#### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Jorge Elias Kalil Filho

eRA COMMONS USER NAME (credential, e.g., agency login): Jorge Kalil

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral

training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Federal University Rio Grande do Sul (UFRGS), Brazil	M.D.	1977	Medicine
University of Paris VII, Paris, France	MSc	1980	Immunogenetics/ Immunopathology
University of Paris VII, Paris, France	DSc	1982	Human Biology
University of São Paulo (USP), São Paulo, Brazil	Professorship	1991	Immunology
Clinical Medicine School of USP (FMUSP), São Paulo, Brazil	Full Professor	1998	Medicine

#### A. Personal Statement

Jorge Kalil, MD, PhD, FRCP, Dr h.c., is Professor of Medicine and Clinical Immunology and Allergy and Director of the Laboratory of Immunology at the Heart Institute, School of Medicine, University of São Paulo. After studying Medicine and doing his residency in Clinical Medicine in Brazil, he went to Paris, where he worked for 5 years (1978-1983) in Jean Dausset's lab (Nobel prize for HLA, 1980) and specialized in Immunology and Immunogenetics. In France, he pioneered in obtaining monoclonal antibodies that were used to dissect the HLA system, both genetics and function. As a result, Kalil pursued in the role of HLA molecules presenting antigens to the immune system and how T-cells recognize them, triggering rejection to a transplanted organ, protection against microbes or autoimmune disease. Pioneering the use of molecular biology tools in Immunology in Brazil, Kalil identified local HLA polymorphisms and described interesting association to diseases. The study of Rheumatic Fever was of particular importance. Still a relevant problem in developing countries, RF is a paradigm of an autoimmune disease triggered by an infection. He described how cross-reactivity is driven by the molecular mimicry; how the disease starts in the whole heart and then is restricted to valves and how the tissue is damaged. On the other hand, by mapping the immune response to M Streptococcal protein, he was able to identify protective epitopes that eventually were used to depict a synthetic vaccine with high protection value. After all pre clinicals, this study will be starting phase 1 clinical trials in humans shortly. By using similar approaches, Kalil described the outcome of Chagas disease. With the cumulated experience on T-cell recognition, he proposed a new HIV vaccine, which is currently being tested in primates. As director of Butantan Institute he supported a project to develop a Dengue vaccine which has become a real possible solution to this disease, bringing Butantan's science and industrial fields to a world-class level.

All these studies enable Kalil to contribute to this study in the areas of antigen presentation and recognition, humoral response, T-cell response, effectivity, regulatory and recovery.

#### B. Positions and Honors

### Positions and Employment

1985- present	Director, Laboratory of Immunology Heart Institute, HC-FMUSP, São Paulo, BR
1005	Discrete History work bility Labourton LIC FMLICE Co. Double DD

1985- present Director, Histocompatibility Laboratory HC- FMUSP, São Paulo, BR

1998- present Professor and head of Clinical Immunology and Allergy, Dept of Clinical Medicine, FMUSP, São Paulo, BR

2001- present Chairman of iii – Institute for Investigation in Immunology - Millenium Institute, World bank/CNPq, BR

2014- present Adjunct Professor at George Washington University, DC, USA

### <u>Present Functions – Committees and Societies</u>

1996- present	Member of the International Council of Histocompatibility and Immunogenetics
2007- present	Member, Board of Directors of InCor – HC-FMUSP, Sao Paulo, BR
2007- present	Member of TWAS - Academy of Sciences for Developing World
2010- present	Member of Executive Committee, IUIS - International Union of Immunological Societies ()
2012- present	Co-Chair FOCIS Center of Excellence, São Paulo
2014- present	Member of SAB of ICGEB - International Center for Genetic Engineering and Biotechnology, United Nations
2015- present	FOCIS Board of Directors in the area of International Development

