

Validation of a Multi-Cell Agent-Based Simulation of Leukocyte Trafficking

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One of the major unanswered questions in atherosclerosis research is where leukocytes enter a plaque: through the lumen and/or from microvessels invading the plaque. Computational simulations of leukocyte trafficking in plaques will provide new insights into this process. We have developed an agent-based simulation of leukocyte trafficking through microvascular networks for which experimental validation is necessary before relevant predictions can be made. Monocyte and neutrophil rolling and adhesion in LysM-GFP knock-in, ApoE^{-/-} mice was examined in the femoral vessels using intravital fluorescent microscopy. Numbers of rolling and adhered leukocytes in vessel segments were quantified over time and the ratio of rolling to adhered leukocytes was compared to computational model results. For monocytes and neutrophils passing through segments of small venules (~ 25 μm), 92% rolled and 2.7% were adherent. In larger venules (~50 μm), 23% rolled and 1% were adherent. In capillary size vessels (≤ 7 μm), 29% rolled and 14% adhered. In a large arteriole (~75 μm), 6.6% rolled, and $< 2.2\%$ adhered. In contrast, the model predicts that the large majority of monocytes adhere without rolling. Therefore, we conclude that the rules governing selectin and integrin function/expression in the model require further evaluation.