An acute-phase protein, alpha 1-acid glycoprotein, is a local regulator to protect sperm from neutrophil phagocytosis in the bovine oviduct

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The oviduct is classically described as a sterile milieu, though pathogens and endotoxins could invade its mucosal surfaces via the uterus, peritoneal cavity and follicular fluid. We have recently shown that polymorphonuclear neutrophils (PMNs), the first line of defense against microorganisms, are present in the bovine oviduct fluid during preovulatory stages. We further suggested that the bovine oviduct provides a PGE-rich microenvironment to protect sperm from phagocytosis by PMNs that they possibly face in vivo, thereby supporting sperm survival in the oviduct. Alpha 1-acid glycoprotein (AGP) is a major acute-phase protein produced mainly in the liver, having an immunomodulatory functions. In this study, investigated, 1) the local production of AGP in the bovine oviduct, 2) the effect of AGP on the phagocytic activity of PMNs for sperm and superoxide production, and 3) the impact of AGP desialylation on the PMN phagocytosis of sperm. AGP gene was expressed in cultured bovine oviduct epithelial cells (BOECs) and AGP protein was detected in oviduct fluid. Pre-exposure of PMNs to AGP at physiological levels impaired PMN phagocytosis for sperm and superoxide generation. The desialylation of AGP eliminated these suppressive effects of AGP on PMN. Scanning electron microscopy revealed that AGP drastically reduced the formation of DNA-based neutrophil extracellular traps (NETs) for sperm entanglement. Additionally, AGP dose-dependently stimulated BOECs to secrete PGE2, and AGP and PGE2 at local levels additively inhibited sperm phagocytosis. The results provide evidence that locally produced AGP may be involved in protecting sperm from phagocytosis by PMNs in the bovine oviduct.