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Ex Vivo Expression of Angiogenic Growth Factors and Their Receptors in Human Penile Cavernosal Cells

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Arteriogenic erectile dysfunction is associated with impairment of vascular perfusion to the erectile components of the penis. Animal studies have identified insulin-like growth factor (IGF-I) and vascular endothelial growth factor (VEGF) as penile angiogenic growth factors, but the role of these factors in humans is not well understood. We evaluated the ex vivo expression of IGF-I, VEGF, and their receptors (IGF-IR, Flt-1, and KDR) in human penile cavernosal smooth muscle cells (HCSMCs) to identify cellular and molecular pathways involved in the regulation of penile tissue vascularity. Primary culture was initiated with explants of human corpora cavernosa, and early passage (3-5) cells were used for these evaluations. Cultures were examined to verify the presence of smooth muscle cells and the absence of endothelial cell contamination. Specific monoclonal antibodies were used to localize growth factors and their receptors. To evaluate gene expression of VEGF, Flt-1, and KDR, total RNA was extracted from cavernosal cells and subjected to reverse transcriptase—polymerase chain reaction (RT-PCR) using custom synthesized primers. To study the effect on cell proliferation, 10 000 cells/well were exposed to varying concentrations of VEGF (0-50 ng/mL). At specified time periods the cells were trypsinized and counted. IGF-I and VEGF and their receptors were localized in the cultures, which were positive for the presence of smooth muscle cells and negative for endothelial cell contamination. RT-PCR evaluation revealed the expression of four splice variants of VEGF messenger RNA (VEGFs 121, 145, 165, and 189) and two of its receptors (Flt-1 and KDR). VEGF165 and VEGF121 were the most abundant forms of messenger RNA and Flt-1 appeared to be the most prominent receptor type in these cells. Exposure to VEGF elicited a twofold to threefold increase in the proliferation of HCSMCs. HCSMCs express both IGF-I and VEGF and their receptors, which may be important in the control of vascularity in human penile architecture.

Key words: Human cavernosal cells, insulin-like growth factor, vascular endothelial growth factor, endothelial NOS, Flk-1, Flt-1

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