ID: 21368

PROPERTY, METABOLISM AND ROLES OF SULFOGALACTOSYLGLYCEROLIPID IN REPRODUCTION

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Sulfogalactosylglycerolipid (SGG, aka seminolipid) is expressed selectively in mammalian male germ cells. SGG biosynthesis occurs in testicular germ cells (TGCs) in both pachytene spermatocytes and round spermatids. Alkylacylglycerol (mainly palmitylpalmitoylglycerol-PPG), SGG's lipid backbone, is first galactosylated by ceramide galactosyltransferase to form galactosylglycerol (GG), which is then sulfated by cerebroside sulfotransferase to become SGG. Our biophysical studies indicate that SGG is an ordered lipid, having propensity to interact with cholesterol. Together with cholesterol, most of SGG on sperm exists in sperm lipid rafts, which have direct affinity for the egg zona pellucida (ZP). On the sperm surface, SGG co-exists with arylsulfatase A (ARSA), which also has direct ZP binding ability. Therefore SGG and ARSA likely act synergistically in sperm-egg interaction. Their co-existence on the sperm surface is due to the binding of SGG to the surface cleft of ARSA. SGG also interacts with high affinity to the active site pocket of lysosomal ARSA, resulting in SGG desulfation. In testicular seminiferous tubules (SFTs), ARSA exists in lysosomes of Sertoli cells, which are somatic cells that are important for development of TGCs into sperm. Sertoli cells are also engaged in phagocytosing residual bodies (excess cytoplasmic components of elongating spermatids) for mature sperm formation. As well, Sertoli cells phagocytose apoptotic germ cells, which amount to 50% of total TGCs. Both residual bodies and apoptotic germ cells contain SGG. Our studies using Arsa knockout mice indicate that phagocytosed SGG is targeted to Sertoli cell lysosomes for desulfation by ARSA. Presumably, galactosylceramidase would then degalactosylate GG to the backbone lipid, PPG, which can be shuttled to adjacent TGCs for a new round of SGG biosynthesis. In Arsa null mice, SGG desulfation does not occur resulting in its intracellular accumulation, a condition that is toxic to Sertoli cells. $Arsa^{-/-}$ Sertoli cells produce higher levels of H_2O_2 than age-matched wild type mice. H_2O_2 would harm developing TGCs and Sertoli cells themselves. These accruing effects lead to decreased numbers of viable TGCs, increased numbers of abnormal sperm, decreased numbers of Sertoli cells and subsequently subfertility of aging $Arsa^{-/-}$ male mice. Our results indicate the importance of sperm SGG in fertilization as well as SGG degradation in Sertoli cells in maintaining male fertility.