

JULY 07, 2005

## 2005 HHMI International Research Scholars in Infectious Diseases and Parasitology

\* Previous HHMI international research scholars

**Alex Andrianopoulos, Ph.D. Associate Professor of Genetics** University of Melbourne Melbourne, Australia

Alex Andrianopoulos will research the human pathogen *Penicillium marneffeii*, a fungus that can grow in either a unicellular or multicellular form, depending on the temperature surrounding it. Andrianopoulos will attempt to identify genes controlling this change in form at the molecular and cellular level. His findings will have both medical and scientific value, as well as important implications for biotechnology.

**Michele Marie Barry, Ph.D. Associate Professor of Medical Microbiology and Immunology** University of Alberta Edmonton, Canada

Michele Barry will study the proteins that interfere with cell death, focusing on the mechanisms human cells use to expel viruses and the ways that viruses fight back in the vaccinia virus. Her research could provide clues for the development of new therapeutic approaches for human diseases.

**Gabrielle T. Belz, Ph.D. Investigator** The Walter and Eliza Hall Institute of Medical Research Melbourne, Australia

Gabrielle T. Belz will investigate the processes that induce the body to produce elevated numbers of CD8+ memory cells, which are key to the function of the human immune system. This study could have significant impact on how vaccines are developed in the future.

\* **Charles Boone, Ph.D. Professor** Banting and Best Department of Medical Research University of Toronto Toronto, Canada

Charles Boone will study the genes responsible for causing vegetative, yeast-like fungi to grow in a filamentous form, which can augment the fungus's virulence. A detailed understanding of the genes controlling these processes will provide new insights into fungal pathogenicity and should identify targets for the development of novel antifungal drugs. Boone plans to disseminate his findings to the research community through an open database.

**Jean-Laurent Casanova, M.D., Ph.D. Professor of Pediatrics** Pediatric Immunology Unit **Director** Laboratory of Human Genetics of Infectious Diseases Necker Medical School and Hospital for Sick Children University of Paris René Descartes **Director** Inserm Unit 550 Paris, France

Jean-Laurent Casanova will conduct research on the potentially fatal condition known as herpes simplex encephalitis, which, for an unknown reason, develops from herpes simplex virus-1 (HSV-1) in a small percentage of infected children. His search for a candidate gene and an understanding of the underlying immunodeficiency of this disease in families may have important medical and biological implications.

\* **Pascale Françoise Cossart, Ph.D. Professor and Head** Unité des Interactions Bactéries-Cellules Institut Pasteur **Director** Inserm Unit 604 Paris, France

Pascale Cossart will study the infection by *Listeria monocytogenes*, a bacterium that is one of the best models of intracellular parasitism. She will characterize the processes by which *Listeria* infect cells, tissues and organs and succeed in breaching host barriers.

\* **Alan F. Cowman, Ph.D. Researcher, Division of Infection and Immunity** The Walter and Eliza Hall Institute of Medical Research Melbourne, Australia

Alan Cowman wants to know how *Plasmodium falciparum*, which causes the most lethal form of human malaria, invades mature red blood cells. This information will be important in determining the potential of the proteins involved in the process as vaccine and drug candidates.

\* **Brendan Crabb, Ph.D. Chief of Laboratory** The Walter and Eliza Hall Institute of Medical Research Melbourne, Australia

Brendan Crabb will study merozoite surface proteins, the prime targets of immune responses and the leading vaccine candidates for control of the deadly human malaria parasite *Plasmodium falciparum*. Specifically his

group will use genetic technologies to study the relative importance of specific merozoite antigens.

**Christoph Georg Fritz Dehio, Ph.D. Associate Professor of Microbiology Researcher, the Biozentrum** University of Basel Basel, Switzerland

Christoph Dehio is conducting research on bacterial pathogens associated with the formation of tumors in humans. In particular, Dehio will study the bacterium *Bartonella henselae* to determine the factors that lead to the formation of a vascular tumor.

