SPC001-**The Personal and Scientific Lifeline of Álvaro José Romanha, a Science Craftsman**

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Álvaro José Romanha was born in Colatina, ES (Brazil), on January 31st, 1951. After attending the Elementary School of Nossa Senhora da Imaculada Conceição, he started his secondary education at Colégio Estadual Conde de Linhares. In 1966, he joined the secondary school at Universidade Federal de Viçosa (COLUNI) to pursue a technical degree in agronomy. Two years later, he moved to Belo Horizonte to finish his secondary education at Colégio Arnaldo, having concluded at Colégio Champagnat. Álvaro started his higher education attending the School of Pharmacy and Biochemistry at Universidade Federal de Minas Gerais - UFMG (1969-1972), obtaining the specialist degree in Biochemistry and Immunology (1972-1976) and PhD in 1982, presenting a thesis entitled "Isoenzymatic Heterogeneity in *Trypanosoma cruzi*" under the guidance of Professor Aníbal Antônio Silva Pereira. On the same year, Álvaro started his two-year postdoctoral training under the supervision of Professor Winston E. Gutteridge at the Wellcome Research Laboratories (UK). Acting as Associated Professor of Biochemistry and Cell Biology at Pontifícia Universidade Católica de Minas Gerais (PUC) between 1976-1979, Álvaro was an Invited Professor at the Postgraduate Programs in Parasitology and in Biochemistry and Immunology at UFMG (1985-1995). From 2011 to 2014, he was a Senior Visiting Professor at the Postgraduate Program in Biotechnology and Biosciences at Universidade Federal de Santa Catarina (UFSC) in Florianópolis, SC. Still as an undergraduate student, Álvaro was hired at the René Rachou Research Center (CPqRR/Fiocruz) in 1971, where he worked up to 2010 in distinct scientific and administrative positions. During his career, Álvaro was President of the Brazilian Society of Protozoology - SBPz (1990-1991), having organized several annual meetings of this society; Coordinator of the FAPEMIG Advisory Committee on Biological Sciences and Biotechnology (1998-2000); Coordinator of the CPqRR Human Research Ethics Committee (2001-2005); Member of the CNPq Committee on Morphology, Microbiology, Immunology and Parasitology (2002-2005); Member of the Advisory Committee at the Mine Network of Biotechnology and Essays Program at the Science and Technology Secretariat of Minas Gerais State (2004-2006); Member of the Hemominas Council (2006-2008); Member of the Scientific Advisory Board of Biological Sciences at the Foundation for Research Support for the State of Amazonia (2006-2009) and level 1A CNPq Research Fellow. In 1984 he established the Laboratory of Biochemistry and Molecular Biology to work on the biochemistry of *T. cruzi* using isoenzymes, a technique he has introduced at that time. During his PhD, Alvaro has described four distinct zymodemes for *T. cruzi* (ZA, ZB, ZC and ZD) that were associated to epidemiological aspects of Chagas' disease. These studies made his laboratory a reference for typing different species of pathogenic protozoa. The repercussion of his studies has led to outnumbered national and international collaborations. During the 90's, due to the consolidation of the laboratory and the expansion of research lines, such as prospection of new molecules with anti-*T. cruzi* activity, molecular characterization of *T. cruzi* and *T. rangeli* strains, molecular mechanisms of resistance of *T. cruzi* to drugs, molecular studies of the parasite-vector and host-parasite interaction and proteomic analysis of *T. cruzi*, the newly created Laboratory of Cellular and Molecular Parasitology under Álvaro's supervision has incorporated the former laboratory. During these years, Álvaro has especially dedicated is attention to the important studies of sterol biosynthesis pathway inhibitors and the cooperative effect of the host immune system and benznidazole treatment in partnership with Judith Molina, Julio Urbina, Ricardo Gazzinelli and Zigman Brener, one of his most prominent scientific mentors and friend. In 2011, Álvaro had a pivotal participation on the establishment of the Research Network on Natural Products Against Neglected Diseases (ResNet NPND) during the Brazil-Germany year of Science, Technology and Innovation, held at the University of Münster, Germany. Along Professors Thomas J. Schmidt (Germany) and Reto Brun (Switzerland), Alvaro was appointed as one of the international coordinators of the ResNet NPND, congregating 23 researchers representing five countries. Within the various research lines coordinated by Álvaro at the CPqRR, it is noteworthy to mention the establishment of the FIOCRUZ-PDITS technological platforms in 2005. The first, dedicated to proteomics, introduced bi-dimensional electrophoresis that enabled the development of several research projects with innovative results. The second was a platform of Pre-Clinical Trials of anti-*Trypanosoma cruzi* (PlaBio Tc) Drug Screening, dedicated to evaluate the *in vitro* activity and *in vivo* cytotoxicity of natural compounds/extracts against amastigote and trypomastigote forms of *T. cruzi* heterologously expressing the enzyme Beta-galactosidase. Throughout his career as scientist, Álvaro has published 175 papers resulting in over 4,300 citations on the Web of Science. Furthermore, he has supervised 18 PhD thesis, 29 Master's dissertations and 15 undergraduate students. Always disseminating "good science", as he says, Álvaro is responsible for an entire generation of outstanding scientists in the area of cellular and molecular parasitology. At CPqRR, one of his former PhD students, Dr. Silvane Murta, is currently a researcher responsible for his important legacy at that institution, maintaining and expanding several research lines implemented by Álvaro, including functional genomics of *T. cruzi* and *Leishmania* spp. Married to Tarcília Frechiani (Dedé), Álvaro has three kids: Camilo, Bernardo and Mateus and a grandchild Eduardo.

