

Expression of HER2 in Mouse Testis and Spermatozoa

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Epidermal growth factor (EGF) superfamily of peptide growth factors (EGF-GFs) plays an important role in gonadal development. Activation of EGF receptors induces dimerization that gives differing responses to different ligands. Of these receptors, HER2 as a cofactor for other EGF receptors acts as a proliferation promoting oncoprotein, and have been implicated in the pathogenesis of a variety of human cancers. In an effort to investigate the role of HER2 in male fertility, the expression of HER2 was investigated in testes and epididymal spermatozoa in mice. Optimized semiquantitative RT-PCR analysis revealed that *her2* mRNA level increased during postnatal development of testis. On western blot, tyrosine phosphorylated HER2 of Mr. 185 kDa was detected in testis extract, suggesting the presence of active HER2. The germ cells within the seminiferous tubule showed varying degrees of HER2 immunoreactivity. In particular, some spermatogonia which located in the close proximity of basement membrane showed strong immunoreactivity of HER2, suggesting possible involvement of HER2 in mitotic expansion of stem spermatogonia. Sertoli cells showed moderate to strong immunoreactivity. Notably, adluminal compartment of Sertoli cell cytoplasm adjacent to the late stage of elongating spermatids showed strong HER2 immunoreactivity in adult testis. HER2 immunoreactivity was also found in Leydig cells in which signal markedly increased according to sexual maturation. In immature Leydig cells primary culture, EGF stimulated expression of *StAR* mRNA together with HER2, suggesting close relationship between EGF receptor signaling and steroidogenic activity during the ontogeny of Leydig cells. Peritubular cells were also positive for HER2 immunoreactivity. In epididymal spermatozoa, strong HER2 immunoreactivity was found in acrosome region of head, and weak signal was found in middle piece and tail, suggesting possible involvement of HER2 in

acrosome reaction and motility of spermatozoa. Taken together, present result suggests that HER2 may play an important role in signal amplification down stream of EGF GF receptor family in mouse testis and spermatozoa.