**Abdoulaye Djimde, Ph.D. Chief of Drug Resistance Laboratory, Malaria Research and Training Center** University of Bamako Bamako, Mali

Abdoulaye Djimde will conduct clinical, entomological, and molecular studies to improve understanding of resistance to current inexpensive and commonly prescribed antimalarial drugs. He will focus on improving the understanding of the mechanisms involved in the spread of *Plasmodium falciparum* resistance to quinine and sulfadoxine-pyrimethamine.

**Jean Dubuisson, D.V.M., Ph.D. Chief of Laboratory at Centre National de la Recherche Scientifique" (CNRS)** Institute of Biology of Lille Institut Pasteur of Lille Lille, France

Jean Dubuisson will study the hepatitis C virus (HCV), a major cause of chronic liver disease worldwide. Basic knowledge of the HCV life cycle is needed to better combat the deadly pathogen. Dubuisson is analyzing this life cycle during multiple stages of HCV development, which may speed the development of improved antiviral drugs targeting HCV entry.

\* **B. Brett Finlay, Ph.D. Peter Wall Distinguished Professor** University of British Columbia Vancouver, Canada

B. Brett Finlay is studying the pathogenic strains of *E. coli* bacteria, which account for significant illness and death worldwide. He will investigate the specific mechanisms by which *E. coli* attaches to and interacts with host cells. Specifically, Finlay hopes to determine which *E. coli* genes are associated with pathogenicity, how *E. coli* interacts with host cells at the molecular level, and how *E. coli* disease mechanisms relate to animal colonization, shedding, and disease.

\* **Simon James Foote, M.B.B.S., Ph.D. Director** The Menzies Research Institute **Research Professor** The Walter and Eliza Hall Institute of Medical Research Hobart, Australia (Menzies) Melbourne, Australia (WEHI)

Simon Foote is attempting to understand how the host defends itself against malaria resistance by infecting genetically similar mice carrying rare mutations with malaria and studying the mutations that allow animals to survive infection. This research should help scientists gain insight into host response to malaria, as well as develop new, more effective anti-malarial therapies.

**Andrea Vanesa Gamarnik, Ph.D. Head of Laboratory** Fundación Instituto Leloir Buenos Aires, Argentina

Andrea Gamarnik will study the molecular mechanisms of dengue virus replication. It is estimated that more than 50 million human dengue virus infections occur annually in the tropical and subtropical regions of the world. Currently, neither vaccines nor antiviral drugs exist to control dengue infections. Her work will facilitate identification of novel antiviral strategies against dengue virus.

**Rajesh S. Gokhale, Ph.D. Staff Scientist** National Institute of Immunology New Delhi, India

Rajesh S. Gokhale will investigate how molecular repertoire in nature is generated from a limited number of genes. His study of "enzymatic crosstalk" in *M. tuberculosis* will provide insight into mechanisms employed by pathogens to generate metabolite diversity.

**\* H. Ulrich Göringer, Ph.D. Professor of Microbiology and Genetics** Darmstadt Technical University Darmstadt, Germany

Hans Goringe is working to develop tools that will be useful in identifying new drugs to combat trypanosome infections, caused by parasitic flagellate protozoa and widespread in the developing world. He will focus on drugs capable of crossing the blood-brain barrier.

**Emanuel Hanski , Ph.D. Professor of Clinical Microbiology** Institute of Microbiology Hebrew University, Faculty of Medicine Jerusalem, Israel

Emanuel Hanski will study invasive strains of group A streptococcus, bacteria that causes necrotizing fasciitis, also known as the flesh-eating disease. He will focus on the identification of factors related to bacterial virulence and their mode of regulation. Identification of these factors and learning how virulence is regulated may lead to better prevention and treatment of this life-threatening disease in humans.

