SEMINAL PLASMA TGFβ ACTIVATES PRO-INFLAMMATORY CYTOKINE SYNTHESIS IN HUMAN CERVICAL EPITHELIAL CELLS

D. J. Sharkey*, *S. A. Robertson

Centre for Reproductive Health, Department of Obstetrics and Gynaecology, University of Adelaide, Adelaide, SA, Australia

Exposure to semen at intercourse in women elicits an inflammation-like response characterised by recruitment of inflammatory cells and expression of pro-inflammatory cytokines including GM-CSF, interleukin-6 (IL-6) and IL-8 (1). Studies in animal models have implicated TGFβ as the major active moiety in seminal plasma, and we have shown previously that TGFβ1 and TGFβ3 are present in high concentrations in human seminal plasma (>100 ng/mL), while TGFβ2 is less abundant. To investigate the physiological significance of each of the three TGFβ isoforms as pro-inflammatory agents in human seminal plasma, we have established *in vitro* model systems to measure human cervical cell cytokine synthesis. Primary cervical epithelial cells prepared from ectocervix of hysterectomy tissues or transformed Ect1 cells were incubated for 12 h with human recombinant TGFβ (isoforms 1, 2 or 3) or with seminal plasma in the presence or absence of isoform-specific TGFβ neutralising antibodies. Epithelial cell supernatants were recovered 24 h later and supernatants were analysed by commercial ELISA to quantify GM-CSF, IL-6 and IL-8 production. Each of the three TGFβ isoforms mimicked seminal plasma and were comparable in their capacity to stimulate >10-fold increases in both GM-CSF and IL-6 expression in a dose-responsive manner. In contrast, unlike seminal plasma none of the TGFβ isoforms induced IL-8 expression. Addition of neutralising antibodies to TFGβ1, TGFβ2 and TGFβ3 each effected >50% reduction in the ability of seminal plasma to induce GM-CSF and IL-6, but did not impair seminal plasma-stimulated IL-8 production. Together these data show that TGFβ1, TGFβ2 and TGFβ3 are major active constituents of seminal plasma, acting to elicit GM-CSF and IL-6 production in cervical epithelial cells. However, TGFβ does not fully account for the pro-inflammatory effects of human seminal plasma, and other active constituents remain to be identified.

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