the lab is to characterize signaling pathways controlled by Ca^{2+}[2] during immunopathological T cell responses leading to inflammation and tissue destruction. Another topic studied by our group is the impact of T cell activation during an inflammatory response on hematopoiesis and bone homeostasis.

Laboratory

Group Leader: Fabio Grassi, *MD, PhD, 2002.*

Members: Anna Casati, *PhD student, 2005* • Denise Ferrera, *PhD student, 2003* • Ursula Schenk, *PhD, 2005* • Micol Ferro, *Undergraduate student, 2005.*

[1] T cell:
T cell or T lymphocyte, a white blood cell, which plays a central role in cell-mediated immunity. The abbreviation "T" stands for thymus since it is the principal organ for T cell development. A polymorphic receptor on the cell surface, the T cell receptor (TCR), confers specificity for distinct targets to every T cell.

[2] Ca^{2+}:
Calcium ions.

STEM CELLS

Markus G. Manz received his degree in Medicine 1995 from the Eberhard-Karls-University in Tuebingen, Germany.

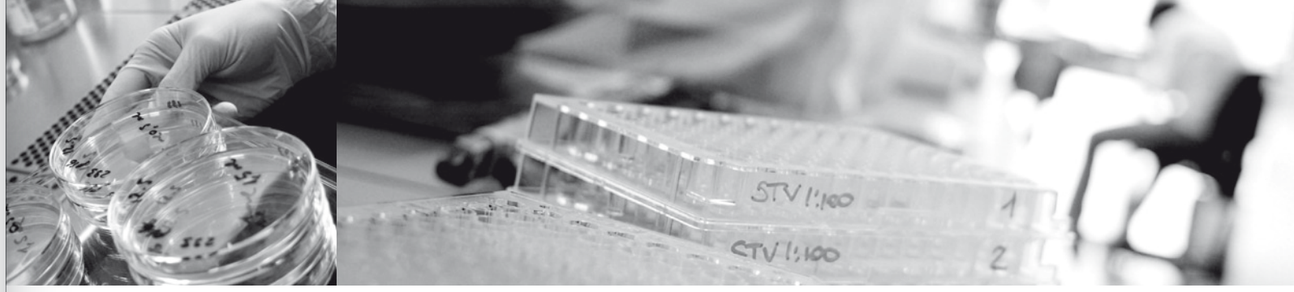
Between 1995 and 1999, he trained in internal medicine at the Tuebingen Medical School, from 1999 to 2001 he worked as a postdoctoral fellow in the laboratory of Irving Weissman at Stanford, USA, and in 2002 he became group leader at IRB.

From 2004 to 2006 he finished his hematogy/oncology training at the University of Tuebingen, while maintaining the IRB lab as an Associate Group Leader.

Since September 2006 he is group leader at the IRB and associated hematologist at the Oncology Institute of Southern Switzerland (IOSI), Bellinzona.

Markus Manz scientific interest focuses on hematopoiesis and immune system development. His research is driven by the urge to understand basic mechanisms of immune system maintenance and regeneration in steady-state and disease, a knowledge that eventually will be valuable for the development of new strategies to interfere with this process, e.g in states of infection, immunodeficiency, autoimmunity, hemato-lymphoid cancers, or in solid organ and hematopoietic cell transplantation.

In 2004 he received the prestigious Artur-Pappenheim Award of the German Society of Hematology and Oncology.



Hematopoiesis

Throughout life, a small fraction of hematopoietic stem cells (HSCs)[1] self-renew in the bone marrow and generate all cells of the hemato-lymphoid system, a system with very high cellular turn-over. Because of its ready accessibility, hematopoiesis is currently one of the best studied mammal adult stem cell differentiation systems, and is likely paradigmatic for other physiologic (e.g. liver, skin, central nervous system) and pathologic (tumors, leukemia) stem cell regenerated compartments. Beyond its model character for basic research, hematopoietic stem cell transplantation (formerly bone marrow transplantation) is so far the only successfully working clinical stem cell therapy, mostly applied for the treatment of malignant hematologic disease or immunodeficiencies. Also, hematopoietic stem cells currently provide the major gateway for clinical gene therapy.

The hierarchically structured, unidirectional differentiation process from HSCs to terminally differentiated cells involves progressive loss of self-renewal ability, proliferation capacity, and lineage differentiation potentials. In my laboratory, we are studying regulation of physiologic and pathologic hemato-lymphopoieis in steady-state, and inflammatory conditions, as well as in neoplasia in both mice and men.

Our hypothesis is that HSC maintenance, subsequent commitment and expansion to different cellular lineages is largely controlled externally, depending on varying demand. To evaluate this, we characterize and isolate human and murine hematopoietic stem- and progenitor cells as well as bone marrow stroma cell components (mesenchymal stroma cells, MSCs), study and subsequently modify their transcriptional profile, and test their responsiveness to physiologic stimuli and to pharmacologic compounds in both in vitro and in vivo assays.

In depth understanding of physiologic maintenance and differentiation pathways from HSCs to mature cells of the hematopoietic system will eventually provide new insights and improved therapeutic methods to treat hematopoietic and immune system diseases.

[1] Hematopoietic Stem Cells (HSCs):
Small population of cells in adult bone marrow that for the life of an individuum are capable to both self-renew (maintain themself) and give rise to all hemato-lymphoid system cells as erythrocytes, platelets, and all white blood cells (immune system cells).

Laboratory

Group Leader: Markus G. Manz, *MD, 2002.*

Members: Patrick Ziegler, *PhD, 2006* • Michael A. Schmid, *PhD student, 2006* • Steffen Boettcher, *MD student, 2006* • Aya Onai, *PhD, 2004-2006* • Nobuyuki Onai, *PhD, 2004-2006* • Roxane Tussiwand, *PhD student, 2003-2006.*

HIV-AIDS

Viral Replication, Pathogenesis and Immunity

Study of retroviruses has led to major advances in fundamental biology, most notably the discovery of oncogenes and the modification of the central dogma[1]. In this spirit, we investigate mechanisms of HIV-1 replication and pathogenesis with the goal of advancing understanding of the basic workings of the cell. Through the development of genetic and biochemical screens[2] we attempt to identify cellular factors of importance to HIV-1 and, more generally, to cell physiology. In effect, we exploit HIV-1, using the virus to elucidate mechanisms of cell cycle progression and cytokinesis, signal transduction and cytokine expression, protein folding and degradation, as well as pathogen recognition and antigen presentation. Our research is basic in nature but by shedding light on mechanisms of HIV-1 replication and immune system evasion we hope to contribute to the development of drugs and vaccines that target this virus.

[1] The Central Dogma of Molecular Biology: *a framework for understanding that genetic information is directional, generally going from DNA to RNA to protein. Study of retroviruses demonstrated that genetic information can also move in the "reverse" direction from RNA to DNA.*

[2] Screens: *procedures for identifying individual genes, gene products, or chemicals that modify, or are responsible for, a phenotype of biological interest.*

Laboratory

Group Leader: Jeremy Luban, *MD, 2006.*

Members: Caterina Strambio de Castillia, *PhD, 2005* • Martha Neagu, *MD, PhD student, 2005* • Thomas Pertel, *PhD student, 2005* • Christina Helbig, *PhD student, 2006* • Nadia Rahm, *2006.*

Jeremy Luban earned an M.D. at the College of Physicians and Surgeons, Columbia University in New York, in 1987. He underwent clinical training in Internal Medicine and Subspecialty fellowship training in Infectious Diseases, as well as postdoctoral training in Biochemistry in the laboratory of Stephen Goff.

He became a Professor at Columbia University with dual appointments in the Department of Medicine (1993) and the Department of Microbiology (1995). In addition to teaching medical students, physicians, and PhD graduate students he served as director of the Columbia-Rockefeller Center for AIDS Research.

His laboratory focuses on host factors that regulate HIV-1 replication and confer innate immunity to this deadly virus. Among the HIV-1 regulatory factors discovered by his lab are the human proteins cyclophilin A and TRIM5.

Dr. Luban became a group leader at the IRB and relinguished his position at Columbia University in 2007.

INFLAMMATION

Mariagrazia Uguccioni received a degree in Medicine from the University of Bologna (Italy) where she specialized in Haematology in 1994.

From 1993 to 2000 she was a member of the Theodor Kocher Institute, University of Bern (Switzerland), and since 2000 she is Head of the Chemokine Expression and Function Laboratory at the IRB.

She is Assistant Professor of Immunology at the School of Rheumatology, University of Bologna, since 2000.

Dr. Uguccioni's research has covered aspects of human haematology and immunology: chemokine activities, leukocyte activation and traffic, natural chemokine antagonists, and chemokine expression in human pathology.

Recently, her group is focusing on chemokine activities in human pathology and has identified a novel regulatory mechanism of leukocyte trafficking induced by synergy-inducing chemokines.

Chemokines: Tissue Expression, Function and Activity Modulation

Our research interest remains focused on CHEMOKINE activities in physiology and pathology, with emphasis on mechanisms governing fine tuning modulation of their expression and activity. The breakdown in the control of leukocyte mobilization contributes to the pathogenesis of chronic inflammation as well as tumour development. Chemokines, are produced constitutively or upon specific induction in virtually all tissues of the human body (Figure 1). We have recently shown *(Paoletti et al., Blood 2005; Sebastiani et al., EJI 2005)* that non-ligand chemokines can enhance the activity of CCL19 and CCL21 on CCR7, and of CCL22 on CCR4, respectively. Western blot and binding experiments have shown the formation of heteromeric complexes suggesting these complexes as the cause of the observed synergism. Interestingly, the available structure and structure-function data, albeit scarce to date, collectively implicate residues in the first β-strand as mediators of heteromeric association and synergism(Sebastiani et al., *EJI* 2005). It is thus tempting to speculate that heteromeric chemokine complexes may mimic those homomeric dimers that form via association of their β-sheets, featuring an interface composed of the first β-strands. However, the molecular reasons as to why a heteromeric complex should be more active than a homomeric one remain, at present, completely obscure, and the analysis of this phenomenon is part of our ongoing research. Surface representations with electrostatic potentials of chemokines show similarities among selective agonists and known natural antagonists, thus indicating this analysis as an additional instrument for disclosing the potential of different chemokines as natural antagonist or synergy inducing molecules.

We have hypnotized that the synergism induced by heteromeric chemokine interactions may be a widespread phenomenon, positively regulating diverse chemokine activities such as chemotaxis, cellular adherence, receptor internalization, and protein kinase phosphorylation. Therefore, we are conducting additional *in vitro* studies to dissect in detail the mechanisms governing these activities.

