WesFoundation

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Researcher - Dr. Raghavan Chinnadurai
Facility - University of Wisconsin Carbone Cancer Center
Location - Madison, WI
Amount - $50,000.00
Biography: Dr. Raghavan Chinnadurai completed Ph.D in Human Biology (Specifically in Molecular Virology) at the Institute of Virology in University Clinic of Ulm, Ulm, Germany. Subsequently he did post doctorate in immunology and cell therapy at Emory University in Atlanta, Georgia. Currently, he is an Assistant Scientist at the department of Medicine in University of Wisconsin-Madison. Dr. Chinnadurai is also an honorary fellow and member at the University of Wisconsin Carbone Cancer Center. Dr. Chinnadurai's research interest is to pursue a multidisciplinary scientific approach to develop Mesenchymal Stromal Cell (MSC) based cell therapeutics and to understand how endogenous non-hematopoietic marrow stem cells such as MSCs shape immune responses in the state of health, inflammation and cancer.
Lay Description: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an important therapy for aggressive leukemia. However, the major cause of mortality after allo-HSCT is graft-vs-host disease (GvHD), which is driven by donor T cells reacting against host antigens. Treatment approaches are needed to mitigate steroid resistant GvHD. In the recent years cell therapy is increasingly being tested to reduce inflammation and injury in inflammatory immune disorders. Mesenchymal stromal cells (MSCs) are adult multipotent stem cells that can be derived from multiple tissue sources such as bone marrow, umbilical cord, adipose tissue, and placenta. Of these, bone marrow derived MSCs are the most commonly tested cell therapy candidate in clinical trials for their anti-inflammatory and regenerative properties. Although early phase clinical trials have demonstrated excellent safety with MSC therapy, clear demonstration of its anti-GvHD efficacy is an ongoing concern. We have identified the potential pitfalls of first-generation MSC based cell therapy and delineated unique mechanisms of MSC's function, fitness and their translational relevance to failed clinical trials and thus inform clues to develop second-generation MSC therapy. In the present study we aim to test the use of MSC products as cell therapy to mitigate GvHD in animal models of allogeneic bone marrow transplantation.

Researcher - Dr. John Colgan
Facility - University of Iowa
Location - Iowa City, Iowa
Amount - $50,000.00
Biography: Dr. John Colgan earned his Bachelor of Science in Biology from Cook College at Rutgers University in New Jersey. He performed his graduate studies at Columbia University in New York City and received a Ph.D. for his thesis on molecular mechanisms that regulate gene transcription in eukaryotic cells. For his postdoctoral training, Dr. Colgan studied virology and immunology at Columbia University College of Physicians in New York City. He joined the faculty at the University of Iowa in 2005 to begin his independent research program, which is focused on identifying pathways critical for the development of white blood cells and the role of these pathways in leukemia development and growth.
Lay Description: Conventional therapies for leukemia rely on toxic drugs that have long and short-term side effects. Further, leukemia can become resistant to these therapies, which correlates with a very poor prognosis. Thus, there is a pressing need to identify new and more precise methods for treating leukemia. Our project is focused on determining the importance of a protein called GON4L in the growth of leukemic cells. Our previous work showed that fast-dividing, white blood cell precursors from which leukemia originates require GON4L for proliferation. Given these results, we expect that GON4L and its associated pathways are critical for driving the development and spread of leukemia, making them excellent therapeutic targets. To determine how loss of GON4L affects leukemic cell growth and survival, we are creating a mouse model for leukemia in which we can induce removal of GON4L in leukemic cells and then test whether they cease to proliferate. To complement this approach, we are using biochemical methods to identify molecular pathways that require GON4L.

Our hope is that understanding GON4L's role in leukemia and its molecular function will help identify new and more effective strategies for treating leukemia.