\* **William Ross Heath, Ph.D. Chief of Laboratory** The Walter and Eliza Hall Institute of Medical Research Melbourne, Australia

William Heath will investigate the effects of the interaction between malarial parasites and dendritic cells, which initiate immunity, on the disease's ability to overcome the efforts of a competent immune system. Heath will study which specific types of dendritic cells capture malaria and how these important immune cells are affected by a full-fledged infection by *Plasmodium*. His research could lay the groundwork for development of new and more effective treatments for human malarial infections.

**Anja Tatiana Ramstedt Jensen, Ph.D. Associate Professor** Institute of Medical Microbiology and Immunology Faculty of Health Sciences University of Copenhagen Copenhagen, Denmark

Anja T.R. Jensen will study molecular differences between malaria parasites causing severe and non-severe malaria in children. Antibody reactivity to the identified molecules will be analyzed in individuals showing different malaria symptoms and living in malaria endemic areas. Her work should help identify antigens for a malaria vaccine.

**Sumalee Kamchonwongpaisan, Ph.D. Researcher** National Center for Genetic Engineering and Biotechnology National Science and Technology Development Agency Thailand Science Park Pathumthani, Thailand

Sumalee Kamchonwongpaisan works on potential molecular targets of antimalarial drugs, with focus on derivatives of artemisinin, one of the most effective antimalarial drugs, and on antifolate drugs that interfere with synthesis of DNA and other essential components of the malaria parasite. Her study will lead to a better understanding of the modes of action of antimalarials, and hopefully to the development of effective new drugs.

**Elena A. Levashina, Ph.D. Researcher** Institut de Biologie Moleculaire et Cellulaire **Laureate** Inserm Avenir program Strasbourg, France

Elena A. Levashina will study the role of the insect immune system in the survival of malaria parasites in the *Anopheles* mosquito, the insect vector that transmits malaria to humans. Her work has implications for development of novel vector control strategies.

**Yuesheng Li, M.D., Ph.D. Chief of Laboratory** Hunan Institute of Parasitic Diseases Yueyang, China

Yuesheng Li's research consists of two linked projects designed to improve understanding of the immunobiology of infection and the pathology of schistosomiasis, a parasitic disease that is widespread in rural areas of Africa, Asia, and Latin America. One component will focus on susceptibility for infection. The other will investigate possible genetic control of susceptibility to advanced disease.

**\* Susana Lopez, Ph.D. Professor of Genetics and Molecular Biology**  
Institute of Biotechnology National Autonomous University of Mexico  
Cuernavaca, Mexico

Susana Lopez will study several aspects of rotavirus-host cell interaction, including the virus's mechanism of entry into cells, transcription and replication of the viral genome, and the mechanism the virus uses to take over the cell's translation machinery. Rotaviruses are the most important cause of severe diarrhea in young children worldwide.

**\* Hugo D. Lujan, Ph.D. Adjunct Professor** Department of Biological Chemistry School of Medicine National University of Córdoba **Scientist**  
Mercedes and Martín Ferreyra Institute for Medical Research, CONICET  
Córdoba, Argentina

Hugo D. Lujan studies *Giardia*, a parasitic protozoa that is a major source of water-borne diarrheal disease. His goal is to better understand the basic molecular mechanisms involved in intracellular protein trafficking and antigenic variation in *Giardia*, which enables the parasite to evade its host's immune responses.

**Vilma Regina Martins Researcher** Ludwig Institute for Cancer Research  
Sao Paulo, Brazil

Vilma Martins is studying the physiological mechanisms underlying cellular prion proteins' loss of function and their roles in prion disease. Prions are microscopic protein particles that are thought to cause certain neurodegenerative diseases, such as so-called mad cow disease. She will work with a group to establish systematic human prion disease screening in Brazil.