### <u>Past Functions – Positions and Societies</u>

1977-1978	Residency Clinical Medicine, Hospital de Clínicas Porto Alegre, BR
1978-1983	Research -Prof Jean Dausset's Laboratory (Nobel Prize Laureate 1980), Paris, France
1980-1981	Residency Immuno-Hematology, Saint Louis Hospital, Paris, France
1981-1982	Head of Laboratory of Hybridomas. Prof Jean Dausset's Lab, Paris, France
1982-1983	Vice-President, Latin American Immunology Society and Clinical Investigation Society
1983-1985	Associate Professor, Medical School Universidade Federal do Rio Grande do Sul (UFRGS)
1985-1988	Assistant and Associate Professor of Surgery, School of Medicine, USP
1986-1998	Member of various Steering National Committees. CNPq, FINEP, PADCT, PRONEX, CAPES
1987-1988	President, Brazilian Society for Transplantation
1991-1992	Visiting assistant Professor, Stanford Medical School, Dep of Pathology, Stanford, USA
1991-1992	Acting director Tissue Typing Lab, Stanford Blood Bank, Stanford, USA
1995-1996	Advisor of the Minister of Health of Brazil
1996-1997	President, Brazilian Society for Immunology
1997-2001	International Scholar Howard Hughes Medical Institute
2003-2007	Deputy Clinical Director of HC-FMUSP, São Paulo, BR
2006-2007	President, Board of Directors of InCor – HC-FMUSP, São Paulo, BR
2006-2007	President, Board of Trustees – Zerbini Foundation, São Paulo, BR
2006-2008	Chairman Department of Clinical Medicine, HC-FMUSP, São Paulo, BR
2011-2017	Director, CEO, Butantan Institute, São Paulo
2013-2016	President, IUIS

### **Honors and Distinctions**

11011	ors and Distinctions
1995	Brazilian Academy of Sciences, Associate Member
1997	Honorary Professor, Universidade Maimónides, Buenos Aires, Argentina
1997	Brazilian Academy of Sciences, Full Member
1998	Honored by the Brazilian President with the Medal of National Scientific Merit
1999	ASHI International Scholar Award, 25 <sup>th</sup> Anual Meeting, New Orleans, USA
2004	Academy of Science for Developing Countries, TWAS, World Prize in Biology
2011	Fundação Conrado Wessel Award in Science
2011	Physician of the Year Hospitalar, São Paulo, BR
2014	Medal of Merit - Brazilian Chamber of Deputies
2012	Chevalier Ordre Nationale du Mérite France.
2013	Doctor Honoris Causa University Pierre et Marie Curie (Sorbonne Universités), Paris, France
2015	Doctor Honoris Causa Universidade Federal do Rio Grande do Sul - UFRGS, BR
2015	Honorary Member of the ASTMH
2015	Fellow of the Royal College of Physicians London, UK
Winr	ner of several National and International Scientific awards

#### C. Contribution to Science

Kalil has over 300 PubMed appearances and over 500 entries at ISI. The number of citations are around 8.000 and the h-index is 45.

In 35 years of career dedicated to science, Kalil contributed on many areas of immunology and specially immunogenetics. His main focus on research is related to MHC molecules, their genetics, expression and, mainly, function. As a consequence Kalil also studied antigen presentation and Tcell recognition, allorecognition, auto recognition, autoimmunity and protective immune responses. Several models were used. Some are summarized.

MHC and other genes. Genetics, expression, function. Kalil pioneered In France in the production of monoclonal
antibodies and developed many of them directed to specific class 1 and class 2 molecules. They were used to help
solving the strutuctural genetics and function of these molecules, Which were major scientific topics atthat time.
Returning to Brazil he introduced in the country molecular tools for identification of polymorphic HLA molecules.

# Monoclonal-antibodies as a tool for phylogenetic studies of major histocompatibility antigens and beta-2-microglobulin

By: Teillaud, JL; Crevat, D; Chardon, P; Kalil, J; Goujetzalc, C; Mahouy, G; Vaiman, M; Fellous, M; Pious, D. IMMUNOGENETICS. Vol:15; 377-384,1982

### HLA class I genes integrated into murine cells are inducible by interferon

By: Rosa, F; Lebouteiller, PP; Abadie, A; Mishal, Z; Lemonnier, FA; Bourrel, D; Lamotte, M; Kalil, J; Jordan, B; Fellous, M. EUROPEAN JOURNAL OF IMMUNOLOGY. Vol: 13,495-499 ,1983

# <u>Influence of HLA Class I-specific and Class II-specific monoclonal-antibodies on DR-restricted lymphoproliferative responses .1. Unseparated populations of effector-cells</u>

By:Sterkers, G; Henin, Y; Kalil, J; et al. - JOURNAL OF IMMUNOLOGY. Vol:131;2735-2740,1983

### Extensive polymorphism of a (CA)(N) microsatellite located in the HLA-DQA1/DQB1 class-II region

By: Macaubas, C; Hallmayer, J; Kalil, J; et al. - HUMAN IMMUNOLOGY. Vol:42;209-220,1995

Transplantation Immunology. Allorecognition. Secondary antigens tolerance. Transplantation and Disease. In this
area contributed to identification of new actors in the humoral immune response but also in allorecognition. He
also made contributions for the understanding of associtation of HLA and disease and their role in the induction
of T cell autoimmune responses.

