Projects to Swiss Bridge Foundation - 2018

PROJECT 1: LEUKEMIA AND SOLID TUMOR IN CHILDHOOD

SUB-PROJECT 1.A: PEDIATRIC LEUKEMIA: CONTRIBUTION OF MOLECULAR-CYTOGENETIC ANALYSIS TO TRANSLATIONAL EPIDEMIOLOGY.

RESPONSIBLE INVESTIGATOR: Maria S. Pombo-de-Oliveira, M.D, Ph.D.; Research Center, Instituto Nacional de Câncer, Rio de Janeiro, Brazil. E-mail: *mpombo@inca.gov.br* **(ORCID ID:0000-0002-1507-004X).**

COLLEAGUES: The Brazilian Collaborative Study Group of Childhood Leukemia. Colaborators Luciana Pizzatti Barboza Ph.D. (UFRJ) and Guilherme Kurtz M.D., Ph.D. (CPQ-INCA). Technologists: Eugênia Terra-Granado Ph.D., Gisele M.Vasconcelos Ph.D., Ingrid Koster.

POS-GRADUATION STUDENTS: Gisele Dallapicola Brisson, Alython AraujoChung Filho, Filipe dos Santos Vicente Bueno, Suellen V. Moura, Daniela P.M.Almeida, Luiza Codaço, Francianne Gomes Andrade.

OBJECTIVES: To test the association of genetic susceptibility conferred by gene variants (*TPMT, GSTT1, GSTM1, CYP3A4, CYP3A5, VDR, NR3C1, NUDT15C416, NT5C2, PRPS, PRDM)* with the bioavailability and pharmacokinetics of glucocorticoids and thiopurines during ALL treatment;To compare, according to constitutive gene profile, the event-free survival and relapse rates in children with ALL adjusted by predictive risk factors (age, WBC count at diagnosis, molecular-cytogenetic subtypes, MRD and initial response to glucocorticoids).

SUB-PROJECT 1.B: EXOME ANALYSIS OF WILMS TUMOR (WT).

RESPONSIBLE INVESTIGATOR: Hector Seuanez Abreu, M.D., Ph.D.; Laboratory of Genetic, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. e-mail: *hseuanez@inca.gov.br*.

COLLEAGUES: Carolina Furtado, Michael Sammeth, Leila Cardoso.

OBJECTIVES: Identification of exonic mutations associated with Wilms tumor. The characterization of the WT exome will be carried out for 23 patients who will be selected on the basis of their histopathology profiles and availability of paired blood samples. Exons will sequenced on the HiSeq 2500 (Illumina) platform in fast mode on 2 cycles of 100-base (2x100) reads using Illumina TruSeq Rapid SBS Kit-HS (200cycle) kit. Sequence data will be analyzed to determine: (1) coverage of exome regions (2) polymorphism calling by comparison to reference sequences, (3) identification of somatic mutations, (3) identification of relevant exons associated to WT.

PROJECT 2: SOLID TUMOR IN ADULTS

SUB-PROJECT 1.A: MOLECULAR MARKERS OF SECOND PRIMARY ESOPHAGEAL TUMORS IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMAS: MOLECULAR SIGNATURES FOR THE POTENTIAL USE IN EARLIER DIAGNOSIS AND THERAPEUTICS.

RESPONSIBLE INVESTIGATOR: Luis Felipe Ribeiro Pinto**,** Ph.D.**;** Head, Molecular Carcinogenesis Program, Instituto Nacional de Câncer (INCA). Praça da Cruz Vermelha 23, 20230-130 Rio de Janeiro, RJ. e-mail: *lfrpinto@inca.gov.br*.

COLLEAGUES: Sheila Coelho Soares Lima, Ph.D. (Researcher, PCM, INCA); Martim Bonamino, Ph.D. (Researcher, PCM, INCA); Nathalia Meireles da Costa, Ph.D. (Researcher, PCM, INCA); Simone Guaraldi, M.D., Ph.D. (endoscopy service, PCM, INCA); Maria Aparecida Ferreira, M.D. (endoscopy service, PCM, INCA); Pedro Nicolau, Ph.D. (Pos-Doc, PCM, INCA); Paulo Thiago Santos, Ph.D. (Pos-Doc, PCM, INCA); Isabela Gonzaga (MSc, PCM, INCA); Marina Nicolau; M.Sc. (PCM, INCA); Diego Oliveira, M.Sc. (PCM, INCA); Tatiana Simão, Ph.D. (Reader, UERJ); Luiz Eurico Nasciutti, Ph.D. (Professor, UFRJ); Antonio, Palumbo, Ph.D. (Pos-Doc, UFRJ).

OBJECTIVES: Therefore, the objectives for the next three years are: 1)The evaluation of the role of the genes previously identified in methylome analysis using in vitro models (cell lineages). The list of the genes to be studied includes FBXL7, SPRR3, FSCN1, and others; 2) The validation of these genes in a prospective screen for esophageal second primary tumors in head and neck cancer patients after lugol chromoendoscopy, including liquid biopsy analysis of the methylated altered genes; 3) Pre-clinical analysis to investigate the effects of the inhibition of PI3K pathway in ESCC, particularly inhibition of the FOXM1 mediated new mechanism we identified to be activated in esophageal tumors (Nicolau et al., Oncotarget 2018); 4) Since the 8th edition of TNM includes the analysis of HPV in oropharyngeal tumors, we are going to evaluate the impact of HPV in a cohort of 400 oropharyngeal cancer patients attended at INCA; 5) To better characterize the main altered signaling pathways in laryngeal tumors, we are going to carry out a RNA-seq of laryngeal squamous cell carcinoma samples that have already been through methylome analysis. This is important because TCGA and other databanks analyze head and neck cancer patients altogether, without adjacent non-tumor tissue, and our analysis have identified wide differences among these tumors; 6) To characterize the immunological profile of laryngeal and esophageal squamous cell carcinomas through RNA-seq.

BUDGET:

	1st year	2nd year	3rd year	Total per budget category
Equipment	none	none	none	none
Consumables	100,000	100,000	100,000	300,000
Travel & Training	none	none	none	none
Literature	none	none	none	none
Sub total	100,000	100,000	100,000	

TOTAL CONTRIBUTION REQUESTED TO SWISS BRIDGE **300,000 CHF**