Protein tyrosine phosphatase - sigma inhibitors for hematopoietic regeneration

Grant Award Details

Grant Type: Quest - Discovery Stage Research Projects
Grant Number: DISC2-09624
Project Objective: Generate and functionally evaluate candidate PTP - sigma inhibitors that antagonize PTP - sigma mediated signaling in hematopoietic stem cells for the purpose of hematopoietic regeneration.

Investigator:
Name: John Chute
Institution: University of California, Los Angeles
Type: PI

Disease Focus: Blood Cancer, Blood Disorders, Cancer
Human Stem Cell Use: Adult Stem Cell
Award Value: $2,116,708
Status: Closed

Progress Reports

Reporting Period: Year 2

Grant Application Details

Application Title: Protein tyrosine phosphatase - sigma inhibitors for hematopoietic regeneration
Public Abstract:  

Research Objective

We propose to develop a lead small molecule inhibitor of PTPσ, a receptor expressed by human blood stem cells, for the purpose of promoting human hematopoietic regeneration.

Impact

Systemic administration of a PTPσ inhibitor can accelerate hematologic recovery in thousands of patients who have received myelosuppressive chemo- or radiotherapy.

Major Proposed Activities

- Generate novel PTPσ inhibitors for functional screening.
- Develop and validate a PTPσ inhibition assay to allow direct testing of candidate PTPσ inhibitors in vitro.
- Develop and validate a Rac1 activation assay and a PTPσ specificity assay and test all candidate PTPσ inhibitors for these activities.
- Determine the in vitro and in vivo hematopoietic regenerative capacity of select PTPσ inhibitors.
- Test the efficacy of select PTPσ inhibitors in a model of BM transplantation and against human HSCs in vitro.
- Perform initial PK and toxicity studies of PTPσ inhibitors and select a lead compound for clinical development.

Statement of Benefit to California:

This research will benefit California in several ways. First, this research provides fundamental new knowledge regarding hematopoietic stem cell biology to the field. Second, we have generated new intellectual property around novel PTPσ inhibitors for which we have filed provisional patent applications with the USPTO. Third, our discoveries will provide the basis for licensure to biotechnology or pharmaceutical companies in California or raise investment from venture capitalists.

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