Aortic dissection is an important cause of death in the western world with an estimated prevalence of 1-2% of total mortality. Although most dissections occur abdominal, the study of thoracic aortic aneurysms (TAA) has provided major new insights into the pathogenesis of this disease. The genetic contribution to TAA is significant as about 20% of all affected individuals have a positive family history for aneurysms. For many years, the study of a monogenic syndromic cause of TAA, Marfan syndrome (MFS), has served as a paradigm for the study of TAA. Detailed pathogenetic studies of humans and mouse models with MFS have lead to the identification of transforming growth factor beta signaling as a key pathway in the pathogenesis of aortic aneurysms. Through the detailed clinical description and the use of state-of-the-art molecular technologies (microarray, next generation sequencing, microRNA profiling, proteomics), our studies aim at the further delineation and unraveling of the pathogenesis of TAA. A better understanding of this disease will ultimately lead to better diagnostic tools, improved counseling and development of new therapeutic strategies.