Hyaluronan and Versican (PGM): Partners in Crime in Vascular Disease

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Figure 1. Sections from ballooned injured carotid artery in rat (right panel) illustrating increases in hyaluronan (red) and proliferating cells (brown). Normal carotid artery stained for hyaluronan and PCNA is shown in the left panel.

Riessen, R. et al., Circulation 93:1141-1147 (1996)

Figure 2. Section from an atherosclerotic lesion from a LDL receptor negative rabbit showing cables of hyaluronan (red) surrounding macrophages (green)
Hyaluronan and versican accumulate in vascular disease and influence a number of events that form the basis for many forms of vascular disease. For example, these extracellular matrix (ECM) components in part regulate the proliferative and migratory activity of the arterial smooth muscle cells (ASMC). Interference with the binding of hyaluronan to the surface of the ASMC blocks the proliferation of ASMC to PDGF. Furthermore, blocking the synthesis of versican (PGM) by antisense or Si RNA also inhibits the proliferation of ASMC. Hyaluronan and versican (PGM) are present at the plaque-thrombus interface of advanced atherosclerotic lesions suggesting a role in thrombosis associated with sudden cardiac death. Constitutive overexpression of the hyaluronan synthases (HAS1, HAS2, and HAS3) by ASMC creates an ECM that supports the adhesion of monocytes in a hyaluronan-dependent manner with the predominant activity associated with the overexpression of HAS1. Similar ECMS can be generated by poly IC treatment of both ASMC and fibroblasts and the propensity for these ECMS to serve as ligands for macrophages is associated with an enrichment of hyaluronan and versican (PGM) in the ECM. Blocking antibodies to versican (PGM) will block monocyte sticking to these ECMS indicating a key role for versican in macrophage adhesion and aggregation. In addition, versican (PGM) inhibits the assembly of other ECMs such as elastic fibers. One mechanism that operates to inhibit elastic fiber formation is the ability of versican to interfere with the kindling of the elastin receptor (elastin binding protein = EBP) to the surface of the ASMC. These studies collectively indicate that hyaluronan and versican play multiple roles as ECM components in the development of vascular disease.

**Keywords:** hyaluronan, versican (PGM), atherosclerosis, monocytes, smooth muscle cells, elastogenesis