Spermatogenesis is a continuous and organized process that occurs throughout the adult male life, by which spermatogonia proceed through mitosis, meiosis and complex cytological transformations resulting in the formation of spermatozoa. This process requires precise and highly ordered regulation of gene expression at both the transcriptional and post-transcriptional levels. Histone methyltransferase ERG-associated protein with SET domain (ESET) represses gene expression and is essential for the maintenance of the pool of embryonic stem cells and neurons. Self-renewal and differentiation of spermatogonial stem cells (SSCs) are the foundation of spermatogenesis. In this talk, I will present our recent findings about the role of histone methyltransferase ESET on SSC survival and its molecular mechanism.