All Time GABBA - Associação de Alumni do Programa Doutoral GABBA

Maria de Sousa Summer Research Program

4ª Edição

O que é?

Estágios de verão de duas semanas, que incluem um prémio monetário para ajudar a suportar os custos de deslocação e alojamento. O programa é organizado pela associação ATG e visa honrar a emérita cientista Maria de Sousa. Os estudantes serão supervisionados por um membro ATG.

Quem se pode candidatar?

Estudantes de Licenciatura e Mestrado, inscritos numa instituição de ensino superior em Portugal.

Quando são as inscrições?

20 de junho a 6 de julho de 2022

Como se poderá candidatar?

Preencher o seguinte formulário: https://forms.gle/vBvewWWWF57FUQCg6.

Projetos disponíveis para 2022:

- Projeto — **Bioinformatic analysis of three-dimensional live mitochondria networks**
  Orientador — Diogo Trigo, PhD
  Local — iBiMED – Institute of Biomedicine, University of Aveiro
  Data — 2 semanas em Setembro

- Projeto — **Towards the characterization of the risk for IL-7R-mediated malignancy in different hematopoietic stages**
  Orientador — João Barata, PhD e Ana Cachucho
  Local — Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisboa
  Data — 2 semanas em Agosto

- Projeto — **Exploring the role of IDH mutations in clonal competition in acute myeloid leukemia**
  Orientador — Delfim Duarte, PhD e Marta Lopes
  Local — Hematopoiesis & Microenvironments Group, i3S – Instituto de Investigação e Inovação em Saúde, Porto
  Data — 2 últimas semanas de Agosto ou 2 primeiras de Setembro

Com o apoio de: AMERICAN PORTUGUESE BIOMEDICAL RESEARCH FUND

Mais informação:

geral@atg.up.pt

All Time GABBA - Associação de Alumni do Programa Doutoral GABBA

Maria de Sousa Summer Research Program

4ª Edição

Bioinformatic analysis of three-dimensional live mitochondria networks

The work developed in this research internship aims to study alterations to the mitochondria network in live neuronal cells, namely: size, shape, velocity, dynamics, or branching. Differentiated neuroblastoma SH-SY5Y cells were treated with different modulators and live-cell 3D images of mitochondria in the whole cell were obtained by confocal microscopy. The student will analyse this data: images have been prepared for analysis and randomized; MATLAB application Mitometer^{R}, already running and optimized for the analysis, will be used. The work will consist in analysing the complex cellular images with the Mitometer application and preparing an output file, organized by specified predetermined parameters.

Towards the characterization of the risk for IL-7R-mediated malignancy in different hematopoietic stages

Acute lymphoblastic leukemia (ALL), the most frequent cancer in children, is an aggressive hematological cancer resulting from clonal expansion of either B (B-ALL) or T lymphoid precursors (T-ALL). Interleukin-7 (IL-7) and its receptor (IL-7R) - a heterodimer of IL-7Rα (encoded by IL7R) and the common γ chain (γc) - are essential for normal lymphoid development. However, we and others have shown that IL-7R-dependent signals can play a key role in ALL initiation, development and maintenance. Around 10% of pediatric T-ALL cases display IL7R gain-of-function mutations leading to IL-7Rα homodimerization and constitutive, ligand-independent signaling. These mutations associate with very poor prognosis in relapsed T-ALL. Similar mutations are found also in high risk B-ALL patients. These findings highlight the oncogenic potential of IL-7R while raising questions as to which stages of hematopoietic development are at higher risk for transformation upon aberrant IL-7R signaling. Using a number of different conditional mutant IL7R mouse models we are characterizing the ability of abnormal IL-7R-mediated signaling to induce leukemia at different stages of hematopoietic development, by looking at leukemia penetrance, immunophenotype, transcriptomic and mutational profile, and a number of other parameters that will enable us to define leukemia aggressiveness. The summer internship student will contribute to some of these efforts under the direct supervision of the PhD student spearheading the project.

Exploring the role of IDH mutations in clonal competition in acute myeloid leukemia

Acute myeloid leukemia is a fast-proliferating blood cancer with poor prognosis and limited treatment options. Each AML has a clonal architecture characterised by dominant clones and minor subclones. In this small project, we will also explore metabolic dependencies in clonal competition of AML cells. Somatic mutations in isocitrate dehydrogenases (IDH1/2) occur in about 20% of AML cases and are early clonal events in AML evolution. IDH1/2 convert isocitrate into α-ketoglutarate (α-KG). IDH1/2 mutations result in neomorphic enzymes that convert α-KG into the oncometabolite 2-hydroxyglutarate (D)-2-HG, which inhibits α-KG-dependent dioxygenases leading to DNA hypermethylation and block in differentiation. Little attention has been given to the impact of the released (D)-2-HG on the surrounding environment, although (D)-2-HG seems to inhibit leukemia cell proliferation. Furthermore, IDH1/2 mutations universally occur in major AML clones but the mechanism for this clonal dominance is not understood. We hypothesize that the (D)-2-HG released by IDHmut clones works as a competition mechanism in AML and negatively affects IDH-WT clones, non-malignant HSCs and T cells. We will transduce previously generated murine AML cells with the pBABE-based retrovirus expressing the mutant IDH1 R132H or the control WT IDH. We will confirm that 2-HG is released by IDH-mutant AML cells in vitro, by quantifying its levels using a validated and commercially available ELISA kit. We will determine the competitive properties of IDH-mutant AML cells by performing in vitro high-throughput screening with the Incell system. This exploratory project will provide preliminary results for the study of IDH1 mutations in clonal competition in AML.

Com o apoio de: AMERICAN PORTUGUESE BIOMEDICAL RESEARCH FUND

Mais informação:

geral@atg.up.pt