IJAE
Vol. 122, n. 1 (Supplement): 128, 2017
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Follicle-stimulating hormone receptor (FSHR) a promising novel target for cancer diagnosis in seminoma and embryonal carcinoma

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Adult testicular germ cell tumors (TGCTs) are the most frequent malignant tumors in male patients aged 15–45 years, their incidence is increasing in recent years. There are two main subclasses of TGCTs: seminomas (SE) and non-seminomatous germ cell tumors (NSGCTs). SE have histological features of primordial germ cells, whereas NSGCTs have varying degrees of differentiation (i.e. embryonal carcinoma, EC), they present distinctive clinical features and differ for therapy and prognosis. NSGCTs tend to be metastatic at presentation, and have a worse prognosis than seminomas at an equivalent stage of disease. Despite general advances in the management of TGCTs, the molecular bases underlying their progression remain almost unknown. The effects of the Follicle-stimulating hormone (FSH), central hormone in mammalian reproductive biology, are mediated by FSHR, which was believed to be expressed primarily in ovary and testis. Recently, FSHR expression has been shown in the blood vessels of different solid tumors, including prostate, urothelial and breast carcinomas, suggesting a role in neoangiogenesis. The expression of FSHR at the periphery of tumors, also suggests that FSHR may be of relevance to the metastatic process. In normal human testis, estrogen physiological actions are mediated by estrogen receptor (ER) β and highly variable ERβ expression has been reported in the different TGCTs. ERβ loss is associated with advanced tumor stage in several cancers and previously, we showed a higher expression of ERβ1 in SE with respect EC. In this study, we evaluated the expression of FSHR in normal and neoplastic human testis tissues. Further, we compared FSHR expression with that of ERβ1 in the same samples. In normal testes, immunohistochemical studies showed the presence of FSHR prevalently in somatic testicular cells, while ERβ1 is expressed both in somatic and germinal testicular cells. Intriguingly, we discovered that FSHR was strongly expressed in EC and absent in SE. Conversely, immunostaining for ERβ1 revealed higher intensity in SE as compared to EC. These data suggest distinct physiopathological roles for the two receptors in TGCTs progression, being ERβ1 protective and FSHR harmful. Our data report for the first time the expression of FSHR in TGCTs, suggesting its possible involvement in testicular carcinogenesis. FSHR may be considered an useful molecular marker to distinguish seminoma from embryonal carcinoma, the most common TGCTs subtypes, and this could be informative in clinical decision making and patient counseling.

Keywords
FSHR, TGCTs, seminoma, embryonal carcinoma