Objective

Our interest is to understand the role of VEGF expression and angiogenesis in leukemogenesis. Recently, emerging data is suggesting that in addition to promoting the growth and metastatic spread of solid tumors, angiogenesis may play an important role also in the pathophysiology of hematological malignancies. Clinical studies indicate that leukemia patients express high levels of pro-angiogenic factors such as VEGF and have increased angiogenesis in the bone marrow. However, these findings are mostly correlative and genetic proof that VEGF expression and angiogenesis support leukemogenesis is still lacking. Furthermore, the molecular mechanisms leading to high VEGF production in leukemia have not been elucidated. The transcription factor HIF-1α is the main positive regulator of VEGF expression.

We therefore hypothesize that HIF-1α upregulation may cause high VEGF expression in leukemic blasts and propose to: 1) Elucidate the cause of VEGF expression in leukemic cells; 2) Study the effect of HIF-1α and VEGF overexpression on normal hematopoiesis; 3) Study the effect of HIF-1α and VEGF overexpression on leukemia onset and progression. We plan to achieve these objectives by an inter-
disciplinary approach consisting of the analysis of in vitro experiments, in vivo data and clinical data. The expression of HIF-1α will be analyzed in leukemia clinical specimens and cell lines in correlation with VEGF levels, angiogenesis and disease progression. In parallel, in vivo studies in mice will address whether overexpression of HIF-1α or VEGF perturbs normal hematopoiesis and promotes leukemogenesis. These mouse models will be instrumental to test the efficacy of anti-angiogenesis and anti-Hif-1α inhibitors in the future. Funding of this proposal will foster the European reintegration of a talented scientist with extensive training in the United States while also strengthening the cooperation of European institutions with prominent research centers in the United States.

Field of science

/medical and health sciences/basic medicine/physiology/pathophysiology
/medical and health sciences/clinical medicine/oncology/leukemia

Programme(s)

Topic(s)

Call for proposal

FP7-PEOPLE-2007-4-3-IRG

Funding Scheme

MC-IRG - International Re-integration Grants (IRG)

Coordinator

OSPEDALE SAN RAFFAELE SRL

Address

Activity type

EU contribution

Website

Administrative Contact

Maria Rosa Pedrazzi (Dr.)
Participants (1)

FONDAZIONE CENTRO SAN RAFFAELE DEL MONTE TABOR

Address
Via Olgettina 60
20132 Milano

Website

Administrative Contact
Maria Rosa Pedrazzi (Dr.)

EU contribution
€ 100 000

Address
Via Olgettina 60
20132 Milano

Website

Administrative Contact
Maria Rosa Pedrazzi (Dr.)

Last update: 16 July 2019

Record number: 89076

Permalink: https://cordis.europa.eu/project/id/224783/

© European Union, 2020