# Mouse Model of Marfan Syndrome Accelerates Aneurysmal Formation through Well-Characterized TGF-β Signaling Pathways

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## Background

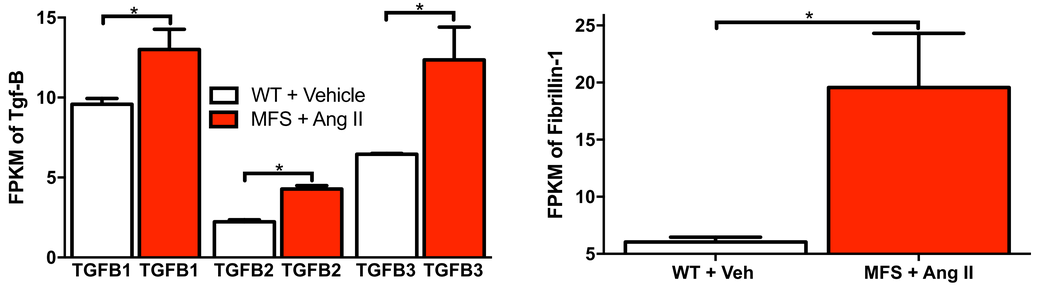
Marfan syndrome (MFS) represents a genetic disorder with ranging clinical presentation, most notably ascending aortic aneurysms. There has been extensive research to elucidate the mechanistic biochemistry of this disease. In this regard, the abundance of TGF-β from a mutation in fibrillin-1 is the suggested etiology. Many important signaling pathways downstream of TGF-β have been well-characterized. Our laboratory has previously demonstrated a unique murine model of MFS resulting in the accelerated formation of ascending aortic aneurysms. This study aims to characterize the relevance of this model to known signaling mechanisms in MFS.

## Methods

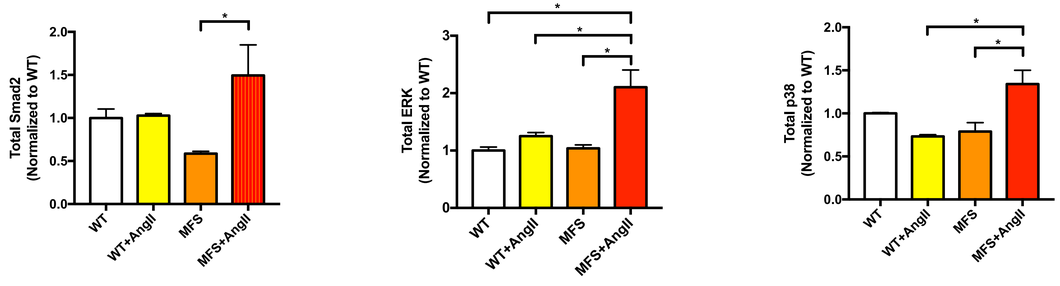
Fbn1C1039G/+ heterozygous mice, with a mutation in fibrillin-1, were supplemented with angiotensin II 4.5 mg/kg daily to accelerate aneurysmal formation. Four mouse groups were analyzed, wild type (wt) (saline +/- angiotensin II) and heterozygous (saline +/- angiotensin II). Aortic tissues from these samples were subjected to RNA sequencing, western blotting and phosphor-imaging in effort to query various TGF-β signaling pathways.

## Results

RNA sequencing of fibrillin-1 and TGF-β revealed significantly greater RNA expression in the accelerated mice. Western blotting of the accelerated model normalized to wt mice showed upregulation of Smad2, ERK and p38 proteins.

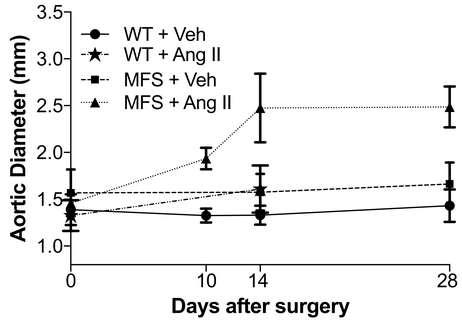



**Left:** Fragments per kb of transcript per million reads mapped of transforming growth factor beta comparing wt mice with an accelerated mouse model. **Right:** Fragments per kb of transcript per million reads mapped of fibrillin-1 comparing wt mice with an accelerated mouse model. *significance is p-value of <0.05




**Left:** Total protein expression of SMAD with wt mice as the control. **Middle:** Total protein expression of ERK with wt mice as the control. **Right:** Total protein expression of p38 with wt mice as the control. *significance is p-value of <0.05

## Murine Model Aortic Diameter




This figure represents the increase in aortic diameter in an accelerated mouse model of MFS.

## Conclusions

Our accelerated MFS mouse model signals through known TGF-β cascades. This novel model appears relevant to the study of MFS aortopathy with the added advantage of offering rapid experimental process.

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