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## **Systemic and local changes in PDGF system associated with post ovariectomy microvascular remodeling in pigs**

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Previous studies in our group demonstrated that terminal microvascular networks in dura mater of ovariectomized (OVX) pigs undergo significant remodeling characterized by a decrease in microvessel density, capillary rarefaction, and increase in blood vessel permeability. It was postulated that post OVX vascular remodeling is estrogen-dependent and could involve changes in the expression of relevant growth factors and receptors on both systemic and local levels.

Systemically, comparison of growth factors and receptors in serum of intact female (IF) and OVX pigs using antibody array revealed most robust changes in expression levels of platelet-derived growth factors (PDGF) -AB and -BB, both of which are potent regulators of growth and survival in vascular tissue. These results were corroborated by Western blot analysis using monoclonal antibody directed against the B chain of PDGF, which recognizes both PDGF-AB and -BB. Densitometry analysis confirmed antibody array results showing a significant decrease in PDGF-AB and -BB expression levels in post OVX animals compared to IF swine. Lower levels of circulating PDGF could translate into a weakened response of systemic repair mechanisms during vascular damage in OVX animals. On a tissue level, however, two months post OVX there was a significant increase in local PDGF expression in OVX animals compared to IF swine accompanied by a corresponding increase in phosphorylation of PDGF receptor alpha. Our current hypothesis is that hypoxic stromal responses, triggered by initial microvessel loss in OVX animals, activate PDGF/VEGF system in an attempt to restore microvasculature via angiogenic processes. Ongoing studies are aimed at identifying other factors and pathways involved in the regulation of post OVX vascular remodeling.