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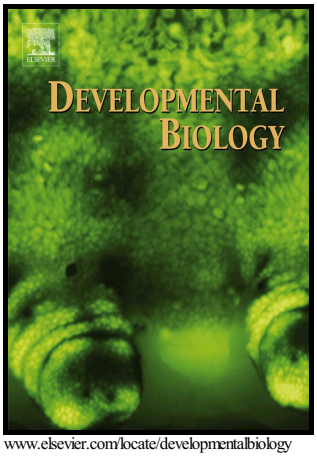

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Lyndsay A Wylie[a], Kevin P Mouillesseaux[b,c], Diana C Chong[a], Victoria L Bautch[a,b,c,d,#]

a. Curriculum in Genetics and Molecular Biology, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.
b. Department of Biology, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.
c. Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.
d. McAllister Heart Institute, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.

*Corresponding author: Victoria L Bautch, PhD ' Professor of Biology,, Department of Biology, CB#3280, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599 USA, Phone: 919-966-6797, Fax: 919-962-8472, bautch@med.unc.edu

ABSTRACT

The BMP pathway regulates developmental processes including angiogenesis, yet its signaling outputs are complex and context-dependent. Recently, we showed that SMAD6, an intracellular BMP inhibitor expressed in endothelial cells, decreases vessel sprouting and branching both *in vitro* and in zebrafish. Genetic deletion of SMAD6 in mice results in poorly characterized cardiovascular defects and lethality. Here, we analyzed the effects of SMAD6 loss on vascular function during murine development. SMAD6 was expressed in a subset of blood vessels throughout development, primarily in arteries, while expression outside of the vasculature was largely confined to developing cardiac valves with no obvious embryonic phenotype. Mice deficient in SMAD6 died during late gestation and early stages of postnatal development, and this lethality was associated with vessel hemorrhage. Mice that survived past birth had increased branching and sprouting of developing postnatal retinal vessels and disorganized tight and adherens junctions. *In vitro*, knockdown of SMAD6 led to abnormal