Laboratory

Group Leader: Mariagrazia Uguccioni, *MD, 2000.*

Members: Maria Gabriela Danelon, *Technician, 2001* • Katrin Kuscher, *PhD student, 2004* • Tamara Visekruna, *PhD, 2005* • Daniel Venetz, MD, *PhD student, 2006* • Denise Bottinelli, *undergraduate student, 2006.*

IMMUNITY

Cellular Immunology

Specific immune responses require the timely interaction of various cell types within specific microenvironments. In the primary response the rare antigen specific naive T cells need to maximize the possibility of encounter with antigen. They do so by continuously recirculating through secondary lymphoid organs where they are stimulated by antigen-presenting mature dendritic cells (DCs). Soluble antigens can reach the lymph node directly but in most cases they are carried by migrating DCs that capture antigen in peripheral tissues and subsequently move through the lymphatics to the draining lymph node.

One goal of our laboratory is to understand how the number, localization and activation state of DCs in lymph node impact on T cell priming and immune responses.

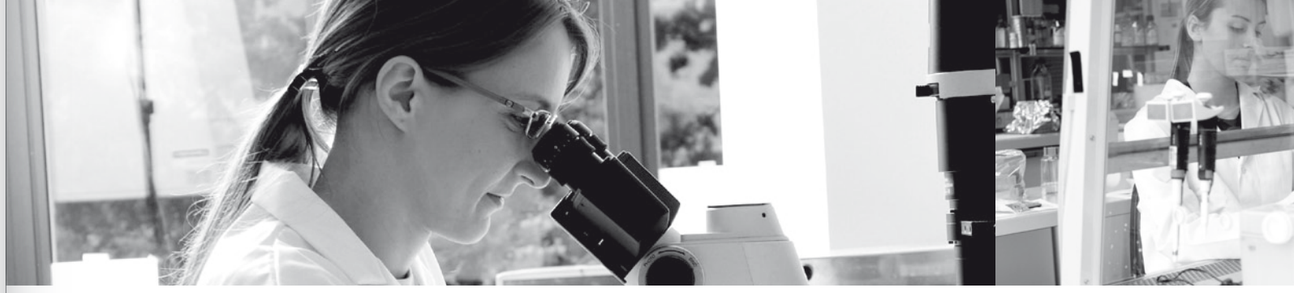
A second goal of our research is to dissect the signals by which DCs determine differentiation of proliferating T cells towards the Th1, Th2 or Th17 lineage and how migratory capacity and effector function are coordinately regulated in differentiating T cells. Based on their migratory capacity and effector function we have originally characterized two subsets of memory T cells: central memory T cells (T_{CM}) express homing receptors for lymph nodes and have no or low level effector function. In contrast effector memory T cells (T_{EM}) lack lymph node receptors and have immediate effector function.

We are investigating the molecular basis underlying the functional properties and the differentiation potential of T_{CM} and T_{EM}, their heterogeneity and the signals required for their generation and maintenance. We are also interested to define the composition of memory subsets in different pathological and physiological conditions to gain insights into the role these subsets play in the immune responses.

Laboratory

Group Leader: Federica Sallusto, *PhD.*

Members: Alfonso Martin-Fontecha, *PhD, 2000* • Annalisa Macagno, *PhD, 2002* • Miroslav Hons, *PhD student, 2004* • Eva V. Acosta-Rodriguez, *PhD, 2005* • Martina Beltramello, *PhD, 2005* • Rebekka A. Geiger, *PhD student, 2005* • Dirk Boumjohann, *PhD student, 2006* • Thomas Duhen, *PhD, 2006* • Andrea Reboldi, *PhD student, 2006.*



Federica Sallusto received her degree in Biology at the University of Rome La Sapienza. Between 1989 and 1996 she worked at the Department of Immunology, of the Italian National Institute of Health first as a postdoctoral fellow and then as a research scientist.

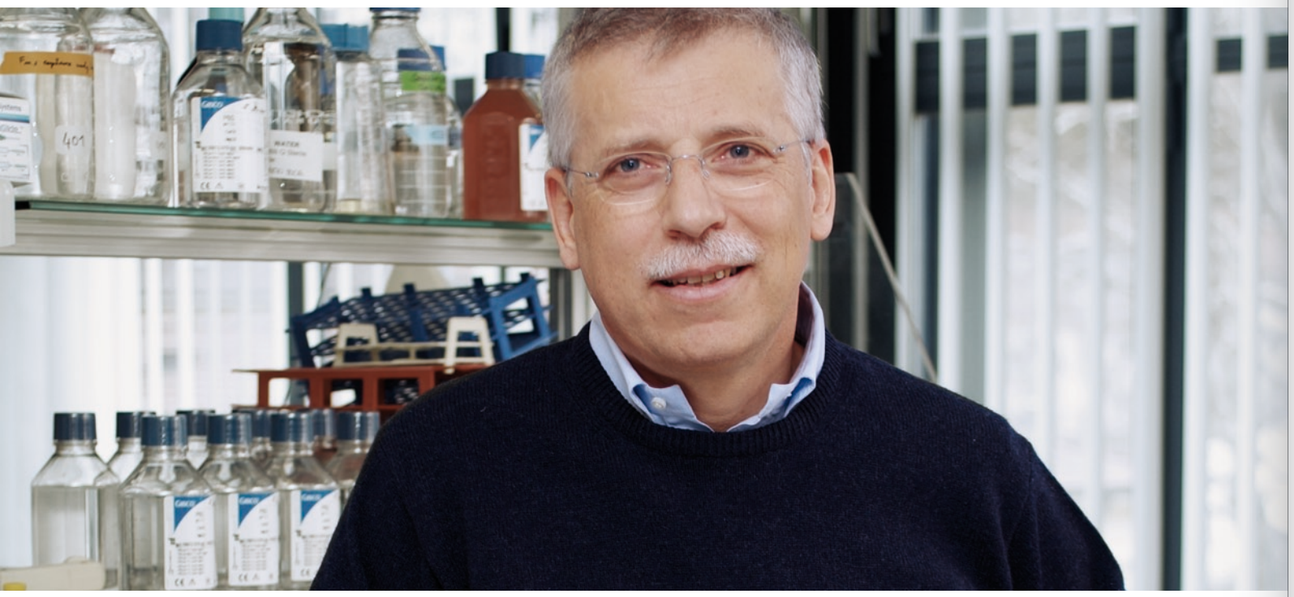
She worked at the Basel Institute for Immunology as a visiting scientist from 1993 to 1994 an as a member from 1996 to 2000.

Her research is focused on dendritic cell biology, T cell activation, differentiation and T cell traffic. Among her original contributions are the development of a method to culture human dendritic cells, the discovery that Th1, Th2 and Th17 cells express distinct sets of chemokine receptors and the definition of central and effector memory T cell subsets.

She published more than 80 papers and was the recepient of the Pharmacia Allergy Research Foundation Award in 1999.

Since 2000 Federica Sallusto is the Head of the Cellular Immunology Laboratory at the IRB.

ANALYTIC VACCINOLOGY



Antonio Lanzavecchia earned a degree in Medicine at the University of Pavia where he specialized in Paediatrics and in Infectious Diseases.

From 1983 to 1999 he was a member of the Basel Institute for Immunology and since 1999 he is the founding director of the IRB in Bellinzona. He has been Professor of Immunology at the University of Genoa and at the University of Siena.
Awarded the EMBO medal in 1988 and the Cloëtta prize in 1999, Dr. Lanzavecchia has published more than 200 papers.

His research has covered several aspects of human immunology: antigen processing and presentation, dendritic cell biology, lymphocyte activation and traffic, T and B cell memory.

Recently he developed a method for the efficient isolation of human monoclonal antibodies from memory B cells, which has been successfully applied to infectious diseases such as SARSCoV, H5N1, HCMV, Dengue, Malaria and HIV-1.

Immune Regulation

The research of our group remains focused on three main themes. First, we study the impact of innate immunity on the adaptive immune response with special emphasis on the activation of dendritic cell and the regulation of polarizing cytokines such as IL-12, IL-23, IL-1 and IL-6. Second, we continue to test in different experimental systems the role of the cumulative strength of stimulation (SoS) on the generation of effector and memory T cells. Current results from our as well as other groups support our initial proposition that SoS is the critical factor in determining the extent of CD4 and CD8 T cell differentiation. We are particularly interested to understand the mechanisms that control the generation of T and B memory cells and the dynamics of memory cells in the central and effector compartment. A third new avenue of research which is progressively expanding is prompted by two methods that have been originally developed in our laboratory that allow an accurate analysis of memory B cell frequencies and the efficient retrieval of human monoclonal antibodies from cells obtained from immune donors.

We feel that our research has the potential to impact in the field of vaccination at least in three areas: i) development of novel adjuvants capable of driving strong and selected immune responses; ii) identification of in vitro correlates of the immune status to evaluate vaccine efficacy and iii) adoptive immunotherapies with antigen-specific T cells or human monoclonal antibodies retrieved from the memory repertoire.

Laboratory

Group Leader: Antonio Lanzavecchia, *MD, 2000.*

Members: Afonso Almeida, *PhD, 2005* • Nadia Bernasconi, *PhD, 2000* • Davide Corti, *PhD student. 2004* • Giulia Di Lullo, *PhD, 2005* • Jens Geginat, *PhD, 2000-2006* • Isabella Giacchetto-Sasselli, *Technician, 2000* • Greta Guarda, *PhD student, 2004* • Laura Lozza, *PhD student, 2005-2006* • Giorgio Napolitani, *PhD, 2002* • Debora Pinna, *PhD student, 2005* • Laura Rivino, *PhD student, 2003-2006* • Claudia Ruprecht, *PhD student, 2002-2006* • Chiara Silacci, *Technician, 2005* • Janine Stubbs, *PhD, 2006* • Stefan Wirths, *MD, 2002-2006* • Erica Dunder, *PhD student, 2006.*

Participating in Discovery

Individual donors and foundations participate in the success of the IRB by sponsoring student fellowships, infrastructure, and special instruments that enable new areas of discovery.