Researcher - Dr. Tomasz Skorski
Facility - Temple University
Location - Philadelphia, PA
Amount - $50,000.00
Biography: I have more than 25 years of experience in studying molecular mechanisms of leukemogenesis. In the past 18 years my laboratory was focused on determination of the role of DNA repair mechanisms in acute (AML, ALL) and chronic (CML) leukemias and also in myeloproliferative neoplasms (MPNs) including the potential of therapeutic interventions. We found that acute and chronic leukemia stem cells (LSCs) accumulate potentially lethal DNA double-strand breaks (DSBs), but homologous recombination (HR) and non-homologous end- joining (NHEJ) protect their survival. Normal cells use BRAC1/2-dependent HR and DNA-PK –mediated NHEJ to prevent DSB-triggered apoptosis. However, leukemia cells may employ alternative mechanisms such as RAD52-mediated HR and PARP1-mediated NHEJ. These changes may be driven by genetic and epigenetic aberrations. Individual patients with leukemias/MPNs displaying deficiencies in specific DSB repair pathway are identified by Gene Expression and Mutation Analysis (GEMA) (1). We explore these differences to target tumor-specific DNA repair mechanisms to achieve synthetic lethality in leukemia cells, with negligible effects on normal cells. These studies will lead to novel therapeutic approaches based on induction of personalized medicine-guided synthetic lethality in leukemias from individual patients. We were first to demonstrate that targeting PARP1 and/or RAD52 combined with standard therapeutic regimens can be successfully applied in individual leukemias identified by GEMA (1-4).
My laboratory received continuous funding since 1999 from NIH (R01, R21, R29), Leukemia and Lymphoma Society (Scholar of the LLS, and research grants), Department of Defense, Leukemia Research Foundation, and Elsa U. Pardee Foundation.
Overview - Although tremendous progress has been made in treatment modalities of acute myeloid leukemia (AML), there is the necessity to improve

and develop novel therapeutic approaches. We propose to develop a strategy based on Gene Expression and Mutation Analysis (GEMA) profiling to identify patients with AML displaying specific preferences for repairing spontaneous and drug-induced DNA damage. DNA repair pathways will be then attacked by PARP inhibitors eventually combined with standard treatment to eliminate leukemia stem and progenitor cells without affecting normal cells and tissues.

Researcher - Dr. Greg Wang
Facility - UNC Chapel Hill
Location - North Carolina
Amount - $50,000.00
Biography: Dr. Wang received his PhD from University of California, San Diego in 2006 under direction of Dr. Mark P Kamps and completed his postdoctoral studies at Rockefeller University with Dr. C David Allis in 2011. In 2012, Dr. Wang joined UNC as a faculty of Biochemistry and Biophysics with a joint appointment in the UNC Lineberger Comprehensive Cancer Center. Research in his lab focuses on mechanistic understandings of how chemical modifications of chromatin define distinct patterns of mammalian genomes, control gene expression, and regulate cell proliferation versus differentiation during development, and how their deregulations lead to cancer (Learn more about: https://www.gregwanglab.com/)
Lay Description: Despite recent advances, many forms of hematological cancers including acute leukemia still remain incurable, exhibiting poor prognosis in the clinic and demanding new treatment strategies. Through recent deep sequencing of primary human leukemia samples, we now know that these cancers frequently acquire somatic mutations within the genes encoding crucial enzymes that modify chromatin, a form of genetic material where DNA is situated. Such mutations can cause deregulation of potentially important genes. However, the detailed molecular and cellular mechanisms are far from clear. We have carried out preliminary studies to show importance of these enzymes in acute leukemia development. The goal of this
WES Leukemia Foundation grant is to identify novel drug targets that leukemia cells rely on for malignant growth, and to develop new compounds to treat leukemia cells based on the underlying mechanisms. We are working closely with a set of outstanding collaborators, which include experts in medicinal chemistry, chromatin biology and leukemia clinics. The successful completion of the grant should promote current understanding of acute leukemia and help yield innovative therapeutics.