Michael Sobel, M.D.

· The Vascular Research Program at the VA Puget Sound Health Care System

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The VA Puget Sound has a robust research infrastructure that supports two principal investigators in the Division of Vascular Surgery: Dr. Michael Sobel, Professor of Vascular Surgery, and Errol Wijelath, Research Associate Professor.

Current projects include the following:

1. Preventing Vein Graft Stenosis in Peripheral Vascular Surgery.

Dr. Sobel and Dr. Katie Moreno, a University of Washington surgery resident on a research fellowship, are conducting this study. This is a prospective, longitudinal observational study of patients undergoing infrainguinal bypass surgery. The leading hypothesis is that derangements in a patient's thrombo-inflammatory responses are associated with pathological vascular healing and clinical events like vein graft stenosis and graft failure. We are developing novel methods to measure the co-activation of platelets and monocytes in the circulating blood, and trying to define phenotypic and clinical subgroups. The long-term goal is to identify the thrombo-inflammatory pathways associated with vein graft failure, for drug targeting.

2. Oncostatin M in Atherosclerosis and Vascular Disease.

Dr. Wijelath has identified this little known cytokine as a key player in the pathological proliferation and migration of vascular smooth muscle cells during the evolution of atherosclerosis and the response to injury. Through the study of atherosclerotic plaques and vascular lesions, as well as advanced molecular biological manipulations of oncostatin M (OSM) receptors *in vitro*, Dr. Wijelath is mapping the pathways of OSM action, and defining its roles in vascular disease.

3. Modulating Endothelialization of Cardiovascular Grafts.

As its funding ends, this joint project involving several Division of Vascular Surgery faculty members is winding down. In this project we discovered and refined a family of novel angiogenic proteins that enhance the effects of vascular endothelial growth factor, and can be used to promote natural endothelialization of prosthetic grafts.

RELATED PUBLICATIONS

1. Suda Y, Arano A, Fukui Y, Koshida S, Wakao M, Nishimura T, Kusumoto S, Sobel M. Immobilization and clustering of structurally defined oligosaccharides for sugar chips: an improved method for surface plasmon resonance analysis of protein-carbohydrate interactions. *Bioconjug.Chem* 17:1125-1135, 2006.
2. Wakao M, Saito A, Ohishi K, Kishimoto Y, Nishimura T, Sobel M, Suda Y. Sugar Chips immobilized with synthetic sulfated disaccharides of heparin/heparan sulfate partial structure. *Bioorg Med Chem Lett* 18(7):2499-2504, 2008.
3. Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest 1*33(6 suppl):815S-8843, 2008.
4. Rahman S, Patel YM, Wijelath E, Sobel M. Therapeutic potential of novel modulators of neovascularization. *Future Cardiol* 4:409-426, 2008.
5. Sato M, Ito Y, Arima N, Baba M, Sobel M, Wakao M, Suda Y. High sensitivity analysis of naturally occurring sugar-chains, using a novel fluorescent linker molecule. *J Biochem (Tokyo)* 146:33-41, 2009.
6. Cushing DJ, Cooper WD, Cohen ML, McVoy JRS, Sobel M, Harris RB. Reversal of heparin-induced increases in aPTT in the rat by PM102, a novel heparin antagonist. *Eur J Pharmacol* 635:165-170, 2010.
7. Saito A, Wakao M, Deguchi H, Mawatari A, Sobel M, Suda Y. Towards the assembly of heparin and heparan sulfate oligosaccharide libraries: efficient synthesis of uronic acid and disaccharide building blocks. *Tetrahedron* 66:3951-3962, 2010.
8. Wijelath E, Kohler TR, Murray J, Namekata M, Yagi M, Sobel M. Enhancement of capillary and cellular ingrowth in ePTFE implants with a proangiogenic recombinant construct derived from fibronectin. *J Biomed Mater Res A* 95:641-648, 2010.
9. Wijelath E, Namekata M, Murray J, Furuyashiki M, Zhang S, Coan D, Wakao M, Harris RB, Suda Y, Wang L, Sobel M. Multiple mechanisms for exogenous heparin modulation of vascular endothelial growth factor activity. *J Cell Biochem* 111:461-468, 2010.

DEPARTMENT CO-INVESTIGATORS

Errol Wijelath, Ph.D. / Katie Moreno, M.D.