If you or your foundation would like to participate in the future development of the IRB please contact:

Tom Brooks, Director of Communications and Development,
tom.brooks@irb.unisi.ch
+ 41 91 820 0327




Science at the Institute

JANUARY
• *DEC-VAC Begins A 5 year EU funded project to develop HIV vaccines based on dendritic cells.*

FEBRUARY
• *Maurizio Molinari receives the Friedrich Miescher Award 2006 for outstanding achievements in the field of Biochemistry.*

MARCH
• *Claudia Ruprecht of the lab of Antonio Lanzavecchia, defends her thesis "On the role of regulatory T cells and microbial products in the control of T and V cell immune responses", at the University of Basel.*

APRIL
• *International Day of Immunology, initiated by European Federation of Immunological Societies (EFIS).*

• *Roxanne Tussiwand of the lab of Markus Manz, defends her PhD thesis at the Università Vita e Salute San Raffaele, Milano.*

MAY
• *Simona Infantino of the lab of Marcus Thelen, defends her thesis "RDC1, and orphan receptor with similarities to Chemokine receptors" at the University of Bern.*

JUNE
• *H5N1 (BIRD FLU) research by Antonio Lanzavecchia is fast-tracked for support by the Wellcome Trust.*

• *Elena Palmesino of Marcus Thelen's lab, defends her PhD thesis "CXR4 associated proteins and their role in cell specific receptor function", at the University of Bern.*

JULY
• *Student Exchange between the lab of Maurizio Molinari and the University of Kyoto.*

• *The Bill and Melinda Gates Foundation funds two projects, PTVDC and VDAC to advance the search for an HIV vaccine. Participating in two studies from IRB Lanzavecchia and Sallusto.*

AUGUST
• *Janine Stubbs joins the IRB as a Post Doc in the Lab or Antonio Lanzavecchia.*

• *Dirk Baumjohann receives Prestigious Boehringer Fellowship.*

SEPTEMBER
• *Jeremy Luban officially joins the IRB as a Group Leader and receives his first SNF Grant.*

• *Markus Manz rejoins IRB as full-term group leader.*

• *Patrik Ziegeler joins the IRB as Post Doc in the Lab of Markus Manz.*

OCTOBER
• *Daniel Venetz receives a Prestigious Cloëtta Foundation Fellowship.*

• *The first annual meeting of the European project INNOCHEM is held in Bellinzona. Mariagrazia Uguccioni scientific coordinator of the project plays host to more than 100 guests from around the world.*

• *The model developed by Markus G. Manz is validated by an important study with University at Zurich.*

• *Nobuyuki Onai from Manz Lab becomes assistant Professor at Aktia University, Japan.*

NOVEMBER
• *Christina Helbig receives a Boehringer Fellowship.*

• *Federica Sallusto and Marcus Thelen recieve Fellowships from the Integramm program of the E.U.*

• *Laura Rivino of the lab of Antonio Lanzavecchia, defends her PhD thesis "Dissecting the human CD4+ T cell memory pool", at the University of Fribourg, Switzerland.*

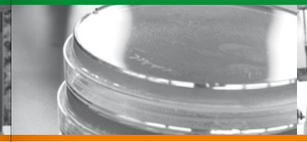
DECEMBER
• *The IRB becomes a Founding Member of the Swiss Institute for Vaccine Research together with the EPFL, the CHUV, and the Ludwig Institute.*

• *Silvia Monticelli joins the IRB as a junior Group Leader.*

• *The European Union issue the first Calls in the F.P.7 program for research.*







Life in the Institute

JANUARY
• *Seminars:*
> Hazel Pinheiro, Ambion Europe Ltd.
> Yair Reisner, Weizmann Institute of Science, Rehovot, Israel.
> Ingmar AFM Heijnen, Kantonsspital Aarau, Aarau, Switzerland.

FEBRUARY
• *Official visit from the Swiss Center for Scientific Calculation (CSCS).*

• *Seminars:*
> Luca Scorrano, Venetian Institute of Molecular Medicine, Padua, Italy.
> Bettina Borisch, CMU, Geneva, Switzerland.
> Dennis R. Burton, The Scripps Research Institute, La Jolla, CA, USA.
> Alexandra Trkola, University Hospital Zurich, Switzerland.
> Andrea Zisch, University Hospital Zurich, Switzerland.

MARCH
• *Seminars:*
> Giancarlo Pruneri, European Institute of Oncology, Milan, Italy.
> Daniela Capello, A. Avogadro Uni. of Eastern Piedmont, Novara, Italy.
> David A. Thorley-Lawson, Tufts University School of Medicine, Boston, USA.
> Fiona Powrie, University of Oxford, UK.

APRIL
• *Visits to the IRB: UBS Bellinzona Ticino Association of Natural Scientists, and Lions.*

• *Meeting with Ticino Middle School Science teachers.*

• *The annual IRB student Retreat is held at the convent in Bigorio.*

• *Seminars:*
> Eric Prossnitz, University of New Mexico, Albuquerque, Mexico.
> Marisa Jaconi, Geneva, University, Switzerland.
> Cameron Simmons, Hospital for Tropical Diseases, HCMC, Vietnam.

MAY
• *The Ticino Delegation to Federal Government visit the IRB as part of a survey of Research in Ticino.*

• *The Horten Foundation holds their annual meeting at the IRB.*

• *Seminars:*
> Stephanie Brooking, Ambion Europe Ltd.
> Gisou van der Goot, University of Geneva, Switzerland.
> Kanta Subbarao, National Institutes of Health, USA.
> Peter Friedl, University of Wurzburg, Germany.
> Carmen Birchmeier, May-Delbrueck-Centrum für Molekulare Medizin, Berlin, Germany.

JUNE
• *HRH Princess Chulabhorn of Thailand visits the IRB.*

• *The first Musica e Molecole evening Jazz features with the Carlo Uboldi Trio. Sponsored by UBS Bellinzona.*

• *IRB News released in new monthly format available in english, german and italian.*

• *Seminars:*
> Signe Hässler, Uppsala University Hospital, Sweden.
> Ralf Ignatius, University of Berlin, Germany.

JULY
• *Work begins on the transformation of a local building into a stateof-the-art research facility and P3 laboratory.*

• *The Swiss National Fund agrees to support the purchase of a calcium imaging system proposed by Fabio Grassi.*

• *Seminars:*
> Onur Boyman, University Hospital of Lausanne, Switzerland.
> Thomas Duhen, INSERM, Lyon, France.

AUGUST
• *The Swiss Science and Technology Office inspect the IRB and prepare a positive evaluation.*

• *Official visit of the Swiss Federal Research Station.*

• *Seminars:*
> Martin Lohse, University of Würzburg, Germany.
> Amanda Proudfoot, Serono International SA, Geneva, Switzerland.
> Douglas Richman, University of California San Diego, USA.

SEPTEMBER
• *United Kingdom Embassy representatives visit the IRB as part of an effort to increase swiss-UK collaboration in science.*

• *Joerg Staheli takes over as Director of the Biopolo Ticino and hosts ELISSI meeting.*

• *The council of the Polytechnic istitutes visit the IRB.*

• *Visit of the Consiglio di Stato of Canton Ticino.*

• *Seminar Claudia Lengerke, Children's Hospital, Boston, USA*

OCTOBER
• *A delegation of Cuban scientists visits the IRB.*

• *Seminars :*
> Anna Mondino, Vita-Salute San Raffaele University, Italy.
> Ian Colditz, CISRO Livestock Industries, Armidale, Australia.
> Anna Villa, CNR-ITB, Segrate, Italy.
> Tim Sparwasser, Technische Universität München, Germany.

NOVEMBER
• *The second Musica e Molecole features the music of Stockhausen. Sponsored by B.S.I.*

• *Alessandro Ciocca is elected to the Consiglio di Fondazione of the IRB.*

• *Seminars:*
> Bernard Malissen, Centre d'Immunologie Inserm- CNRS, Marseille, France.
> Anjana Rao, The CBR Institute for Biomedical Research, Boston, USA.
> Paul O'Shea University of Nottingham, UK.
> Luca Varani, Stanford University School of Medicine, Stanford, USA.

DECEMBER
• *The Consiglio di Stato of Ticino approves funding for research for 2007-2012.*

• *High school students from Locarno complete their optional biology course with a project at the IRB.*

• *Middle School Students visit the IRB for a lecture on immunology.*

• *Seminars:*
> Ira Mellman, Yale University School of Medicine, New Haven, USA.
> Rolf Zinkernagel, University Hospital Zürich, Zürich.
> Nicole Suciu Foca, Columbia University, New York, USA.

Multiplying Discovery

Students trained at the IRB continue their scientific careers in institutes and universities around the world.

Education. PhD Programme and PhD students

The IRB provides high level scientific education for graduate students. The PhD programme, in collaboration with Swiss and foreign universities, includes experimental work carried out at IRB under the direct supervision of a group leader as well as seminars, lessons, and an annual PhD student retreat. Starting from 2004 the Institute organizes an International PhD lecture course that includes lectures and journal clubs. In addition, the Istitute participates in an international PhD programme coordinated by the Vita Salute San Raffaele University of Milan, Italy. The IRB also provides education for undergraduate students (short stages and experimental diploma thesis).

Elena Palmesino

"CXCR4 associated proteins and their role in cell specific receptor function".

Elena Palmesino and Marcus Thelen.

Understanding chemokine receptor-mediated signaling in different cellular environments is the main focus of the project. Ample evidence from our laboratory and by others indicate that coupling of a given G-protein coupled receptor to downstream signaling cascades must be regulated in close proximity to the receptor and may vary between cell types. As a model we investigate the signaling properties of the chemokine receptor CXCR4 which regulates trafficking of leukocytes and tissue cells and is involved in tumor metastasis. The receptor also mediates cell survival and is important in organogenesis. However, CXCR4-stimulated intracellular signaling depends on the cell system. To characterize receptor-associated proteins, that determine the fate of CXCR4-medited cell activation, we developed a solubilization protocol that does not affect the structural integrity of CXCR4, and in which solubilized CXCR4 retains is ability to bind CXCL12. Current investigations should lead to the identification of receptor associated proteins in different cellular systems. Analysis of the expression patterns of the proteins will provide clues on their function in the regulation of CXCR4 activity.

PhD Granted by University of Bern, Switzerland.
Tutor: Professor Andrew Ziemiecki

Simona Infantino

"RDC1, an orphan receptor with similarities to chemokine receptors".

Simona Infantino and Marcus Thelen.

The orphan receptor RDC1 may function as a chemokine receptor. We have characterized its expression pattern in leukocytes, in particular on B cells. So far, we have tested most of the known human chemokines as potential ligands, but could not identify a specific agonist. Receptor internalization on primary and transfected cells was measured as agonist induced response. Recent results obtained in collaboration with our partners in Paris suggest that CXCL12 binds RDC1 and induces its internalization in T cells. However, results form our laboratory indicate that primary B cells do not respond to CXCL12, but to a yet unknown agonist. We assume that the physiological relevant ligand could be an unknown molecule. To this end supernatants derived from different cell culture systems, mimicking the environment where RDC1 positive cells reside, are tested for potential activity on RDC1 and will be fractionated using standard biochemical techniques. Once a ligand has been identified we will study its expression patter and physiological significance.

PhD Granted by University of Bern, Switzerland.
Tutor: Professor Andrew Ziemiecki

Laura Rivino

"Dissecting the human CD4+ T cell memory pool."

Laura Rivino, David Jarrossay, Federica Sallusto, Antonio Lanzavecchia & Jens Geginat.

Two types of regulatory T cells have been described: "natural" $CD25^+Foxp3^+$ Tregs and adaptive IL-10-secreting "Tr1" cells with unknown phenotype. Induction and maintenance of CCR6 on TCR-activated human T cells required TGF-b and absence of polarising cytokines. In human blood CCR6 was expressed on myeloid DC, on most natural Tregs and on a fraction of antigen-experienced $CD4^+CD25^-Foxp3^-$ T cells. $CD25^-CCR6^+$ T cells possessed high IL-2 and IL-10 producing capacities, but produced IL-10 only following weak TCR stimulation. They were auto-reactive and proliferated with *ex vivo* isolated autologous DC upon IL-10 neutralization in a MHC class II-restricted manner. Moreover, only $CCR6^+$ T cells proliferated with the self-antigen MelanA in healthy donors, while MelanA-reactive cells were predominantly $CCR6^-$ in Viltiligo autoimmune patients. However, $CCR6^+$ T cells responded also to various recall antigens and we isolated several weakly auto-reactive T cell clones that secreted IL-10 upon suboptimal stimulation, but that produced IL-2 and proliferated vigorously upon strong stimulation with tetanus toxoid. We propose that $CCR6^+$ T cells contain context-dependent "Tr1/memory" cells that could behave Tr1-like upon recognition of cross-reactive antigens under steady-state conditions, but act as conventional memory cells in recall responses.