**\* Geoff McFadden Professor** School of Botany University of Melbourne  
Melbourne, Australia

Geoff McFadden's work will focus on a tiny, vital organelle within the malaria parasite called an apicoplast. His goal is to understand how drugs that disrupt the apicoplast work and how the apicoplast is powered. The

information gained could assist in malaria drug development.

**Grant McFadden Scientist** Robarts Research Institute **Professor** University of Western Ontario London, Canada

Grant McFadden will investigate the cellular components of two anti-viral pathways that his research team uncovered during earlier studies of poxvirus infection in mammalian cells. He hopes the studies will better define the molecular mechanisms that control the host-virus species barrier and provide insights into host pathways that viruses must circumvent when invading a new host species.

\* **Robert Menard Chief of Laboratory** Institut Pasteur Paris, France

Robert Menard studies *Plasmodium*, the genus of parasites that cause malaria. He plans to identify and characterize the proteins produced by *Plasmodium* in two of its early stages, before it infects red blood cells and causes symptoms of malaria. What he learns may be useful in developing protection strategies against the early stages of malaria infection.

\* **Shulamit Michaeli Professor** Faculty of Life Sciences Bar-Ilan University Ramat-Gan, Israel

Shulamit Michaeli will examine the regulation of gene expression at the RNA level in parasitic trypanosomes. These organisms are an excellent model for studying RNA processing mechanisms because they regulate their genes mainly at the post-transcriptional level and harbor unique mechanisms such as trans-splicing and editing. Better understanding of the complex RNA world of these parasites, which cause diseases such as Chagas and sleeping sickness, may lead to development of RNA-based therapies.

\* **Valerie Mizrahi Professor** School of Pathology University of the Witwatersrand, Johannesburg **Alternate-Director** DST-NRF Centre of Excellence for Biomedical TB Research Johannesburg, South Africa

Valerie Mizrahi plans to study the mechanisms of DNA metabolism, culturability, and resuscitation in *Mycobacteria tuberculosis*, the organism that causes human tuberculosis. Development of more effective tools for TB control requires understanding the mechanisms underlying TB's remarkable ability to adapt to adverse conditions and persist in a dormant state from which it can reactivate to cause disease.

**Maria Manuel Mota Group Leader** Instituto de Medicina Molecular **Faculty of Medicine** University of Lisbon Lisbon, Portugal

Maria Mota hopes to determine the host molecules and mechanisms required for development of the malaria parasite *Plasmodium* inside the liver cells of its host. She plans to apply a systematic RNA interference (RNAi) screen to determine which molecules are required for successful parasite development.

**\* Laszlo Nagy Associate Professor** Department of Biochemistry and Molecular Biology University of Debrecen Medical and Health Sciences Center Debrecen, Hungary

Laszlo Nagy will use pharmacological and genetic approaches to delineate the pathways regulated by PPAR $\gamma$ , a transcription factor that plays a key lipid-handling role in macrophages, immune-system cells that control inflammation. He plans to use targeted elimination of PPAR $\gamma$  from mouse macrophages to determine its effect on infectious disease models.

**Miguel Navarro Chief of Laboratory** Instituto de Parasitologia y Biomedicina Lopez-Neyra Consejo Superior de Investigaciones Cientificas Granada, Spain

Miguel Navarro will examine the way parasites like *Trypanosoma brucei*, which causes African sleeping sickness, elude the host's immune response by changing their protein coatings. His research will use molecular and cell biology tools including nuclear architectural positional analysis, proteomics, and functional complementation of promoter activity.

**\* Sergei A. Nedospasov Professor and Head** Laboratory of Molecular Immunology Engelhardt Institute of Molecular Biology Russian Academy of Sciences and A.N. Belozersky Institute of Physico-Chemical Biology Moscow State University Moscow, Russia

Sergei Nedospasov plans to use a mouse model to study the effects of a continuous blockade of TNF (tumor necrosis factor), a key factor in innate immunity. Similar blockades occur in arthritis. He hopes to define the parameters of the weakening of the host's defense, which could be useful in developing more effective therapeutic strategies.