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CO001 - **EVOLUTION OF THE NUCLEUS: LAMINA AND THE NUCLEAR PORE COMPLEX IN TRYPANOSOMES**

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The nuclear envelope (NE) is the defining structure of the eukaryotic cell. Prominent structures of the NE are the nuclear pore complexes (NPC) and the filamentous lamina underlying the nuclear membranes. Until recently, these structures were only characterised in model organisms that belong to a relatively narrow eukaryotic group. Here we provide more insight into the evolution of the NE from pan-eukaryotic homology searches and phylogenetic analyses of the individual NE components and recent experimental data on the composition of the NE from the diverged eukaryotic parasiteTrypanosoma brucei. We found that an NPC very similar to that in humans was already present in the last eukaryotic common ancestor (LECA). Although lamins were assumed a derived feature of animal nucleus, we found lamin homologs with shared domain architecture and sequence motifs in diverse protists. The additional NE components facilitating connections between the nucleoskeleton and the NPC, cytoskeleton and chromatin were likely also integrated into the LECA lamina. Our data further suggest that different nucleoskeletal structures that support the nuclear membranes, organise chromatin and connect nucleus to the cytoskeleton operate at the nuclear periphery of trypanosomes. These findings contribute to the understanding of the origin and evolution of the eukaryotic cell. **Supported by**Medical Research Council, Wellcome Trust
Keywords: Trypanosoma; nuclear transport; chomatin

CO002 - **IDENTIFYING AND VALIDATING NEW TARGETS FOR NEGLECTED TROPICAL DISEASES**

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The protozoan kinetoplastid parasites Leishmania spp, Trypanosoma brucei and Trypanosoma cruzi are responsible for potentially fatal diseases that affect over 22 million people worldwide, with an estimated 450 million people at risk. Current therapies are expensive and not widely accessible. In addition, drug toxicity and emerging resistance are major concerns and there is a major need for new tractable drug targets. In this presentation we will present examples of both phenotypic and target based approaches towards this goal. In particular, we have identified the essential kinetoplastid sphingolipid synthase (SLS) as an attractive pharmaceutical target due to the divergence of function compared with the mammalian orthologue. Although retaining a high degree of similarity these enzymes show varying sensitivity to aureobasidin A, a known natural product derived inhibitor of fungal SLSs. In order to better understand this membrane bound enzyme and develop structure-activity relationships we have synthesised a library of analogues of the natural ceramide substrate and used these in biochemical studies of the enzyme. In a complementary approach we have developed screening assay to identify potential inhibitors against the Leishmania major enzyme. Several structural classes of potential lead compounds showing good selectivity for the protozoan enzyme have been identified and studies to explore and refine these initiated. **Supported by**MRC, The Royal Society London, CNPQ
Keywords: Leishmania ; drug targets; sphingolipid synthases

CO003 - **SPHINGOLIPID BIOSYNTHESIS IN THE APICOMPLEXAN PROTOZOA: DIVERGENT ENZYMES IN KEY HOST:PATHOGEN INTERACTIONS**

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Toxoplasma gondii is an obligate, intracellular eukaryotic apicomplexan protozoan parasite that can cause fetal damage and abortion in both animals and humans. Sphingolipids are essential and ubiquitous components of eukaryotic membranes that are both synthesized and scavenged by the Apicomplexa. However, we have demonstrated that the scavenging of sphingolipids is non-essential for the proliferation of Toxoplasma. Turning our attention to the parasite biosynthetic pathway we have characterised key enzymes that demonstrate divergence from their well conserved eukaryotic orthologues. For example, we have shown that the apicomplexan serine palmitoyltransferase, an enzyme catalysing the first and rate-limiting step in sphingolipid biosynthesis, is evolutionarily related to the prokaryotic serine palmitoyltransferase. The status of this enzyme and others in the biosynthetic pathway as potential drug targets will be discussed.
Keywords: Toxoplasma; host; sphingolipid

CC001 - **RNA-BINDING PROTEINS AND RNA GRANULES: A COMPLEX RESPONSE TO A SINGLE STRESS SIGNALING FOR *T.CRUZI* DIFFERENTIATION.**

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Gene expression regulation comprises several events involving transcriptional and post-transcriptional steps. RNA binding proteins (RBPs) are key regulators in all these events. They comprise a diverse family of proteins with a variety of RNA binding domains (RBD) involved in splicing, nuclear-cytoplasmic transport, translation and mRNA decay. The RBD interact and recognize RNA motifs based on sequence or structure. In addition to the RBD, many RBPs also display protein-protein domains subjected to post-translational modifications. There are different classes of RBPs based on the presence of specific domains. The association of RBPs with mRNAs is very dynamic responding to changes in the cell environment. Indeed, as a response to any cellular stress there occurs a reprogramming of the translated mRNAs as a consequence of the combinatorial set of RBPs associated to the mRNAs forming messenger ribonucleoprotein (mRNP) complexes. The stability, localization and functioning of a given mRNA depends on its associated proteins. Most of the RBPs characterized in protozoa arise from trypanosomatids. These organisms are a unique model to study post-transcriptional regulation processes, due to the low relevance of transcriptional control in gene expression regulation. The investigation of RBPs dynamics during *T. cruzi* metacyclogenesis, and in particular following a nutritional stress that precedes the differentiation of the parasites, shows a remarkable switch of the mRNAs bound to a given RBP or the mRNAs being translated. Proteomic analysis of mRNPs isolated from the parasite shows canonic RBPs displaying RRM, CCCH or Pumulio domains, as well as RNA granule proteins, translation factors and potential moonlighting metabolic proteins. The identification of the mRNA targets associated to specific RBPs indicates that they form post-transcriptional operons. The complexity and dynamics of the RNA-protein interactions suggests that RBPs are major carriers of post-transcriptional gene expression regulation in *T.cruzi*.
Keywords:T. cruzi; gene expresssion; metacyclogenesis