

## Commentary: Toward a biologic understanding of autograft dilatation in the Ross procedure—creating opportunities to rescue the neoaortic root



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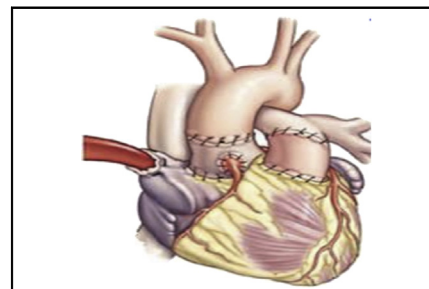
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The aortic root has a sophisticated architecture that results in hemodynamic performance and longevity beyond any prosthetic replacement.<sup>2</sup> The seminal step by Mr Ross to enlist the aortic valve's living twin as its replacement has produced outstanding results at experienced centers.<sup>3,4</sup> Several considerations have hampered the widespread adoption of the Ross procedure, one of which has been autograft dilatation, with consequent valvular failure.<sup>4,5</sup> A focused effort to understand the clinical drivers of this process has reduced its incidence and highlighted its independent predictors.<sup>5,6</sup> An advanced technical understanding of the neoaortic root has also minimized the risk of autograft dilation, including techniques such as subcoronary implantation, and additional external supports.<sup>5-8</sup> Despite these advances, detailed data about cellular changes that drive such autograft dilation have been lacking to date.

In this issue of the *Journal*, Chiarini and colleagues<sup>9</sup> address this evidence gap with their sophisticated analysis of proteomic changes in the media of dilated autografts from patients undergoing late reoperation as compared with normal pulmonic and aortic media. They describe a pattern of distinct changes in protein profiles with respect to the cytoskeleton, the extracellular matrix, and regulators of cell signaling.<sup>9</sup> These molecular data provide new insight into the changes at the protein level that are present in dilated autografts. The identified proteomic profiles appear to be unique to the dilated autograft, akin to a molecular signature. The investigators from Verona are to be congratulated for describing this unique proteomic signature of the failing autograft that could serve as a platform to advance the understanding of the molecular mechanisms behind the pathogenesis of autograft dilation.

Furthermore, their clinical series included several subjects without autograft dilatation (excluded in their present



The Ross procedure. Reprinted with permission.<sup>1</sup>

### Central Message

The proteomic profiles of the dilated autograft may identify molecular predictors and isolate therapeutic targets for the failing neoaortic root. Future trials should explore these molecular signatures in the Ross procedure.

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study).<sup>9</sup> The analysis of tissue from these functioning autografts could yield even more specific information about the molecular drivers of dilation. In addition, further descriptive studies such as the important work by this talented group from Verona could lead to a truly mechanistic understanding of the cellular processes that determine autograft dilation, akin to the molecular breakthroughs in aortic dilation associated with Marfan syndrome.<sup>10,11</sup>

As our understanding of the molecular landscape of the dilated autograft evolves, multiple important questions arise. Are the observed proteomic signatures the cause or the consequence of the failing neoaortic root? Are these proteomic signatures modifiable? Are there molecular targets for drug therapy in this setting as in the evolving medical approaches to aortic dilation in Marfan syndrome?<sup>10,11</sup> Could the vulnerable autograft be protected from dilation during the years of somatic growth with targeted medical therapy?

Although this work is certainly ongoing and these questions are currently unanswered, Chiarini and colleagues have nevertheless opened the door to these intriguing approaches for refining outcomes yet further in the Ross procedure. Their seminal work in the characterization of the proteomic signature for the failing autograft could ultimately lead to an enhanced recognition of the molecular

pathophysiology, proteomic predictors, and therapeutic targets in this setting as part of the intense team effort to optimize the Ross procedure for our patients.<sup>1,7-11</sup>

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