# Sanderson et al. (Abstract)

Cellular Therapy and Transplantation (CTT), Vol. 3, No. 9
doi: 10.3205/ctt-2010-No9-abstract78


Abstract accepted for "4th Raisa Gorbacheva Memorial Meeting on Hematopoietic Stem Cell Transplantation", Saint Petersburg, Russia, September 18–20, 2010

Contribute a comment



## Heparanase promotes the aggressive phenotype of myeloma tumors and is a novel target for myeloma therapy

**Ralph D. Sanderson, Yang Yang, Anurag Purushothaman, Joseph P. Ritchie, Vishnu C. Ramani**

Department of Pathology, University of Alabama at Birmingham, USA

Correspondence: Ralph D. Sanderson, University of Alabama at Birmingham, 814 Shelby Building, 1530 Third Avenue South, Birmingham, AL, 35294-2182, USA, E-mail: Sanderson@uab.edu

### Abstract

Heparanase is an endoglucuronidase that cleaves heparan sulfate chains. Heparanase expression is upregulated in many types of cancer, particularly in those tumors exhibiting an aggressive phenotype. In myeloma patients, heparanase is often present in high levels in the bone marrow where it is associated with enhanced angiogenesis and poor patient prognosis. Using in vitro and in vivo models of myeloma, we have probed the mechanism of heparanase action in myeloma and discovered that the enzyme actively promotes tumor growth, angiogenesis, metastasis, and osteolysis. This occurs through heparanase-mediated upregulation of expression of a number of proteins known to drive an aggressive tumor phenotype including HGF, MMP-9, VEGF, and RANKL. In addition, heparanase enhances shedding of syndecan-1 (CD138), a heparan sulfate proteoglycan present at high levels on the myeloma cell surface. This is important because the heparan sulfate chains present on the shed syndecan-1 bind to effector proteins such as HGF and VEGF and enhance their ability to promote signaling. This further stimulates myeloma growth and angiogenesis. When mice bearing myeloma tumors were treated with inhibitors of heparanase enzymatic activity, tumor growth and progression were significantly attenuated. Together these results demonstrate that heparanase plays a critical role in enhancing myeloma progression and that targeting heparanase may be a viable therapeutic strategy for treating myeloma and other cancers.

**Keywords:** myeloma, tumor microenvironment, heparan sulfate, therapy, angiogenesis

<-- Previous abstract  Contents  Next abstract -->

Contribute a comment

Top