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## JOURNAL ARTICLE

# Voltage-dependent calcium channels and G regulatory protein mediate the human sperm acrosomal exocytosis induced by N-acetylglucosaminyl/mannosyl neoglycoproteins

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Mammalian spermatozoa must undergo an exocytotic event during fertilization, the acrosome reaction (AR). In most species studied this process is induced by specific glycoproteins of the oocyte extracellular matrix, the zona pellucida (ZP), and it involves guanine nucleotide-binding regulatory proteins (G-proteins), resulting in an uptake of extracellular calcium by the sperm. In the bull, this event has been reported to be mediated by voltage-dependent calcium channels (VDCC). Previous observations showed that neoglycoproteins (NGPs) with N-acetylglucosamine or mannose (GlcNAc-BSA or Man-BSA) residues induce the AR in capacitated human spermatozoa. We report here that the pretreatment of spermatozoa with 125 ng/ml pertussis toxin (PTx) inhibited GlcNAc-BSA- or Man-BSA-induced AR, whereas 1 microgram/ml cholera toxin had no effect. These data indicate that the transduction mechanism for GlcNAc-BSA- and Man-BSA-induced AR involves G-proteins of the inhibitory type (GI). An increase in the AR rate was observed when capacitated spermatozoa were incubated with increasing concentrations of potassium ions (K<sup>+</sup>) in Biggers-Whitten-Whittingham (BWW) modified medium (2.6 +/- 0.3-fold at 80 mM K<sup>+</sup>). This induction was observed only when the pH was raised to 8.5, and it was inhibited by verapamil, nitrendipine, omega-conotoxin, nickel ions (Ni<sup>2+</sup>), lanthanum ions (La<sup>3+</sup>), or cadmium ions (Cd<sup>2+</sup>) in a concentration-dependent manner, indicating the participation of VDCC activated by membrane depolarization. The GlcNAc-BSA- or Man-BSA-induced AR was completely inhibited by preincubation of spermatozoa with VDCC blockers and calcium antagonists, indicating a link between the binding of sugar residues of the NGPs and channel activation. The AR induced by membrane depolarization with high K<sup>+</sup> medium was not inhibited by PTx, suggesting that Ca<sup>2+</sup> entry is downstream to GI-protein activation. These data show that the induction of the AR in human spermatozoa by GlcNAc- or Man-NGPs involves VDCC and GI-like regulatory proteins similar to the induction described for ZP in other mammalian species.

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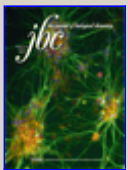
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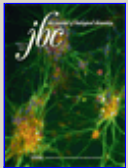
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