**\* Rafael Radi Professor of Biochemistry** Facultad de Medicina, Universidad de la República Montevideo, Uruguay

Rafael Radi will test the hypothesis that during mammalian infection with *Trypanosoma cruzi*, the parasite that causes Chagas disease, the interplay between the metabolism of the amino acid L-arginine and

oxidation-reduction processes of both the parasite and host target cells determine cell survival or death. He will test the hypothesis using biochemical, cellular, and *in vivo* model systems. The finding may permit development of novel and effective infection control strategies.

**Isabel Roditi, D.Habil, Ph.D. Director** University of Bern Bern, Switzerland

Isabel Roditi wants to learn more about surface proteins that govern survival and transmission of *Trypanosoma brucei*, the parasite that causes sleeping sickness, by its insect host, the tsetse fly. Using a fully transmissible strain of *T. brucei* will enable her to monitor the parasite throughout its life cycle in the fly. The long-range goal of such studies is to find ways to interrupt transmission of the disease.

\* **Philippe J. Sansonetti Professor and Head** Unité de Pathogénie Microbienne Moléculaire Institut Pasteur **Director** Inserm Unit 389 Paris, France

Philippe Sansonetti studies *Shigella*, Gram-negative bacteria that cause dysentery. His goal is to decipher the molecular and cellular bases of *Shigella*'s rupture, invasion, and inflammatory destruction of the intestinal lining. He also plans to analyse the mechanisms of immunity against *Shigella*, hoping to use his findings to develop vaccine candidates.

\* **D. Louis Schofield Chief** Laboratory of Malaria Immunology The Walter and Eliza Hall Institute of Medical Research Melbourne, Australia

Louis Schofield will investigate the role of innate immunity and the parasite toxin in susceptibility and resistance to severe malaria. He hopes that determining the role of the toxin and innate responses in disease and the role of anti-toxin antibodies and counter-regulatory mechanisms in clinical immunity to malaria will provide a rational basis for the development of interventions that prevent malaria fatalities.

\* **Dominique Soldati-Favre Associate Professor** Department of Microbiology and Molecular Medicine University of Geneva Geneva, Switzerland

Dominique Soldati-Favre wants to identify and characterize the proteases that enable a family of parasitic protozoa called *Apicomplexa* to attach themselves to and actively invade host cells. Proteases are enzymes that break down proteins into peptides and amino acids. The parasite *Toxoplasma gondii*, which causes toxoplasmosis, will be used to do functional, biochemical and

structural analyses of candidate proteases. Validation of the proteases as potential drug targets will be conducted in *Plasmodium falciparum*, the malaria parasite.

**\* Natalie C.J. Strynadka Associate Professor** Department of Biochemistry and Molecular Biology University of British Columbia Vancouver, Canada

Natalie Strynadka will use X-ray crystallography and other biophysical analysis tools to study the structure and function of proteins that play key roles in antibiotic resistance and bacterial pathogenicity. The goal is design of novel antibiotics.

**Santuza M.R. Teixeira Associate Professor** Department of Biochemistry and Immunology Federal University of Minas Gerais Minas Gerais, Brazil

Santuza Teixeira studies genomic variability in *Trypanosoma cruzi*, the parasite that causes Chagas disease. She plans to analyze DNA sequences of several gene families that encode antigens or surface molecules of *T. cruzi*. She also will look at differences in gene expression and in the activity of DNA repair machinery in the parasite.

**Gisou F. van der Goot Associate Professor** University of Geneva Geneva, Switzerland

Gisou van der Goot wants to understand the mechanisms by which anthrax toxin manages to delay the onset of normal immune responses. She will use a variety of cell biological, morphological and biochemical techniques, including an RNAi screen, to analyze the molecular mechanisms that govern the delivery and presentation of the toxin and its enzymes in the cell.

\* Previous HHMI international research scholars