Commentary: Of mice and men

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Central Message

Preclinical models of disease provide powerful tools to investigate pathology progression. Cardiothoracic surgeons are poised to contribute to understanding underlying mechanisms and affect treatment.

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In this month's issue of *The Journal of Thoracic and Cardiovascular Surgery*, Gensicke and colleagues¹ present their data on their development of a preclinical murine model of Marfan syndrome with accelerated aortic aneurysm formation. The attempt to take complex clinical presentations and pathology and reduce them to a rather straightforward model that is reproducible, uses gene targeting, and recapitulates a meaningful clinical phenotype is daunting. Although from a broad application standpoint, developing a mouse that gets a marfanoid aneurysm is a far cry from the surgical treatment of aorta and aortic root aneurysms, the future effect on understanding the mechanisms of disease and developing novel targeted therapeutics is paramount to advancing multimodal interventions. Murine models of disease allow the development of knockout strains and numerous antibody-bases and analytic methods of analysis to be used.

During the past 3 decades, we have come to understand the mutation of the fibrillin gene and its importance in the progression and presentation of Marfan syndrome.² Gensicke and colleagues¹ have used a murine model with a mutation in the fibrillin-1 gene and have supplemented it with angiotensin II. This combination of fibrillin mutation and angiotensin administered daily promote accelerated aneurysm formation. This approach builds on the interaction of transforming growth factor β (TGF- β) on aneurysm progression. The interaction of TGF- β and an angiotensin receptor blocker (eg, losartan) has been used in slowing disease progression clinically.³

Gensicke and colleagues¹ are to be commended for pursuing basic and translational science research as busy

academic surgeons and their effects continue to drive the field forward. The support of the senior author, Dr Turek, is a meaningful example of how societal support (American Association for Thoracic Surgery and The Marfan Foundation) and that of surgeon-scientists can advance scientific knowledge. Although the clinical effects are still in the early stages, the fundamental basis of this model and sharing it with the broader community are having an effect now.⁴

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