Sponsored by the **American Heart Association** and the **National Institutes of Health** and conducted at **Ohio State University**.

Protandim attenuates intimal hyperplasia in human saphenous veins cultured ex vivo via a catalase dependent pathway.

The study, conducted by researchers at The Ohio State University, examined the biochemical mechanisms that underlie the ability of **Protandim** to suppress intimal hyperplasia (over-proliferation of cells that line the vessel wall), a common adverse event that limits the effectiveness of several types of vascular surgery.

Abstract Summary

Human saphenous veins (HSVs) are widely used for bypass grafts despite their relatively low long-term patency. To evaluate the role of reactive oxygen species (ROS) signaling in intima hyperplasia (IH), an early stage pathology of vein-graft disease, and to explore the potential therapeutic effects of up-regulating endogenous antioxidant enzymes, we studied segments of HSV cultured ex vivo in an established ex vivo model of HSV IH. Results showed that HSV cultured ex vivo exhibit an ~3-fold increase in proliferation and ~3.6-fold increase in intimal area relative to freshly isolated HSV. Treatment of HSV during culture with **Protandim**, a nutritional supplement known to activate Nrf2 and increase the expression of antioxidant enzymes in several in vitro and in vivo models, blocks IH and reduces cellular proliferation to that of freshly isolated HSV. **Protandim** treatment increased the activity of SOD, HO-1 and catalase 3-, 7-, and 12-fold, respectively, and decreased the levels of superoxide (O(2)(•-)) and the lipid peroxidation product 4-HNE. Blocking catalase activity by co-treating with 3-amino-1,2,4-triazole abrogated the protective effect of **Protandim** on IH and proliferation. In conclusion, these results suggest that ROS-sensitive signaling mediates the observed IH in cultured HSV and that up-regulation of endogenous antioxidant enzymes can have a protective effect.

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