

Heterogeneity in the Proliferative Capacity of Smooth Muscle Cells (SMCs)

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In cardiovascular disease, artery walls remodel through an increase in SMC numbers. The predominant hypothesis for this is that SMCs in the tunica media undergo phenotypic modulation into a proliferative cell type. However, direct evidence for SMC phenotypic modulation is scant. We therefore exploited time-lapse microscopy methods to track the fate of freshly isolated, contractile SMCs. As SMCs isolated from different smooth muscle (SM) tissues are heterogeneous in nature, we have used time lapse microscopy in combination with immunocytochemistry to investigate the proliferative capacity of SMCs from portal vein (PV), carotid artery (CA) and distal colon.

The adventitia/endothelium and mucosa/serosa were mechanically removed before isolating cells by enzymatic digestion and trituration. Highly elongated, contractile SMCs that stained for both SM α -actin (SMA) and SM myosin heavy chain (SM-MHC) were obtained from all tissues. Significantly, both colon and PV tissues also contained large numbers of spherical cells that did not stain for SMA or SM-MHC (nonSMCs). In standard culture conditions, the SMCs showed limited proliferative capacity: with the exception of one SMC that divided once (out of 15 tracked cells), colon SMCs did not proliferate. Of 11 PV SMCs tracked, 7 SMCs did divide, though none progressed beyond the 3rd generation (daughter of daughter) by confluency. Conversely, the nonSMCs proliferated rapidly (reaching the 5th generation in 5 days) and dominated the resulting cultures. In contrast, all CA cells stained for both SMA and SM-MHC i.e. no nonSMCs were present. Whilst most CA SMCs underwent apoptosis early in culture (27 of 31 cells), those that survived went on to proliferate at varying rates (up to the 6th generation in 5 days). These results illustrate the complexities involved in creating models of SMC proliferation.