# Identification of patients at high risk of graft loss by pre- and posttransplant monitoring of anti-HLA class I IgG antibodies by enzyme-linked immunosorbent assay

By: Monteiro, F; Buelow, R; Mineiro, C; Rodrigues, H; Kalil, J. - TRANSPLANTATION. Vol:63;542-546 ,FEB 27 1997

### Genetic heterogeneity in susceptibility to autoimmune hepatitis types 1 and 2

By: Bittencourt, PL; Goldberg, AC; Cancado, ELR; Porta, G; Carrilho, FJ; Farias, AQ; Palacios, SA; Chiarella, JM; Abrantes-Lemos, CP; Baggio, VL; Laudanna, AA; Kalil, J.AMERICAN JOURNAL OF GASTROENTEROLOGY. Vol:94;1906-1913, JUL 1999

## Cytotoxic T lymphocyte antigen-4 gene polymorphisms do not confer susceptibility to autoimmune hepatitis types 1 and 2 in Brazil

By: Bittencourt, PL; Palacios, SA; Cancado, ELR; Porta, G; Carrilho, FJ; Laudanna, AA; Kalil, J; Goldberg, AC. AMERICAN JOURNAL OF GASTROENTEROLOGY. Vol:98; 1616-1620, JUL 2003

### Analysis of major histocompatibility complex and CTLA-4 alleles in Brazilian patients with primary biliary cirrhosis

By: Bittencourt, PL; Palacios, SA; Farias, AQ; Abrantes-Lemos, CP; Cancado, ELR; Carrilho, FJ; Laudanna, AA; Kalil, J; Goldberg, AC

JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY. Vol. 18; 1061-1066, SEP 2003

3. Immunopathogenesis' of Rheumatic Fever. Genes of susceptibility infiltrating lymphocytes, crossreactive epitopes, description of the pathogenesis and natural history of disease. In this area he showed how an infectious agent can break tolerance and induce autoimmune disease. For the first time showed infiltrating T cell clones with cross recognition of a peptide from the infectious agent and a human structure.

# <u>Association of human-leukocyte class-II antigens with rheumatic-fever or rheumatic heart-disease in a Brazilian population</u>

By: Guilherme, L; Weidebach, W; Kiss, MH; Snitcowsky, R; Kalil, J.CIRCULATION. Vol:83;1995-1998, JUN 1991

## Human heart-infiltrating T-cell clones from rheumatic heart-disease patients recognize both streptococcal and cardiac proteins

By: Guilherme, L; Cunhaneto, E; Coelho, V; Snitcowsky, R; Pomerantzeff, PMA; Assis, RV; Pedra, F; Neumann, J; Goldberg, A; Patarroyo, ME; Pileggi, F; Kalil, J.CIRCULATION. Vol:92; 415-420, AUG 1 1995

## Rheumatic heart disease - Proinflammatory cytokines play a role in the progression and maintenance of valvular lesions

By: Guilherme, L; Cury, P; Demarchi, LMF; Coelho, V; Abel, L; Lopez, AP; Oshiro, SE; Aliotti, S; Cunha-Neto, E; Pomerantzeff, PMA; Tanaka, AC; Kalil, J. - AMERICAN JOURNAL OF PATHOLOGY. Vol:165;1583-1591,NOV 2004

### StreptInCor: a model of anti-Streptococcus pyogenes vaccine reviewed.

Guilherme L, Postol E, Ferreira FM, DeMarchi LM, Kalil. AutoImmun Highlights. 2013 Oct 4;4(3):81-5. doi: 10.1007/s13317-013-0053-8. eCollection 2013 Dec. Review

4. Immunopathogenesisof Disease. Chagas Disease. Description how a hidden or disappeared pararsite cause disease after 30 years. What are the keygenetic components that drive the de development of the disease. Why some have silent and others very aggressive clinical forms.