PhD Granted by University of Fribourg, Department of Medicine, Biochemistry unit.
Tutor: Professor Sandro Rusconi

Roxane Tussiwand

"Flt3 in dentritic cell development."

Roxanne Tussiwand and Markus Manz.

In vivo steady-state type I natural IFN-producing and dendritic cell (DC) development is largely dependent on Flt3 signaling. Natural IFN-producing and DC progenitors and their respective downstream cell populations express the flt3 receptor, and Flt3 ligand (Flt3L)_/_ mice have reduced while Flt3L-injected mice develop markedly increased numbers of both cell types. We could show that SU11657, a small multitargeted receptor tyrosine kinase inhibitor with Flt3 affinity, suppressed *in vitro* natural IFN-producing and DC development in Flt3L-supplemented mouse whole bone marrow cell cultures in a dose dependant manner, while DC development in GM-CSF-supplemented cultures was not affected. *In vivo* SU11657 application led to a significant decrease of both natural IFN-producing and DCs, comparable to the reduction observed in Flt3L_/_ mice. Conversely, Flt3L plasma levels increased massively in inhibitor-treated animals, likely via a regulatory feedback loop, without being able to compensate for pharmacological Flt3 inhibition.
No obvious toxicity was observed, and hemopoietic progenitor cell and stem cell function remained intact as assessed by myeloid colony-forming unit activity and in vivo bone marrow repopulation assays. Furthermore, upon treatment discontinuation, IFN-producing and DCs recovered to normal levels, proving that treatment effects were transient. DC and IFN-producing cells play an important role in regulation of immune responses and we were able to show that *in vivo* administration of SU11657 could prevent development of EAE in a mouse model system. Collectivly, these findings might lead to new pharmacological strategies in prevention and treatment of autoimmune diseases and complications of organ or blood cell transplantation.
International PhD Program in Basic and Applied Immunology; Università Vita e Salute San Raffaele, Milano

PhD Granted by Università Vita e Salute San Raffaele, Milano.
Tutor: Professor Ruggero Pardi

Claudia Ruprecht

"On the role of regulatory T cells and microbial products in the control of T and B cell immune responses".

Claudia Ruprecht and Antonio Lanzavecchia.

Self-nonself discrimination is the basic property of the immune system that allows rejection of pathogens without attacking self-specific structures. Discrimination of self and nonself is based on both structural features of the antigen as well as on the context, in which the antigen is encountered. While specific recognition of nonself-antigens in presence of microbial products induces potent immune responses, several suppressing mechanisms exist that limit immune reactions to specifically recognized antigens in a context devoid of microbial agents.

A prominent example of suppressing mechanisms is regulation of T cell responses by regulatory T cells (Tregs). Treg-mediated suppression is induced upon T cell receptor (TCR) stimulation of Tregs and therefore dependent on Treg specificity. We found that TCRs derived from mouse regulatory and conventional T cells cover a similar spectrum of affinity towards self-antigens, which implies that Tregs express a similar TCR repertoire as conventional T cells. This result suggests that Treg-mediated suppression is not induced by recognition of self-antigen but rather regulated by recognition of the immunological context.

Characterization of Treg function in autoimmune diseases is hampered by the fact that Tregs in an inflamed tissue cannot be discriminated from infiltrating activated conventional T cells. We report that at the site of autoimmune reactions Tregs can be distinguished from activated T cells by the expression of CD27. Using this novel Treg marker we show that the suppressive activity of Tregs isolated from inflamed tissues is not limited in vitro, which precludes a Treg-intrinsic defect. However we have observed that cytokines as IL-7 and IL-15, which are present in the autoimmune inflammatory milieu, potently block Treg-mediated suppression in vitro. These results suggest that in vivo IL-7 and IL-15 may interfere with Treg function at the sites of ongoing autoimmune reactions.

Recognition of a context containing signs of microbial invasion leads to the counterbalancing of suppressing mechanisms and to the induction of potent immune responses. Such a context is characterized by the presence of pathogen-associated molecular patterns (PAMPs) that are recognized by Toll-like receptors (TLRs) expressed on a variety of cell types. We show that TLR triggering is critically required for the induction of productive T-dependent human naïve B cell responses. B cell receptor (BCR) triggering and T cell help induced initial B cell proliferation but were not sufficient to sustain prolonged survival and accumulation of B cells. Extensive proliferation, isotypic switch and differentiation to Ig-secreting cells were promoted by microbial agents acting on TLRs expressed by naïve B cells upon BCR stimulation. This finding demonstrates that humoral immune responses (as cellular immune responses) are critically dependent on context discrimination via detection of PAMPs.

PhD Granted by University of Basel, Switzerland.
Tutor: ***Professor Antonio Rolink***

Lectures and seminars given by IRB scientists in 2006

IRB scientists are invited to give lectures and seminars around the world.

Maurizio Molinari

1• USGEB Meeting 2006, "Protein folding in the Endoplasmic Reticulum." Friedrich-Miescher Award 2006.
Geneva,Switzerland / *23-24.02.2006*

2• Neuroscience Seminar, "From protein folding and quality control to a novel approach to reduce production of the toxic amyloid-beta peptide."
EPFL Lausanne, Switzerland / *28.03.2006*

3• First Meeting of the Association Medicine Anti-Aging, "The Endoplasmic Reticulum: a factory for proteins and diseases."
Lugano, Switzerland / *6.04.2006*

4• Seventh International Calreticulin Workshop, "Functions and Dinamics of ER/SR Proteins". "Protein folding and quality control in chaperone deficient cell lines."
Niagara Falls, Ontario, Canada / *22-24.04.2006*

5• 151st Meeting of the Società Ticinese Scienze Naturali, "The Endoplasmic Reticulum: a factory for proteins and diseases."
Bellinzona, Switzerland / *6.05.2006*

6• Meriläin Kartano Meeting, "Protein Quality Control in UGT1-deleted cells."
Utajärvi, Finland *8-10.10.2006*

7• Science et Cité, Musica e Molecole. "Dall'Uomo alle Molecole alla Musica."
Bellinzona, Switzerland / *19.06.2006*

8• Basic Virology Course, Institut Pasteur, "The folding of viral glycoproteins in the endoplasmic reticulum."
Paris, France / *7.09.2006*

9• 8th Jenner Glycobiology and Medicine Symposium, "N-Glycan processing determines the fate of folding-competent and -defective glycoproteins."
Scripps Research Institute & Neuroscience Research Institute California, La Jolla, USA
17-20.09.2006

10• Simposio Invecchiamento, Demenza e Ricerca. "Approaches to reduce production of the toxic peptide Ab."
Lugano, Switzerland / *21.09.2006*

11• Simposio Alzheimer 1906-2006 Un secolo di scoperte, "Alzheimer 100 anni dopo: traguardi e prospettive della ricerca medica."
Locarno, Switzerland / *28.09.2006*

Marcus Thelen

12• *RDC1: an orpahn receptor?* Polyphor Basel, Switzerland / *06.02.2006*

13• Chemotactic Cytokines, Gordon Research Ronference, Chairman presentation "Must CXCR7 follow the fate of Pluto?"
Centre Paul Langevin, Aussois, France
17-22.09.2006

14• Analysis of Signaling Networks downstream of G-protein Coupled Receptors.
University of Ulm, Ulm Germany / *27.10.2006*

15• Chemokine Receptor Signal transduction: Common and distinct features
University of Rome, Roma Italy / *20. 11. 2006*

Fabio Grassi

16• "Calcium dependent shaping of T cell activation."
Institut A. Fleming, Vari, Greece *04.04.2006*

17• "αβ T cell development."
Institut Pasteur, Paris, France / *06.11.2006*

18• "Signal transduction in T cell development."
San Raffaele Scientific Institute, Milan, Italy
22.11.2006

19• "Regulation of T cell responsiveness and inflammation by calcium signaling."
University of Pavia, Italy / *12.12.2006*

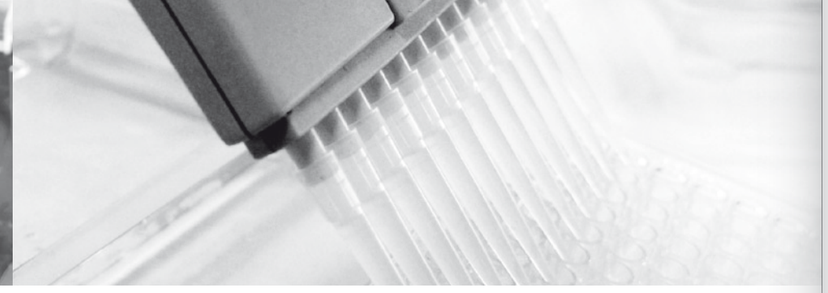
Markus Manz

20• ASM: "huAIS-RG mice-new options to test human lymphotropic viruses?"
Washington DC, USA / *26.02.2006*

21• "huAIS-RG mice-opportunities and limitations."
Baylor Institute for Immunology Research, Dallas, TX, USA / *09.05.2006*

22• "huAIS-RG mice-opportunities and limitations."
Mount Sinai School of Medicine, New York, USA / *10.05.2006*

23• "huAIS-RG mice-new options to test human lymphotropic viruses?"
American Association of Immunologist, Washington DC, USA / *13.05.2006*



24• *"huAIS-RG mice-new options to test human lymphotropic viruses?"*
Childrens Hopital & Harvard Medical School, Boston, USA / *15.05.2006*

25• *"Dendritic Cell Homeostasis"*
Institut für Mikrobiologie, TU München
29.06.2006

26• *1st International MUGEN Conference."Human Immune System Mice."*
Athens, Greece / *11.09.2006*

27• *Haematopoietic Stem Cells VI: "Flt3 in dendritic cell development."*
Universität Tübingen, Germany / *16.09.2006*

28• *First International Workshop on Humanized Mice: "HIV infection in humanized* mice."
Tokyo, Japan / *12.10.2006*

29• *"HIV infection in humanized mice"*
Riken Institute, Yokohama, Japan / *13.10.2006*

30• *"Humanized mice."*
Medizinische Hochschule Hannover
29.11.2006

Jeremy Luban

31• *"Structural studies on TRIM5alpha."*
Department of Infectious Diseases, University Hospital, Zurich, Switzerland / *2006*

