Toward an Agent-Based Model of Atherosclerotic Plaque Development: Leukocyte Trafficking in the Microvasculature

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Coronary disease research has shown that the white blood cells, or leukocytes, are an important contributor to atherosclerotic plaque growth and rupture. One of the major unanswered questions in this field is how and why these cells arrive in plaques, and whether new treatments can be developed to target these cells and heal blood vessels, preventing death from heart attacks. The larger arteries in which plaques form have walls that are too thick to get oxygen from the blood flowing in the vascular lumen, and need a microvascular blood supply of their own, the *vasa vasorum*. Leukocytes that affect plaque formation could arrive in the vessel wall either from the coronary vascular lumen or the *vasa vasorum.* Because it is not possible to block blood flow in either of these areas *in vivo* without causing severe tissue damage or death, and it is impossible to selectively inhibit cell adhesion and trafficking in the *vasa vasorum* vs. coronary arteries, a computational model of these processes will be useful in determining whether treatment with drugs that block growth of the *vasa vasorum* into plaques could prevent accumulation of leukocytes and plaque growth. The mechanisms by which leukocytes adhere to vessel walls and extravasate, as well as predicted locations of extravasation represent a critical component of atherosclerosis and an important submodel to be validated. Expanding on an agent-based / finite-element framework for modeling blood flow presented at Swarmfest 2006, we discuss the development of a rule set for leukocyte rolling, adhesion to the vessel wall, and transmigration, and demonstrate the implementation of the rule set in NetLogo. We then present strategies for validation of this submodel, and discuss results from preliminary validation experiments using intravital microscopy to examine monocyte rolling and adhesion in the mouse. Finally, we propose a framework for inclusion of this submodel in a larger agent-based model of atherosclerosis.

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