Title: Faculty
Name: Jingwu Xie
Organization: Indiana Univ
Address: 980 W. Walnut St
City: Indianapolis
State: Indiana
Zip Code: 46202
Country: United States of America
Email: jinxie@iupui.edu
Area of Research: Microenvironment
Title of abstract: Effects of hedgehog signaling activity on hematopoietic lineages
Authors: Dongsheng Gu, Xiaoli Zhang, Ling Yang and Jingwu Xie
Abstract Organization: Wells Center for Pediatric Research, Department of Pediatrics, Indiana University School of Medicine
Abstract: The hedgehog (Hh) pathway is a major regulator for cell differentiation, tissue polarity, cell proliferation and carcinogenesis. About one third of human cancer is associated with activated Hh signaling, with SMO as the key player and Gli molecules as downstream transcriptional factors. It is believed that inhibiting Hh signaling is a novel option for cancer therapeutics. Despite the significance of Hh signaling for human cancer, the molecular mechanism by which Hh signaling promotes carcinogenesis remains unclear. In particular, we have little understanding on the role of Hh signaling in regulation of tumor microenvironment.

In this study, we tried to examine the role of hedgehog signaling on the myloid lineage using genetic engineered mice with either expression of constitutively activated smoothened molecule SmoM2 or inducible removal of Smo in the bone marrow. We showed that expression of SmoM2 in the bone marrow resulted in an increase in the population of myeloid-derived cells. Conversely, removal of Smo from bone marrow is deficient in producing myeloid-derived cells in vitro. However, myeloid cell specific expression of SmoM2 had not changes in myeloid cell population, suggesting that Smo exerts its effects through paracrine signaling mechanisms. Further investigation indicates that Smo-mediated effects on myeloid cells was through induction of several growth factors and cytokine, including TGFbeta and IL-11. Taken together, our data demonstrate an important role of hedgehog signaling on myeloid lineage differentiation through paracrine mechansms.