BRCA1 and BRCA2 protein expressions in an ovotestis of a 46, XX true hermaphrodite

ABSTRACT

BRCA1 and BRCA2 breast cancer susceptibility genes encode proteins, the normal cellular functions of which are complex and multiple, and germ-line mutations in individuals predispose both to breast and to ovarian cancer. There is nevertheless substantial evidence linking BRCA1 and BRCA2 to homologous recombination and DNA repair, to transcriptional control and to tissue proliferation. There is controversy regarding the localization of BRCA1 and BRCA2 proteins to either nucleus or cytoplasm and whether the expression is present in premeiotic germ cells or can still be expressed in mitotic spermatogonia. We report herein an immunohistochemical study of BRCA1 and BRCA2 distribution in a rather unsual tissue (an ovotestis), which addresses this issue.

INTRODUCTION

Introduction Hereditary predisposition to breast cancer can be attributed to germline mutations in the BRCA1 or BRCA2 breast cancer susceptibility genes. Germline mutations in the BRCA1 and BRCA2 genes are associated with the development of breast and ovarian cancers. BRCA2 is associated the development of breast cancer in both women and men, and a moderate increased risk for the development of ovarian cancer. Zabludoff et al investigated the tissue distribution of Brca1 mRNA in adult mouse tissues and reported that Brca1 mRNA levels were most abundant in the testis and the ovary. They also found that high level Brca1 mRNA expression in the testis of mice was detected in meiotic cells and postmeiotic round spermatids and, in contrast, little or no Brca1 mRNA was expressed in premeiotic germ cells. A low level of Brca1 mRNA was also detected in Sertoli cells. Blackshear et al, on the contrary, demonstrated in the mouse that Brca1 and Brca2 mRNA are expressed in mitotic spermatogonia in addition to early meiotic prophase spermatocytes; Sertoli cells and Leydig interstitial cells were found consistently negative for Brca1 and Brca2 transcripts. In the normal mouse adult ovary, Brca1 and Brca2 transcripts were localized specifically to granulosa cells, thecal cells and oocytes of developing follicles as well as luteal cells of recently formed corpora lutea and surface epithelium. Considering these results, we further investigated the presence of human BRCA1 and BRCA2 proteins in an ovotestis by immunochemical analysis with a different panel of antibodies against BRCA1 and BRCA2.

CONCLUSION

In conclusion, we show using different antibodies that BRCA1 proteins, like BRCA2, are widely expressed in two varieties of non-embryogenic human tissues associated with the cell cycle. BRCA1 and BRCA2 proteins are expressed during growth and differentiation in the ovary. Moreover, they are expressed beyond the spermatogenesis. This is consistent with proposed functions for BRCA1 and BRCA2 genes.