32• *"Cyclophilin, TRIM5 and innate resistance to HIV-1."*
Department of Microbiology and Molecular Medicine, University of Geneva / *2006*

33• *2nd Swiss Workshop on Basic HIV Research. "Host factors that restrict HIV-1"*
Morat/Murten, Switzerland / *2006*

34• *4th International Conference on Innate Immunity:"Innate immunity to HIV-1."*
Corfu, Greece / *2006*

35• *FASEB Summer Res. Conf. on Virus Assembly. "HIV-1 CA and Cyclophilin A."*
Saxtons River, VT, USA / *2006*

36• *7th Annual Symposium on Antiviral Drug Resistance."Cyclophilin and TRIM5 in Innate Immunity HIV-1."*
Chantilly, VA, USA / *2006*

37• *Nouvelles Pandemies, Les Comprendre, Les Combattre. Les "Dix-Neuvièmes Entretiens" du Centre Jacques Cartier: "Cyclophilin and innate immunity to HIV-1"*
Lyon, France / *2006*

38• *"Cyclophilin, TRIM5, and HIV-1."*
Department of Virology, Universitätsklinikums Heidelberg / *2006*

39• *HIV-1 Pathogenesis Meeting:"Characterization of human TRIM5 mutants for CA-binding ability and retroviral restriction activity."*
Keystone, Colorado, USA / *2006*

40• *HIV-1 Pathogenesis Meeting:"CypA and TRIM5 independently regulate HIV-1 infectivity."*
Keystone, Colorado, USA / *2006*

41• *Autoimmunity and AIDS pathogenesis. Scientific Board Meeting.*
Swiss HIV Cohort Study, Bern, Switzerland / *2006*

42• *Second EuroStemCell International Conference: Advances in Stem Cell Research. "AIDS pathogenesis model in mice after adoptive transfer of hematopoietic elements derived from human embryonic stem cells."*
Lausanne, Switzerland / *2006*

Mariagrazia Uguccioni

43• *XXV EAACI Congress, "Tuning Chemokine Activities."*
Vienna / *10-14.06.2006*

44• *"Chemokine expression in autoimmunity."*
Istituto di Reumatologia, Bologna / *06.2006*

Federica Sallusto

45• *Symposium "From Cell Biology to Cancer Immunotherapy". "Regulation of leukocyte trafficking in lymph nodes during the immune response."*
Institut Curie, Paris / *15-16.10.2006*

46• *Keystone Symposium "Chemokines and Chemokines Receptors", "Leukocyte trafficking to the inflamed lymph node".*
Snowbird / *15-20.01.2006*

47• *NIH, IIG Seminar series, Seminar: "Leukocyte traffic in immune stimulated lymph nodes."*
Bethesda / *25.01.2006*

48• *Karolinska Immunology Retreat, "Cell traffic regulation in the immune response".*
Rosenön / *10-11.03.2006*

49• *European Association for the Study of the Liver (EASL), 41st Annual Meeting, "The lesson from basic science: the role of adaptive immunity in viral infections"*
Vienna / *26-30.04.2006*

50• *MAIN Network of Excellence, Students' Meeting "Deciphering the Cell Migration Code", "Leukocyte migration in immune stimulated lymph nodes."*
Gwatt / *13-16.05.2006*

51• *Seminar: NIH/NIAID, Twinbrook Seminar Series, "Regulation of dendritic cell functivon by microbial products."*
Rockville / *23.05.2006*

52• *Pediatric Dengue Vaccine Initiative, Third Research Network Meeting, Arlie Center, "Isolation and characterization of human monoclonal antibodies against Dengue viruses."*
Warrenton / *1-4.06.2006*

53• *XXV EAACI Congress, "Chemoattractants and their receptors in inflammation."*
Vienna / *10-14.06.2006*

54• *DC-THERA Imaging Platform Course: In vivo dendritic cell migration, Nijmegen Centre for Molecular Life Sciences. "Dendritic cell and lymphocyte migration in lymph nodes."*
Nijmegen / *10-14.07.2006*

55• *The 2006 World Transplant Congress, "The link between innate and adaptive immunity."*
Boston / *22-27.07.2006*

56• *Cytokines 2006, Joint Conference of ICS, ISICR and ECS, "The impact of cytokine and chemokine networks on T cell priming."*
Vienna / *27-31.08.2006*

57• *First European Congress of Immunology, "Memory T cell subsets."*
Paris / *6-10.09.2006*

58• *International Graduate school in Molecular Medicine and International PhD Program in Cell and Molecular Biology, Lecture Course "Signal Transduction in T and B cell activation, development and differentiation", "Memory T cell origin and maintenance."*
Milan / *18-22.09. 2006*

59• *Seminar: "Cell traffic in lymph nodes during immune responses."*
University of Bern, Bern Immunology Club seminar series / *27.09.2006*

60• *Collaborative Research Centre 621 (SFB 621 "Pathology of the Intestinal Mucosa") Symposium, "Leukocyte traffic to the inflamed lymph node."*
Hannover / *28-30.09.2006*

61• *GSK Bio, Third Extramural R&D Symposium, "Understanding the generation and function of memory T cells."*
Louvain-la-Neuve / *9-10.10.2006*

62• *32nd Annual La Jolla Immunology Conference, "Memory T cell subsets: function and trafficking."*
La Jolla / *10-12.10.2006*

63• *Ernst Shering Foundation Symposium "Immunotherapy in 2020","Vaccination."*
Postdam. / *22-24.10.2006.*

Antonio Lanzavecchia

64• *Keynote address at Keystone Symposium: Determinants of Host Resistance, Susceptibility or Immunopathology to Pathogens. "The Immune Battle Against Infectious Organisms: From Mouse Models to Human Disease."*
Keystone Resort, Keystone, Colorado / *2006*

65• *Keystone Symposium: Lymphocyte Activation and Signaling. "Signals that Drive Immunological Memory."*
Keystone, Colorado / *2006*

66• *Corso di formazione al Collegio Ghislieri, "Linfociti memoria e immunità a lungo termine."*
Pavia, Italia / *24.01.2006*

67• *ZMBH colloquia series, "Human monoclonal antibodies and analytic vaccinology".*
Heidelberg, Germany / *17.02.2006*

68• *Serata di formazione per i farmacisti, "I vaccini del futuro."*
Scuola Arti e Mestieri, Bellinzona, Switzerland
21.02.2006

69• *Seminar:"Human naïve and memory B cells: identification, activation, and exploitation."*
University of Alabama, Birmingham, USA
02.03.2006

70• *Nomura Science Enterprise Lecture series: "Active and passive vaccination."*
King's college, London, UK / *08.03.2006*

71• *Seminar at CRUK: "On the cellular basis of immunological memory."*
Lincoln's Inn Field Laboratories, London, UK
10.03.2006

72• *Seminario IOSI: "Le basi cellulari della memoria immunologica."*
Ospedale Regionale Bellinzona, Switzerland
22.03.2006

73• *Workshop DC-Crest: "Dendritic cell activation."*
Celerina, Switzerland / *27.03.2006*

74• *VRC Symposium"Vaccination and immunological memory."*
Natcher Building / *26.04.2006*

75• *Keynote lecture at the Third Workshop SIICA, "Memoria B e anticorpi monoclonali".*
Certosa di Pontignano, Siena, Italy
02-03.05.2006

76• *Annual Meeting of The American Association of Immunologists: "B lymphocyte activation."*
Boston, USA / *2006*

77• *Lecture "Naïve/memory CD4 T cells."*
ENII-MUGEN Summer School, Sardegna, Italy
19.05.2006

78• *Presentation of IRB research to Prof. Dr. H.R.H Princess Chulabhorn Mahidol.*
IRB, Bellinzona / *02.06.2006*

79• *Seminar "Exploring and exploiting immunological memory."*
Novartis Institute for Tropical Diseases, Singapore / *05.06.2006*

80• *Keynote lecture, Gaslini advanced course in basic and applied immunology, "Exploring and exploiting immunological memory."*
Genoa, Italy / *13.06.2006*

81• *RCAI-JSI International Symposium on Immunology.*
Tokyo / *16.06.2006*

82• *5th International Congress on Recombinanat Antibodies IBC,"Human monoclonal antibodies from memory B cells."*
Zurich, Switzerland / *27.06.2006*

83• *Frontiers meeting on Emerging Zoonotic Infections,"Human monoclonal antibodies from memory B cells."*
Wellcome Trust Conference Centre, Hinxton, Cambridge, UK / *03.07.2006*

84• *European Congress of Immunology, "Human monoclonal antibodies to treat infectious diseases" and "B cells never forget: monoclonal antibodies from memory B cells."*
Paris, France / *07-08.09.2006*

85• *International conference on dendritic cells: "TLR synergy in dendritic cell activation."*
Edimburgh, UK / *19.09.2006*

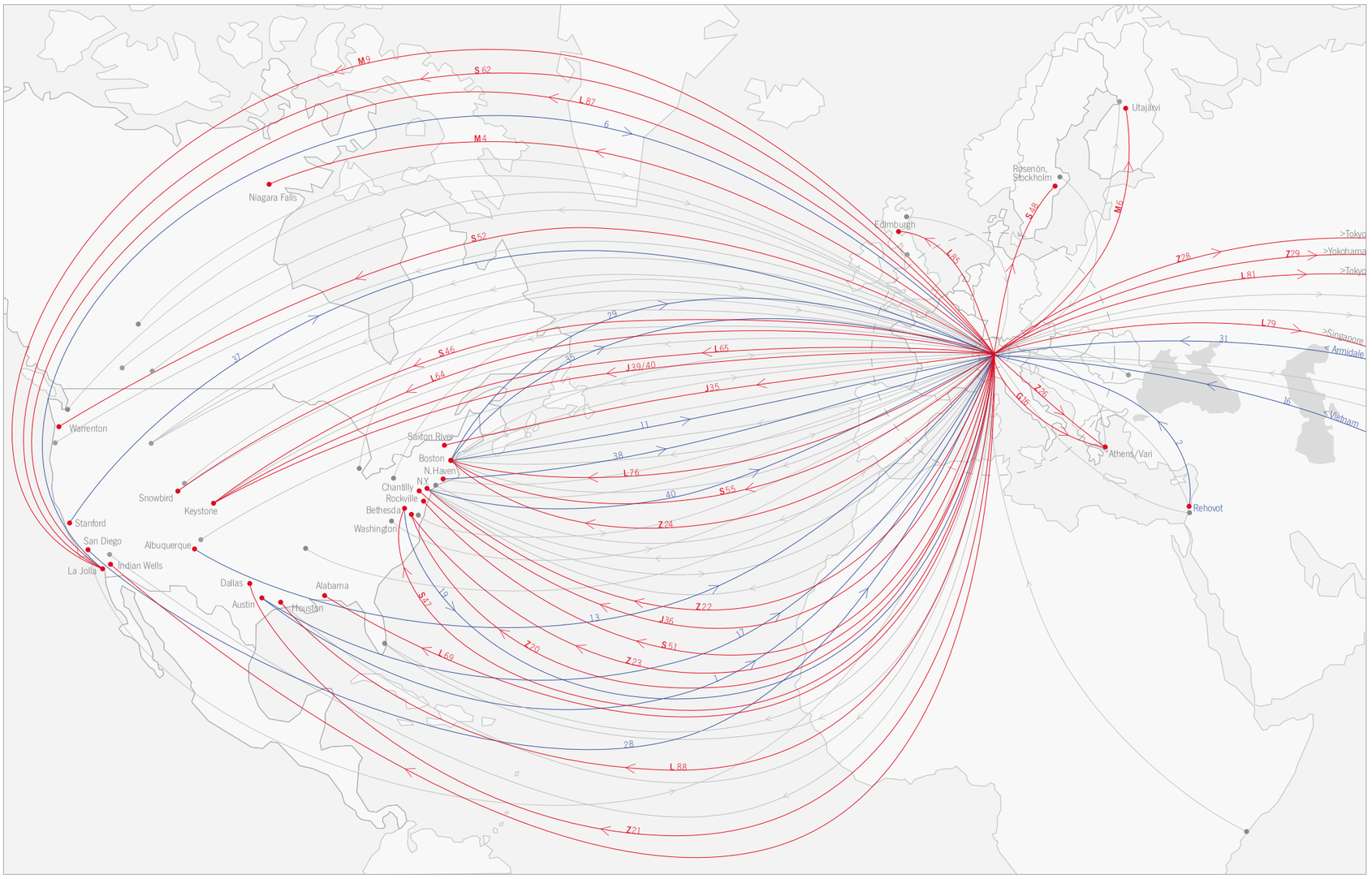
86• *Vaccinology Frontiers Meeting at The Elvetham, Hartley Wintney, "Human monoclonal antibodies from memory B cells"*
Hampshire, UK / *09.10.2006*

