

## ***RUNX1* Research Program – Mark Foundation for Cancer Research STRIVE Grant Program (Seeking Transformational Research Venture)**

### ***STRIVE Grant Description***

The role of inflammation and the immune system in cancer is undeniable. Inflammation can predispose to cancer and promote cancer growth and treatment resistance. The immune system can orchestrate both a pro- and anti-cancerous state. In the last decade one of the most significant discoveries made in the field of hematology was the newly defined disorder called clonal hematopoiesis of indeterminate potential (CHIP), also known as aging-related clonal hematopoiesis (ARCH), which is associated with an increased likelihood of progression to hematologic malignancies. Interestingly, since then, CHIP itself has been shown to increase risk of myocardial infarction and ischemic stroke due to proinflammatory interactions between the mutated leukocytes and vascular endothelium. Current research suggests that the transformation to malignancy requires changes in the cellular microenvironment, such as increased inflammation or decreased immune function that selects for clones with mutations that support proliferation and dissemination of transformed cells. Understanding this interplay between cell-autonomous and cell-extrinsic factors is key to understanding how cancer initiates and ultimately progresses.

In the case of *RUNX1* familial platelet disorder (*RUNX1*-FPD; also known as FPDMM or FPD/AML), a rare inherited hematologic malignancy (HM) predisposition disorder, there is evidence that all of these factors are likely at play and driving the 35%-50% lifetime risk of developing an HM in this patient population. In one institution's cohort of precancerous *RUNX1*-FPD patients under the age of 50, 67% had evidence of CHIP. Furthermore, results from ongoing research have shown that inflammation is present in the bone marrow of precancerous patients at baseline and that there may be a preponderance of immune-related health issues in patients including allergies, reactive airway disease and eczema. Outside of its role in hematopoietic stem cell fidelity and proper megakaryopoiesis and platelet function, *RUNX1* is important in the development and differentiation of cells in both the innate and adaptive immune compartments as well.

The Mark Foundation for Cancer Research and the *RUNX1* Research Program have partnered to support innovative studies that aim to delineate the role of inflammation, the immune system and clonal evolution from CHIP to clonal hematopoiesis of oncogenic potential (CHOP) to overt malignancy in *RUNX1*-FPD. Understanding how germline *RUNX1* mutations impart changes in the immune system and the overall inflammatory profile within patients can lead to critical insights into cancer disease initiation and progression mechanisms. All proposed projects must be oriented towards developing novel cancer prevention interventions for *RUNX1*-FPD.

Some specific areas of interest include:

- Evaluating whether there are shared, druggable mechanisms that drive progression of clonal hematopoiesis to malignancy in the general population and in *RUNX1*-FPD

patients.

- Determining whether the microbiome or environmental exposures influence clonal hematopoiesis to promote malignant transformation and progression.
- Defining whether clonal evolution and malignant transformation is impacted by the cellular and molecular mechanisms that underlie the inflammatory manifestations observed in *RUNX1*-FPD patients such as eczema, reactive airway disease and allergies.

#### **Grant terms**

- Applicants may request funding of up to \$250,000 for a period of 12-18 months. The budget and duration requested must be realistic and reflect the estimated cost and timeline for the proposed study.
- Number of grants funded will depend on the number of outstanding, high-impact study proposals that address the objectives outlined in the RFA.
- Successful studies showing significant promise after the term of the grant agreement may have the potential for additional funding.

#### **Application Process:**

- Applicants must first submit a letter of intent (LOI), which will be reviewed by an independent panel of expert scientific investigators who will determine eligibility for a full application.
- The LOI must include the following content:
  1. *Project Summary* - Summary of the main objectives of the proposed study and how potential findings would support the development of cancer prevention for *RUNX1*-FPD. [one-page limit]
  2. *Project Plan Description* – A brief communication articulating the experimental strategy proposed to achieve the main objectives outlined in the *Project Summary*. [one-page limit]
  3. *References* – Provide citations of cited references in the *Project Summary* and *Project Plan Description*. [no page limit]
  4. *NIH-style Bio-sketch* for all key personnel (i.e. Principal Investigator (PI), Co-PI, essential collaborators) [no page limit]
- All LOIs must be submitted in electronic form, as a single pdf, by email to: [info@runx1-fpd.org](mailto:info@runx1-fpd.org).

#### **Applicant Eligibility:**

- Applicants must be established independent investigators in a tenure-track or tenured position at the Assistant Professor level (or equivalent), or higher, at a recognized 501(c)(3) university or non-profit institution.

#### **Key Dates:**

- LOI submission deadline – February 8, 2021
- Anticipated notification of accepted LOIs – March 15, 2021
- Full applications deadline – April 26, 2021
- Anticipated grant award notification – June 18, 2021



### **About the Mark Foundation for Cancer Research**

The Mark Foundation for Cancer Research actively partners with scientists to accelerate research that will transform the prevention, diagnosis, and treatment of cancer. We fulfill our mission by supporting groundbreaking science carried out by individual investigators, multi-disciplinary teams, and early-stage companies in the United States and across the globe. Recognizing the obstacles that prevent scientific advances from improving patient outcomes, we maintain a nimble, high-impact approach to funding basic and translational cancer research that bridges the gap between bench and bedside through grants and venture investments.

### **About the RUNX1 Research Program**

At the RUNX1 Research Program, our mission is to improve the quality of life and prevent cancer in patients with RUNX1 familial platelet disorder (RUNX1-FPD). We do this by promoting awareness, providing education and funding world-class collaborative research alongside an empowered patient community.