



Journal of Andrology, Vol 16, Issue 5 432-440, Copyright © 1995 by The American Society of Andrology

JOURNAL ARTICLE

Sperm immobilizing activity of a synthetic bioactive peptide 20-44 of 37-kDa cationic antimicrobial protein (CAP37) of human neutrophils

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We have previously reported that human sperm coincubated with human peripheral blood neutrophils in the presence of complement (C)-fixing antisperm antibody (ASA)-positive sera are rapidly internalized and degraded within the neutrophil phagolysosome. However, the mechanism by which motile sperm are processed within the phagolysosome is unknown. Various spermicidal/antimicrobial proteins contained in azurophilic granules that can be secreted into the phagolysosome may play a role in sperm disposal. In this study, we examined the expression of a 37-kDa cationic antimicrobial protein (CAP37) during sperm phagocytosis and the effect of its synthetic bioactive fragment, Peptide 20-44 (P20-44), on sperm motility, acrosomal integrity, and mitochondrial functionality. CAP37 expression by neutrophils undergoing ASA- and C-dependent sperm phagocytosis was increased as measured by flow cytometry. Exposure of motile sperm to a cationic P20-44, the bioactive antimicrobial fragment of CAP37, resulted in the loss of sperm motility without disruption of the acrosomal membrane. The sperm immobilizing activity (SIA) of P20-44 was modulated by the length of incubation, the concentration of the peptide, and the pH of the assay medium. SIA induced by P20-44 was partially reversible and was unaffected by the presence of anionic heparin or seminal plasma. Similar to the antimicrobial activity of P20-44, the SIA was also dependent on the presence of a disulfide bond between cysteine residues at positions 26 and 42 and was inhibited by Lipid A. However, the mechanism of action of P20-44 on sperm is not totally dependent on the molecule's cationicity, because five other cationic antimicrobial peptides had no detectable effect on sperm viability. Thus, the mechanism of action of P20-44 on human sperm is different from its cationic antibactericidal effect. These findings established that motile human sperm are sensitive to CAP37 or its synthetic bioactive peptide and suggested that this protein could play a role in neutrophil-mediated immune destruction of sperm in the female genital tract. P20-44 of CAP37 may be useful in investigating the regulation of human sperm motility and to construct "hybrid peptides" with enhanced potency as a component of vaginal contraceptive that could doubly be effective by killing infectious agents and inhibiting sperm transport.

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