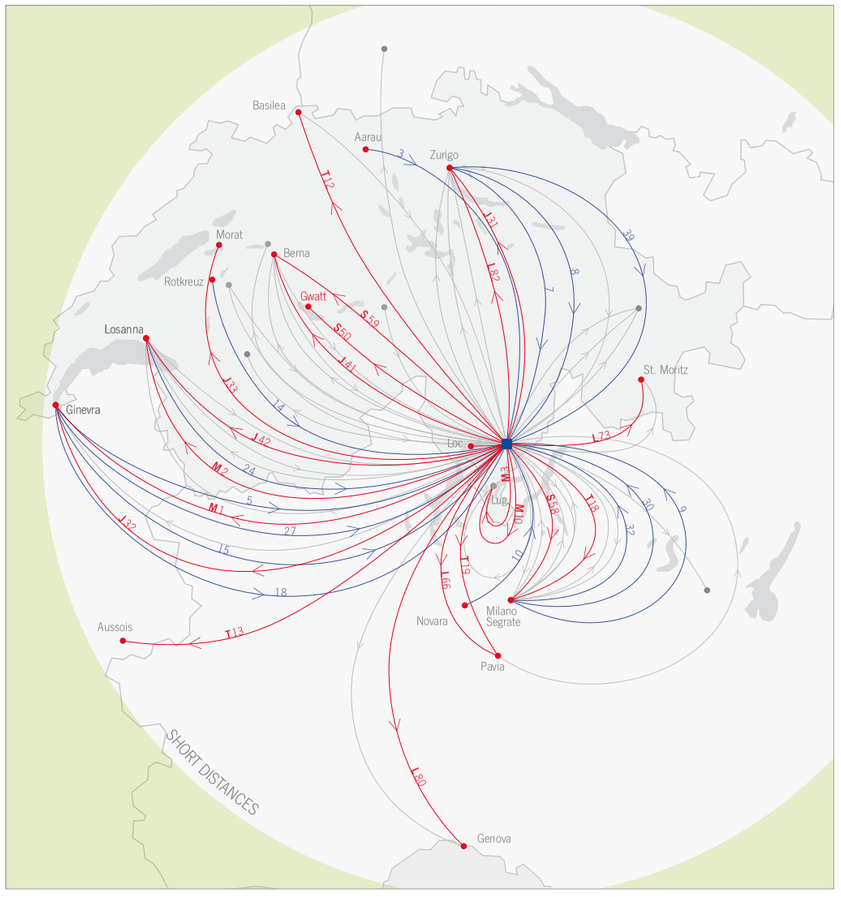
87• *32nd La Jolla Immunology Conference, "The role of TLRs in dendritic cells and B cell activation."*
La Jolla, California, USA / *12.10.06*

88• *Baylor Symposium on Human Immunology and Biodefense, "T, B and Dendritic cells."*
Houston, USA / *04.11.2006*

89• *IRB Corso avanzato di formazione sulle neoplasie linfatiche: "Nuovi aspetti dell'immunologia, in particolare nei linfomi."*
Bellinzona, Switzerland / *2006*

90• *Cours d'immunologie approfondie 2006-2007 «T lymphocyte-dendritic cell interactions: intermediates, effector and memory cells».*
Institut Pasteur, Paris, France / *18.11.06*





LEGEND

- Seminars 2006 by IRB
- Seminars before 2006
- Numbers refer to the list
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- Seminars 2006 from outside
- Seminars before 2006
- Numbers refer to the list
> pages 44 - 45

- Seminars location, 2006
- Previous seminars location
- IRB, Bellinzona

U Mariagrazia Uguccioni
L Antonio Lanzavecchia
M Maurizio Molinari
Z Marcus Manz
S Federica Sallusto
T Markus Thelen
G Fabio Grassi
J Jeremy Luben

Not in the mab because located in:
Bellinzona M 5 / M 7 / L 68 / L 72 / L 78 / L 89
Locarno M11




Special PhD Lecture and Seminars Programme

World-renowned scientist come to Bellinzona to give lectures either as part of the special PhD Lecture Series or as part of the many collaborations between IRB scientist and their international colleagues.

2006-2007 Lecture Series supported by the Jacob Foundation

2006

a• *Bernard Malissen*
T cell development and activation
8.11.2006

b• *Anjana Rao*
Transcriptional regulation of lymphocyte differentiation
13.11.2006

c• *Ira Mellman*
Biology of antigen processing
1.12.2006

d• *Rolf Zinkernagel*
Immunological memory
4.12.2006

2007

e• *Hilde Cheroutre*
Non-classical T cells
18.01.2007

f• *Klaus Ley*
Cell recruitment in inflammation
18.01.2007

g• *Mette Rosenkilde*
Pharmacology of 7TMR antagonists
1.03.2007

h• *Wilhelm Krek*
Signaling networks in human diseases
13.03.2007

i• *Charles M. Rice*
Hepatitis C virus
23.03.2007

l• *Radek Skoda*
Myeloproliferative diseases
20.04.2007

m• *Ton N. Schumacher*
Adaptive immunotherapy of cancer
24.05.2007

Seminars at IRB

2006

1• Hazel Pinheiro – "MicroRNAs as Potential Diagnostic and Prognostic Markers of Disease"
Ambion Europe Ltd / *10.01.2006*

2• Yair Reisner – "Hematopoietic stem cell transplantation across major genetic barriers: tolerance induction by "megadose"stem cells and other veto cells"
Immunology Department, Weizmann Institute of Science, Rehovot, Israel / *26.01.2006*

3• Ingmar AFM Heijnen "Flow cytometric disease monitoring in B-cell neoplasms"
Zentrum für Labormedizin, Kantonsspital Aarau, Aarau, Switzerland / *31.01.2006*

4• Luca Scorrano – "Keeping mitochondria in shape: a matter of life and death"
Venetian Insti-tute of Molecular Medicine, Dulbecco Telethon Institute, Padua, Italy
02.02.2006

5• Bettina Borisch – "Human lymphomas – what do we learn from their cell membrane organization?"
Department of Pathology, CMU, Geneva, Switzerland / *08.02.2006*

6• Dennis R. Burton – "The neutralizing antibody problem and HIV vaccine design"
Department of Immunology, The Scripps Research Institute, La Jolla, CA, USA / *09.02.2006*

7• Alexandra Trkola – "Humoral Immunity to HIV-1: Neutralization and beyond"
Division of Infectious Diseases and Hospital Epidemiology Department of Medicine, University Hospital Zurich, Switzerland / *23.02.2006*

8• Andrea Zisch – "Therapeutic manipulation of adult angiogenesis: early, late, unexpected response to VEGF"
Department of Obstetrics, University Hospital Zurich, Switzerland / *28.02.2006*

9• Giancarlo Pruneri – "Prelevance and clinical relevance of cyclin D1 abnormalities in plasma cell myeloma"
Division of Pathology and Laboratory Medicine, European Institute of Oncology, Milan, Italy
07.03.2006

10• Daniela Capello – "Molecular pathways in HIV-related lymphomas"
Division of Hematology Unit, Dept. of Medical Sciences and IRCAD, A. Avogadro Univ. of Eastern Piedmont, Novara, Italy / *15.03.2006*

11• David A. Thorley-Lawson - "Mechanisms of Epstein-Barr virus persistent infection for real and in virtual reality"
Department of Pathology, Tufts University School of Medicine, Boston, USA / *20.03.2006*

12• Fiona Powrie – "Factors that control the balance between effector and regulatory T cells in the intestine"
Sir William Dunn School of Pathology, University of Oxford, UK / *29.03.2006*

13• Eric Prossnitz – "Estrogen-mediated Signaling via GPR30"
Cell Biology & Physiology, University of New Mexico, Albuquerque, Mexico / *05.04.2006*

14• Applied Biosystems – "Gene expression and Genotyping."
Applera Europe B.V., Rotkreuz Branch, Rotkreuy, Switzerland / 13.04.2006

15• Marisa Jaconi – "Human embryonic stem cells, cardiac differentiation and therapies of the heart: the future is now?"
Department of Pathology and Immunology Faculty of Medecine, Geneva University, Switzerland / *21.04.2006*

16• Cameron Simmons – "Disease Pathogenesis: Dengue and H5N1 influenza in Vietnam"
Oxford University Clinical Research Unit, Hospital for Tropical Diseases, HCMC, Vietnam
24.04.2006

17• Stephanie Brooking – "RNAi-Design, Execution and analysis"
European RNA silencing specialist, Ambion Europe Ltd / *04.05.2006*

18• Gisou van der Goot – "Anthrax toxin: cellular entry and cytophatic effects"
Department of Microbiology and Molecular Medicine, University of Geneva, Switzerland
05.05.2006

19• Kanta Subbarao – "Vaccines against potential pandemic strains of influenza"
Laboratory of Infectious Diseases, NIAID, NIH, Bethesda / *08.05.2006*

20• Peter Friedl – "How migrating T cells acquire signals: a dynamic view on the immunological synapse"
Molecular Cell Dynamics Laboratory, DFG Center for Experimental Biomedicine and Department of Dermatology, University of Wurzburg, Germany / *11.05.2006*

