The chromatin remodeler Brg1 directs adventitial progenitor-to-myofibroblast differentiation and vascular fibrosis.

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Vascular fibrosis describes irreversible stiffening of the blood vessels that develops in response to many forms of cardiovascular disease including hypertension and atherosclerosis. We identified a unique population of multipotent smooth muscle-derived progenitor cells that reside in the adventitial layer of mouse arteries and express the stem marker Sca1 (**AdvSca1-SM cells**). After acute vascular injury, AdvSca1-SM cells expand in the adventitia, differentiate into myofibroblasts, and greatly contribute to vascular fibrosis. The chromatin remodeling protein Brahma-related gene 1 (Brg1) is upregulated in AdvSca1-SM cells in response to vascular injury, but how Brg1 influences AdvSca1-SM differentiation remains unknown. Using *in vitro* systems and animal models, we aim to define the role of Brg1 in AdvSca1-SM cells. We hypothesize that Brg1 modulates chromatin to preferentially drive AdvSca1-SM cell differentiation towards pathologic myofibroblasts and inhibition of Brg1 will disrupt AdvSca1-SM – myofibroblast differentiation and reduce vascular fibrosis.

Results: Mice subjected to carotid ligation and treated with the Brg1 inhibitor PFI-3 exhibit decreased vascular fibrosis, smaller neointima, and decreased expansion of AdvSca1-SM cells as compared to control mice. *In vitro*, AdvSca1-SM cells stimulated with TGF-β express myofibroblast genes and exhibit enhanced contractility, and co-treatment with PFI-3 blocks TGF-β induced myofibroblast gene expression and contractility. Ultimately, these results support the conclusion that Brg1 is a major regulator of AdvSca1-SM myofibroblast differentiation and may be a targetable protein to treat vascular fibrosis.