# <u>Autoimmunity in Chagas-disease cardiopathy - Biological relevance of a cardiac myosin-specific epitope cross-reactive to an immunodominanttrypanosoma-cruzi antigen</u>

By: Cunhaneto, E; Duranti, M; Gruber, A; Zingales, B; Demessias, I; Stolf, N; Bellotti, G; Patarroyo, ME; Pilleggi, F; Kalil, J. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. Vol. 92; 3541-3545,APR 11 1995

# Autoimmunity in Chagas' disease - Identification of cardiac myosin-B13 Trypanosomacruzi protein crossreactive T cell clones in heart lesions of a chronic Chagas' cardiomyopathy patient

By: Cunhaneto, E; Duranti, M; Gruber, A; Zingales, B; Demessias, I; Stolf, N; Bellotti, G; Patarroyo, ME; Pilleggi, F; Kalil, J. JOURNAL OF CLINICAL INVESTIGATION. Vol:98;1709-1712, OCT 15 1996

## <u>Chronic Chagas' disease cardiomyopathy patients display an increased IFN-gamma response to Trypanosomacruzi infection</u>

By: Abel, LCJ; Rizzo, LV; Ianni, B; Albuquerque, F; Bacal, F; Carrara, D; Bocchi, EA; Teixeira, HC; Mady, C; Kalil, J. JOURNAL OF AUTOIMMUNITY. Vol:17; 99-107, AUG 2001

# <u>Cardiac gene expression profiling provides evidence for cytokinopathy as a molecular mechanism in Chagas' disease cardiomyopathy</u>

By: Cunha-Neto, E; Dzao, VJ; Allen, PD; Stamatiou, D; Benvenutti, L; Higuchi, ML; Koyama, NS; Silva, JS; Kalil, J; Liew, CC. AMERICAN JOURNAL OF PATHOLOGY. Vol:167; 305-313, AUG 2005

5. Other infectious diseases. Immunopathogenesis and development of vaccines. Kalil contributed with many groups in the genetics, immunopathology, protective immunity and development of vaccines to infectious agents

### Genetic-control of the immune-response to a synthetic vaccine against plasmodium-falciparum

By: Patarroyo, ME; Vinasco, J; Amador, R; Espejo, F; Silva, Y; Moreno, A; Rojas, M; Mora, Al; Salcedo, M; Valero, V; Goldberg, Ak; Kalil, J. - PARASITE IMMUNOLOGY. Vol: 13; 509-516, SEP 1991

Genetic localization of a locus controlling the intensity of infection by Schistosomamansoni on chromosome 5q31-q33

By: Marquet, S; Abel, L; Hillaire, D; Dessein, H; Kalil, J; Feingold, J; Weissenbach, J; Dessein, AJ. NATURE GENETICS. Vol. 14; 181-184, OCT 1996

### Clinical Evaluation Strategies for a Live Attenuated Tetravalent Dengue Vaccine

Ricardo Palacios; Beatriz Thome, Gabriella Mondini; Patricia E Braga; Jorge Kalil Vaccine In press.

# A Vaccine Encoding Conserved Promiscuous HIV CD4 Epitopes Induces Broad T Cell Responses in Mice Transgenic to Multiple Common HLA Class II Molecules

Susan Pereira Ribeiro , Daniela Santoro Rosa , Simone Gonçalves Fonseca, Eliane Conti Mairena, EdilbertoPostól, Sergio Costa Oliveira, Luiza Guilherme, Jorge Kalil, Edecio Cunha-Neto ; Pub: June 11, 2010; DOI: 10.1371/journal.pone.0011072

### D. Research Support

Receiving many grants over the past 35 years, here are the National Institute of Science and Technology grants. Created first as a Millennium Institute and later became the National Institute of Science and Technology (INCT). These loans refer to the virtual Institute created in Brazil with 30 PI in 8 States of the Federation. In 2009, when the balance of publications was made, iii was responsible for 25% of publications on immunology in Brazil. This Institute aims to raise Immunology to a worldclass level.

### Completed:

Project: PADCT iii- MILÊNIO

ConvênioCNPq 62.0062/01-0 duration 2001 - 2005 approved value R\$ 4.330.000,00 used R\$ 2.000.000,00 on importsdollar rate R\$ 2,34 equivalent to USD 854.000,00

### Project: Project Instituto de Investigaçãoem Imunologia (iii)

Process INCT/CNPq 420166/2005-0 duration 2006 - 2009 approved value R\$ 2.769.000,00 Dollar rate at start 2006 R\$ 2,34 Final dollar rate 2009 R\$ 2,38

### **Ongoing:**

Project: Instituto de Investigação em Imunologia (iii)

Project funds INCT duration 01/03/2009 - 28/02/2016 Fund FAPESP R\$ 1.680.354,60 USD 1.267.235,00 Dollar rate at 01/03/2009 R\$ 2,38 Fund CNPq R\$ 3.772.307,11

Project: ResearchSupport USP/NucleusInstituto de Investigação em Imunologia (iii)

Project funds USP duration 01/03/2009 - 28/02/2019 Fund FAPESP R\$ 2.000.000,00 Dollar rate 28/02/2015 R\$ 2,88