21• Carmen Birchmeier – "Genes that control the development of migrating muscle progenitors"
May-Delbrueck-Centrum für Molekulare Medizin, Berlin, Germany / *18.05.2006*

22• Signe Hässler – "Aire deficient mice, an animal model of endocrine autoimmunity"
Department of Medical Sciences, Uppsala University Hospital, Sweden / *08.06.2006*

23• Ralf Ignatius – "Use of TLR ligands as adjuvants in HIV vaccine studies in the rhesus macaque model"
Institute for Microbiology and Hygiene Charité – University of Berlin, Germany / *28.06.2006*

24• Onur Boyman, "Antibody-cytokine complexes as tools to modulate immune responses"
Div. of Immunology and Allergology, Dept. of Medicine, University Hospital of Lausanne, Switzerland / *06.07.2006*

25• Thomas Duhen – "Study of pDC, from the innate to the adaptive immune response"
INSERM U503, Centre d'Etudes et de Recherches en Virologie et Immunologie, Lyon, France
17.07.2006

26• Martin Lohse – "Optical recording of receptor activation and signalling"
Institute of Pharmacology and Toxicology and Rudolf Virchow Center, University of Würzburg, Germany / *21.08.2006*

27• Amanda Proudfoot – "The chemokine system: multi-faceted therapeutic targets"
SPRI, Serono International SA, Geneva, Switzerland / *24.08.2006*

28• Douglas Richman – "HIV Neutralizing Antibody"
Departments of Pathology and Medicine, University of California San Diego, USA / *29.08.2006*

29• Claudia Lengerke – "Patterning hematopoiesis in embryonic stem cells"
Children's Hospital, Boston, USA / *12.09.2006*

30• Anna Mondino – "The making and breaking of tumor-specific T cell memory"
Biotechnology School, Vita-Salute San Raffaele University, Italy / *10.10.2006*

31• Ian Colditz - "Regulation of neutrophil migration through inflammatory lesions"
CISRO Livestock Industries, Armidale, Australia
13.10.2006

32• Anna Villa – "RAG mutations and severe combined immunodeficiency"
CNR-ITB, Segrate, Italy / *26.10.2006*

33• Tim Sparwasser – "Regulating the regulators: in vivo targeting of DC subsets and tregs using BAC technology"
Institut für Med. Mikrobiologie, Immunologie und Hygiene, Technische Universität München, Germany / *27.10.2006*

34• Bernard Malissen – "Lymphoproliferative disorders proper to defective LAT signalosomes"
Centre d'Immunologie Inserm-CNRS, Marseille, France / *08.11.2006*

35• Anjana Rao – "Signalling to transcription: the calcium/calcineuring/NFAT signaling pathway"
The CBR Institute for Biomedical Research, Boston, USA / *13.11.2006*

36• Paul O'Shea – "Raft-dependent modulation of receptor-mediated signaling reactions in cell membranes"
Cell Biophysics Groups, School of Biology, University of Nottingham, UK / *15.11.2006*

37• Luca Varani – "A solution method for rapid footprint mapping of pMHC/TCR interactions"
Stanford University School of Medicine, Dept.of Structural Biology, Stanford, USA / *16.11.2006*

38• Ira Mellman – "Cell Biology of dendritic cells"
Dept. Cell Biology, Ludwig Institute for cancer Research Yale, University School of Medicine, New Haven, USA / *01.12.2006*

39• Rolf Zinkernagel – "Against dogma and against feelings"
University Hospital Zürich, Institute of Experimental Immunology, Zürich / *04.12.2006*

40• Nicole Suciu Foca – "Tolerogenic effect of soluble ILT3 in human malignancies"
Department of Pathology, Columbia University, New York, USA / *05.12.2006*

Enabling Discovery

The IRB mission is made possible by a partnership of public and private donors, an efficient administration, and the dedicated members of the Foundation Council.



The Institute

The Institute is run by the Foundation for the Institute for Research in Biomedicine with a Foundation Council of 13 members and an Executive Committee of 4. The Scientific Advisory Board oversees the scientific strategy and guarantees the scientific quality of the IRB program. A dedicated and highly efficient administrative staff manages the day to day operations of the institute under the guidance of the Director and the Administrative Directors.

Structure

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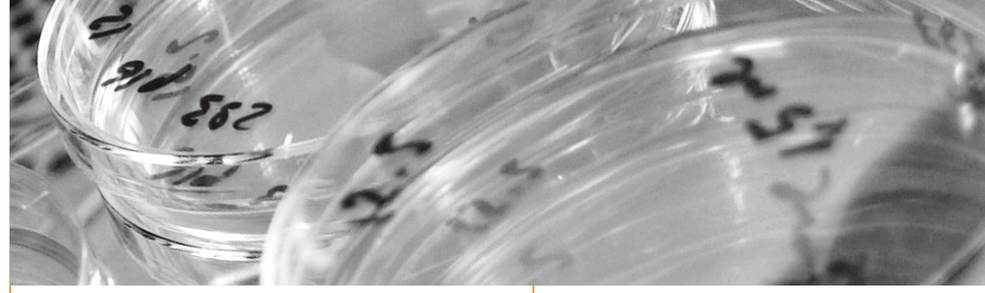

Research Staff

Group Leaders

Fabio Grassi, *MD, PhD*
T Cell Development

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Immune Regulation

Jeremy Luban, *MD*
Viral replication, pathogenesis, and immunity.

Markus Manz, *MD*
Hematopoiesis

Maurizio Molinari, *PhD*
Protein folding and quality control

Federica Sallusto, *PhD*
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Marcus Thelen, *PhD*
Signal Transduction

Mariagrazia Uguccioni, *MD*
Chemokines: tissue expression, function and activity modulation

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Financial Data 2006

Core funding of the IRB is provided by public and private donors; The Helmut Horten Foundation, The Confederation, The Canton of Ticino and the City of Bellinzona, as well as individual donors.

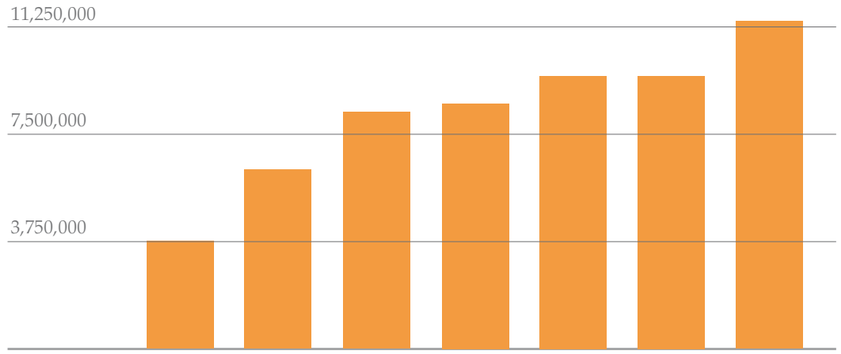
Balance Sheet as 31 of December 2006

ASSETS		31.12.2006	31.12.2005
1.	*Liquidity*	2,394,252	3,777,159
2.	*Various Receivables*	1,915,242	612,987
3.	*Temporary Receivables*	1,034,999	1,297,686
	Current Assets	**5,344,493**	**5,687,833**
4.	*Buildings*	5,274,944	4,317,440
5.	*Furnishing & Equipment*	3,583,000	4,078,000
	Fixed Assets	**8,857,944**	**8,395,440**
	TOTAL ASSETS	14,202,438	14,083,273

Profit and Loss Account for the year 2005 and 2006 (In Swiss Francs)

COSTS		31.12.2006	31.12.2005
1.	*Personnel Costs*	4,903,221	4,613,152
2.	*Consumables*	1,677,051	1,559,230
3.	*Maintenance of Buildings and Equipment*	359,778	283,142
4.	*Investments*	677,524	145,023
5.	*Amortizations*	674,135	678,451
6.	*Rent and related Costs*	883,886	877,692
7.	*Administrative Costs and Various*	974,792	1,205,714
8.	*Travel, Congresses and Guests*	306,606	161,071
9.	*Various costs for Research*	851,908	238,742
	Total Costs	**11,308,902**	**9,762,217**
10.	*Contributions from the Confederation*	1,105,000	690,000
12.	*Contributions from the City of Bellinzona*	500,000	500,000
13.	*Contributions from the Helmut Horten Fnd.*	1,500,000	1,500,000
14.	*Other Contributions*	974,706	964,428
15.	*Research Projects*	4,851,391	3,734,124
16.	*Other Revenue*	1,047,872	564,035
	Totale revenue	**9,978,969**	**7,952,588**
	OPERATIONAL DEFICIT	1,329,932	1,809,629

Evolution of Costs 2000-2006



COSTS	2000	2001	2002	2003	2004	2005	2006
Personnel	1,825,910	3,456,425	4,498,136	4,749,499	5,008,522	4,613,152	4,903,221
General	1,991,623	2,763,354	3,883,763	3,958,932	4,789,958	5,149,065	6,405,681
TOT. COSTS	3,817,533	6,219,779	8,381,899	8,708,431	9,798,480	9,762,217	11,308,902

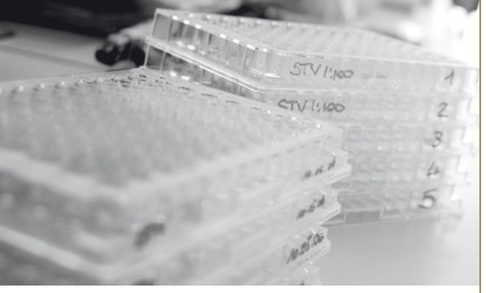
Liabilities

LIABILITIES		31.12.2006	31.12.2005
1.	*Debt for delivery and services*	487,441	465,715
2.	*Accruals*	272,979	575,164
3.	*Funds for Research Projects*	1,199,979	587,274
4.	*Funds for Laboratories*	1,370,249	1,328,398
5.	*Various Funds*	264,996	189,996
	Current Liabilities	**3,595,645**	**3,146,547**
6.	*Long Term Loans*	3,800,000	2,800,000
	Long Term Liabilities	**3,800,000**	**2,800,000**
7.	*Capital Resources*	8,136,726	9,946,355
8.	*Operationed deficit*	-1,329,932	-1,809,629
	Equity of the Foundation	**6,806,793**	**8,136,726**
	TOTAL LIABILITIES	14,202,438	14,083,273

Research projects are funded through competitive grants from agencies such as the Swiss National Fund, The European Union and the National Institutes of Health (USA), as well as from private foundations such as the Wellcome Trust (UK) and the Bill and Melinda Gates Foundation (USA).

Contributing Discovery

Knowledge created at the IRB impacts understanding of immunology through publications, seminars and the constant movement of IRB students and scientists.



Publications 2006

This list covers publications for the year in chronological order.

The numbers refer to the total list of IRB publications since 2000.

