Thrombospondin 1
A Protective “Matri-cellular” Signal in the Stressed Heart

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administer such an “agent”? In fact, therapeutic use of TSP-1 could potentially play dual roles in the injured heart, one that is initially beneficial, by delimiting hypertrophic growth and providing the necessary strength in the early stages after hemodynamic overload, and a second role that is maladaptive, by mediating progressive myocardial fibrosis that could lead to increased myocardial stiffness, contractile dysfunction, and increased cardiac arrhythmias. In addition, we cautiously need to keep the many other functions of TSP-1 in mind, which could result in undesirable effects on both the cardiovascular system and other organs. An elegant approach to bypass this potential problem would be to obtain a more detailed and defined structure-function analysis of TSP-1. Mapping the specific biological functions of TSP-1 to a defined structural region will probably allow us to fine-tune novel therapies based on TSP-1 peptide fragments or analogues that either mimic a specific TSP-1–mediated function or act as a dominant negative in the stressed heart, while limiting undesirable adverse effects. Nevertheless, because of the critical involvement of TSP-1 in the regulation of fundamental pathways during cardiac injury, repair, and fibrosis, further in-depth analysis of its endogenous roles will undoubtedly provide novel insights into the mechanistic basis of various cardiac diseases.

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## Disclosures

None.

## References

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