Cyclic mechanical strain regulates secretion of angiogenic cytokines

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Cyclic strain clearly regulates vascular development and regeneration, but the mechanisms underlying these effects remain unclear. We hypothesized that cyclic strain may play an important role in regulating the interaction between endothelial cells and smooth muscle cells during early stages of angiogenesis by modulating the secretion of specific cytokines. In order to test this hypothesis, we applied cyclic tensile strain at a frequency of 1 Hz and 7 % strain amplitude to two-dimensional cultures of human umbilical vein endothelial cells (HUVECs) and human smooth muscle cells (hSMCs) seeded on treated poly(dimethylsiloxane) substrates, and measured the secretion of cytokines known to have critical roles during early and later stages of the angiogenic process. Preliminary data demonstrates that cyclic strain of HUVECs led to a 3-fold upregulation of Ang-2, a molecule that acts to dissociate ECs and SMCs in angiogenesis, during the first 48 hours of strain, with respect to static conditions. In contrast, secretion of Angiopoietin-1 (Ang-1), a competitor of Ang-2 that serves to stabilize EC-SMC association, was not dramatically effected by strain. This data indicates that cyclic strain affects a 2.5 fold increase in the ratio of Ang-2/Ang-1 secretion by cultures of ECs and SMCs, and this may likely alter the balance of dissociation and association of ECs and SMCs. Cyclic strain was also found to induce a 7-fold upregulation in the secretion of platelet derived growth factor-ββ (PDGF-ββ), a chemotactic molecule secreted by ECs during the later stages of angiogenesis to recruit SMCs, although over a later time frame than Ang-2 upregulation. These results suggests that cyclic strain may play a role in modulating angiogenesis by altering the balance of angiogenic factors, and by temporally mediating the upregulation of factors towards angiogenic activation versus that of stabilization.