Books

2006

139. Consequences of ERp57 deletion on oxidative folding of obligate and facultative clients of the calnexin cycle.
Solda T., Garbi N., Hammerling G. J., and Molinari M. / *J Biol Chem 2006; 281:6219-6226*
IF: 5.9

140. Activation of the Flt3 signal transduction cascade rescues and enhances type I interferon-producing and dendritic cell development.
Onai N., Obata-Onai A., Tussiwand R., Lanzavecchia A., and Manz M. G. / *J Exp Med 2006; 203:227-238*
IF: 14.0

141. Characterization of severe acute respiratory syndrome coronavirus membrane protein.
Voss D., Kern A., Traggiai E., Eickmann M., Stadler K., Lanzavecchia A., and Becker S.
FEBS Lett 2006; 580:968-973
IF: 3.4

142. Plastic downregulation of the transcriptional repressor BCL6 during maturation of human dendritic cells.
Pantano S., Jarrossay D., Saccani S., Bosisio D., and Natoli G. / *Exp Cell Res 2006; 312:1312-1322*
IF: 4.1

143. Expression and regulation of the orphan receptor RDC1 and its putative ligand in human dendritic and B cells.
Infantino S., Moepps B., and Thelen M.
J Immunol 2006; 176:2197-2207
IF: 6.4

144. A hyper-dynamic equilibrium between promoter-bound and nucleoplasmic dimers controls NF-kappaB-dependent gene activity
Bosisio D., Marazzi I., Agresti A., Shimizu N., Bianchi M.E., Natoli G. / *EMBO J 2006; 25:798-810*
IF: 10.1

145. Regulation of peripheral T cell activation by calreticulin.
Porcellini S., Traggiai E., Schenk U., Ferrera D., Matteoli M., Lanzavecchia A., Michalak M., and Grassi F. / *J Exp Med 2006; 203:461-471*
IF: 14.0

146. Notch1-dependent lymphomagenesis is assisted by but does not essentially require pre-TCR signaling.
Campese A. F., Garbe A. I., Zhang F., Grassi F., Screpanti I., and von Boehmer H. / *Blood 2006; 108:305-310*
IF: 10.1

147. ***Toll-like receptor stimulation as a third signal required for activation of human naive B cells.***
Ruprecht C. R. and Lanzavecchia A. / *Eur J Immunol 2006; 36:810-816*
IF: 4.9

148. Differences in CXCR4-mediated signaling in B cells.
Palmesino E., Moepps B., Gierschik P., and Thelen M. / *Immunobiology 2006; 211:377-389*
IF: 1.8

149. A cyanobacterial LPS antagonist prevents endotoxin shock and blocks sustained TLR4 stimulation required for cytokine expression.
Macagno A., Molteni M., Rinaldi A., Bertoni F., Lanzavecchia A., Rossetti C., and Sallusto F.
J Exp Med 2006; 203:1481-1492
IF: 14.0

150. Follicular B helper T cell activity is confined to CXCR5(hi)ICOS(hi) CD4 T cells and is independent of CD57 expression.
Rasheed A. U., Rahn H. P., Sallusto F., Lipp M., and Muller G. / *Eur J Immunol 2006; 36:1892-1903*
IF: 4.9

151. Cyclophilin, TRIM5, and innate immunity to HIV-1.
Sokolskaja E. and Luban J. / *Curr Opin Microbiol 2006, 9:404-408*
IF: 8.0

152. Understanding and making use of human memory B cells.
Lanzavecchia A., Bernasconi N., Traggiai E., Ruprecht C.R., Corti D., and Sallusto F. / *Immunol Rev 2006; 211:303-309*
IF: 8.4

153. A new role for CCR5 in innate immunity--binding to bacterial heat shock protein 70.
Mackay C. R. and Sallusto F. / *Eur J Immunol 2006; 36:2293-2295*
IF: 4.9

154. N-linked glycan recognition and processing: the molecular basis of endoplasmic reticulum quality control.
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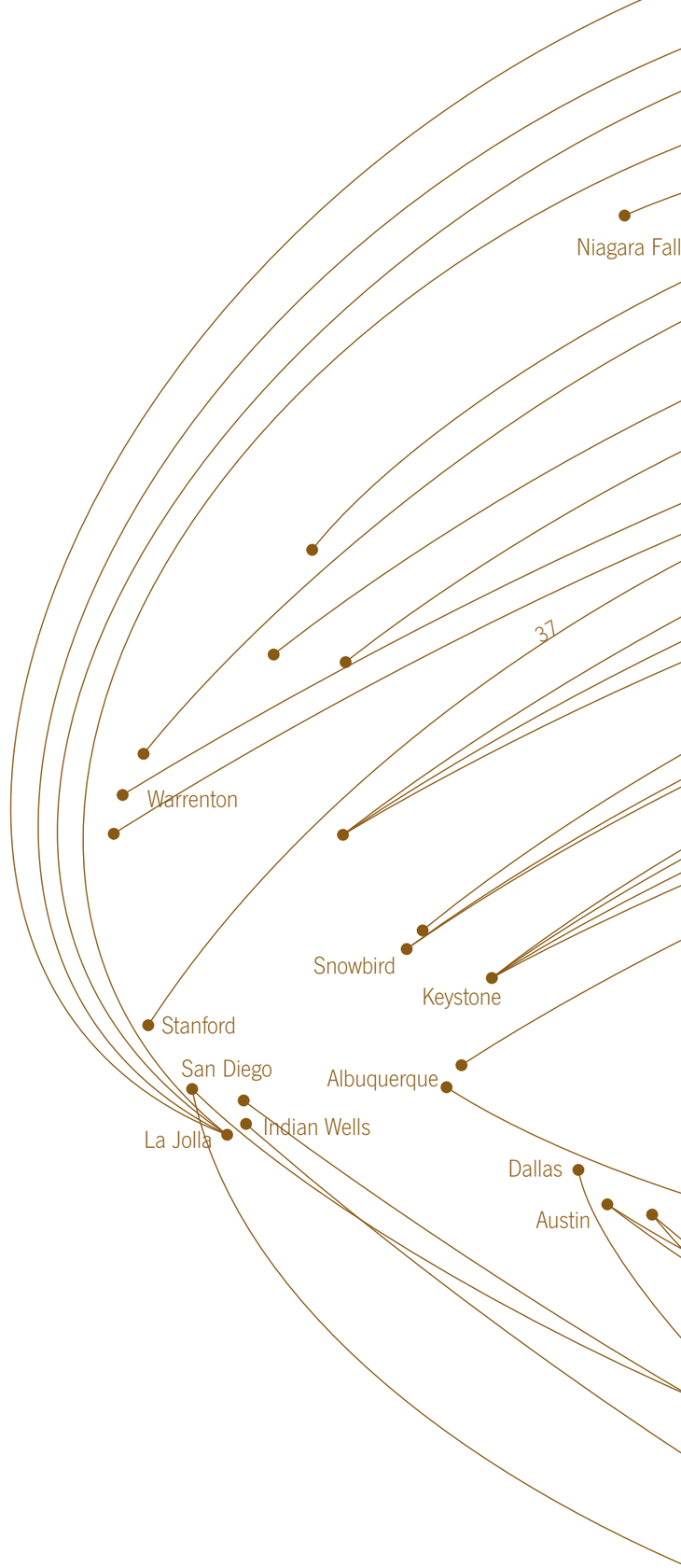

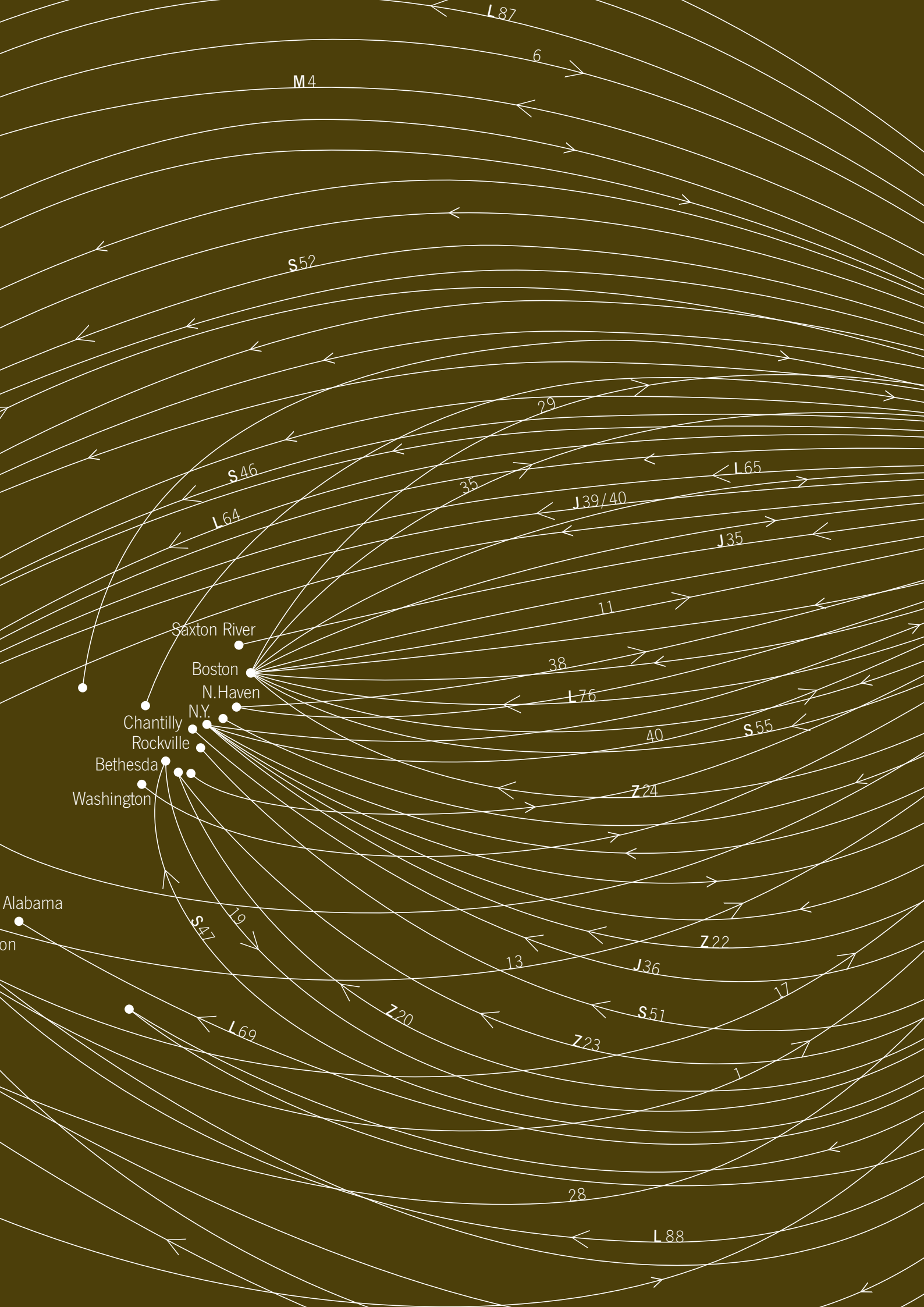
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