McGill UNIVERSITY

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Contribution of the sperm's inner acrosomal membrane proteins to fertilization

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Fertilization is the cornerstone of development where the two differentiated cells, sperm and egg set the stage for embryogenesis, for which competency of the gametes is essential. Yet only rudimentary knowledge is available on the molecules and mechanisms involved in sperm-egg interactions leading to zygotic development. This is underscored in consideration that 30-50 % of male-factor infertility cases have no known cause. Our strategy in gaining an understanding of these mechanisms is to isolate and molecularly dissect sperm compartments that are implicated in the fertilization process. The identities of the proteins provide clues to the compartment's significance and lead to the design of specific probes to test the predicted functions of these proteins during fertilization and/or spermiogenesis. Utilizing this approach, my team and I investigated the function of the inner acrosomal membrane (IAM). This sperm component plays a critical role during fertilization as it is exposed by the acrosome-reaction and then binds the sperm firmly to the zona pellucida (ZP) of the egg, a compulsory step for subsequent IAM-directed sperm penetration of this extracellular matrix. We have identified and/or localized and characterized the following IAM associated proteins: IAM38/ZPBP1/SP38, binding receptor to ZP2; MMP2 and Acrosin, potential ZP penetrating enzymes; SAMP14, plasminogen activator receptor; SAMP32/SPACA1, trans-membrane protein which potentially organizes and attaches some of these proteins to the IAM. By decreasing the sperm concentration during insemination in vitro to recreate sperm scarcity as in the fertilizing environment in vivo, it was found that the introduction of plasminogen, normally present in oviductal fluid, restored the fertilization rate to levels before the sperm scarcity was introduced. We provide evidence that plasminogen conversion occurs by a SAMP14-activating receptor mechanism on the IAM and that the resulting plasmin activity on its own and through MMP2 activation on the IAM improves sperm penetration ability not only through the ZP of the oocyte but through the cumulus as well. Our results suggest that factors present in the female reproductive tract may be able to rescue some of the sperm fertilizing deficiencies found in male factor infertility. Barriers that stand in the way of IVF include low sperm concentration in samples and failure of sperm to penetrate the ZP. In such cases, modulating the insemination conditions by addition of plasminogen could improve the success rate of IVF and reduce the time and cost of ART by reducing the need for ICSI after conventional IVF.

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