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Cell on the move: Remodeling of the vascular wall

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Prolonged exposure to vasoconstrictors causes structural narrowing of the smallest arteries in the vascular system the repositioning of the smooth muscle cells that compose the vessel's wall. This is important because the structural narrowing of arterioles is associated with hypertension and an increased incidence of life-threatening vascular events such as myocardial infarction and stroke. Our working hypothesis is that in order for this narrowing to occur, smooth muscle cells must degrade the extracellular matrix (ECM) that keeps them in place in a process dependent on the activity of certain enzymes called matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9. Previously we have shown that inhibition of MMP activity prevents the structural remodeling from occurring, indicating MMPs are involved in the process. To further test our hypothesis, rat cremaster arterioles were isolated, cannulated, pressurized, and treated with the vasoconstrictors Angiotensin-?? (ANG-II) and Norepinephrine (NE) for four hours, in order to induce structural narrowing. Time control arterioles were cannulated and pressurized for four hours without ANG-II or NE treatment. Non-cannulated control arterioles were snap-frozen in liquid nitrogen immediately after isolation and stored at -70℃. Activity and expression of MMP-2 and MMP-9 were measured using gelatin zymography and western blot analysis respectively. Consistently, MMP-2 activity and protein amounts were greater in control vessels without cannulation than in the cannulated vessels, even untreated. MMP-9 was not detectable. Our previous results indicate that MMPs are involved in the structural narrowing of arterioles that occurs in response to prolonged vasoconstriction. Although additional work is needed to determine which specific MMPs are involved in the process, our results indicate that MMP-2 activity and protein are reduced during prolonged vasoconstriction. Additional experiments are now being conducted to determine whether these reductions result from secretion and activation of MMP-2 in response to isolation and prolonged vasoconstriction of the arterioles.