427j Effect of Cyclic Stretch on the Migration of Endothelial Cells

Cole T. Quam, Luis Cheng Sun, Ming-Wei Li, and Yan-Ting Shiu

Vascular endothelial cells (ECs) line the inner wall of blood vessels and are constantly subjected to cyclic stretch as a result of pulsatile blood flow. Compromising the endothelial lining can lead to a variety of vascular complications such as intimal hyperplasia, stenosis, and atherosclerosis. Rapid closure and repair of a denuding EC injury generally occurs through the migration of adjacent ECs into the denuded area. Although the migration of ECs has been studied extensively, the effect of cyclic stretch on EC migration and the underlying molecular mechanisms are not yet clearly known. In the present study, we used a custom-designed stretch machine to study the effect of cyclic stretch on the migration of ECs in a wound healing scenario, as well as the role of intracellular reactive oxygen species (ROS) in mediating the effect of cyclic stretch. Bovine aortic ECs were cultured and grown to confluence on fibronectin-coated silicone elastic sheets. A strip of ECs was removed by a cell scraper (which created a denuding EC injury), and the injured EC monolayer was kept as either static controls or cyclic stretched for 3 hours at 10% longitudinal elongation, 1 Hz. The migration of ECs into the denuded area was examined by phase contrast microscopy, and the intracellular ROS was detected by a fluorescent probe, 5-(and-6-) chloromethyl-2',7'-dichlorodihydrofluorescein diacetate, acetyl ester. We found that cyclic stretch significantly inhibited the migration of ECs into the denuded zone while increased the concentration of intracellular ROS. Because previously ROS was shown to inhibit EC migration under static conditions, we then hypothesized that cyclic stretch may inhibit EC migration through the ROS pathway. To test this hypothesis, EC monolayers were prepared as described above and then treated with a ROS inhibitor, diphenyl iodium chloride, for 1 hour before being injured and subjected to cyclic stretch for 3 hours. Surprisingly, this ROS inhibitor did not improve the migration speed of ECs under cyclic stretch, suggesting the involvement of a different signaling pathway that mediates the inhibitive effective of cyclic stretch.