ANALYSIS OF BRCA1 GENE METHYLATION IN GLIOMAS AND MENINGIOMAS

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Objective

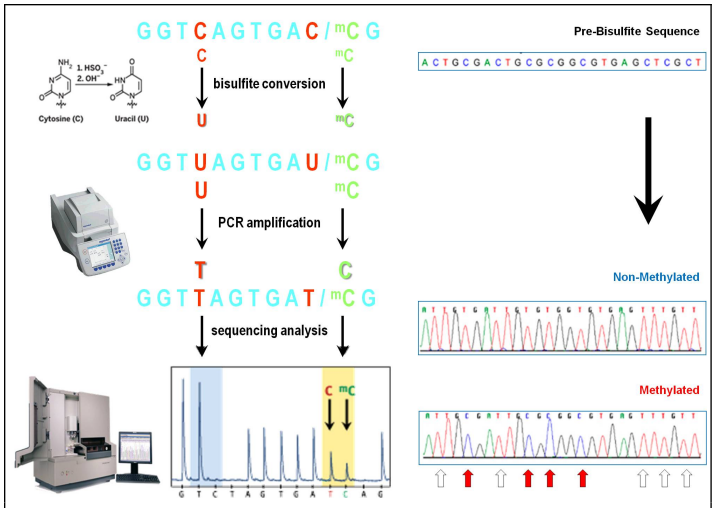
We aim to analyze the methylation status of *BRCA1* in gliomas and meningiomas of different histopathological grades.

Introduction

The methylation of tumor suppressor genes has been implicated as an important mechanism triggering the tumorigenesis. *BRCA1* (17q21) are classically associated with susceptibility to hormone-dependent cancers, especially breast and ovarian tumors. The higher incidence of meningiomas in females and the proliferation in response to hormones prompted the possible impact of *BRCA1* methylation in menigothelial tumors and stirring interest for your research also in glial tumors.

Methods

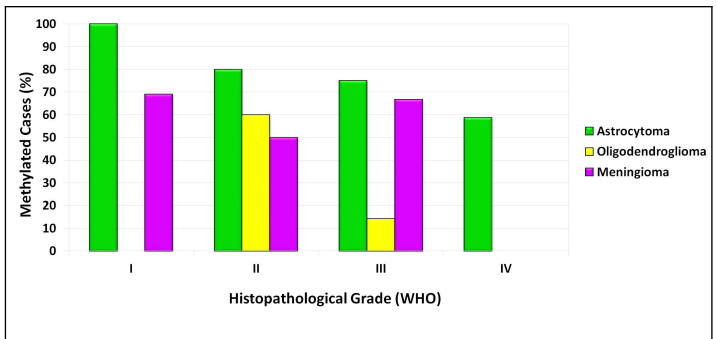
We analyze the methylation status of *BRCA1* by MSP-PCR in 42 gliomas (30 astrocytomas and 12 oligodendrogliomas) and 33 meningiomas of different histopathological grades.



Schematic illustration of sodium bisulfite treatment and methylation-specific PCR (MSP) followed by DNA sequencing for the study of DNA CpG methylation.

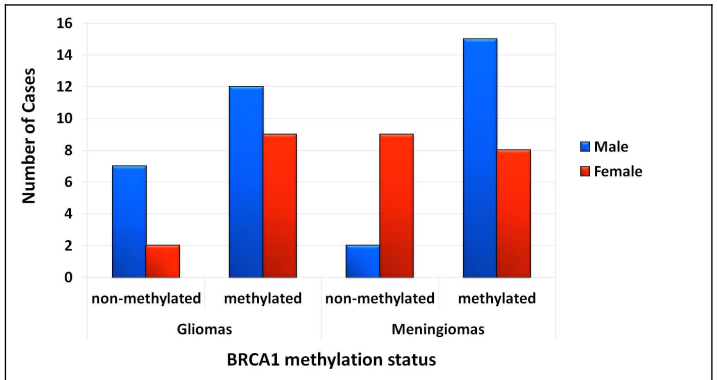
Results

- The distribution by age, sex, tumor location and histopathology of patients reproduced, in general, global trends;
- *BRCA1* methylation was observed in 60% of tumors (70% of astrocytomas, 33% of oligodendrogliomas and 58% of meningiomas);
- The occurrence of methylation tended to decrease in high grade tumors;



Percentages of methylated cases for BRCA1 according to histopathological grade of gliomas and meningiomas.

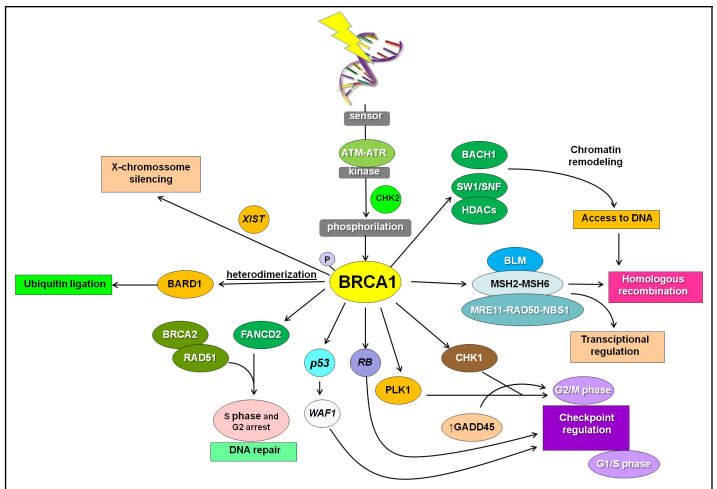
- For meningiomas, an association between *BRCA1* methylation and male gender was evident (p=0.0009);
- Astrocytomas showed a higher rate of methylation compared to oligodendrogliomas (p=0.01).



Distribution of cases by gender according to BRCA1 methylation status in gliomas e meningiomas.

Discussion

It is suggested that the *BRCA1* methylation in gliomas may be associated to the TP53 gene alterations and its reduction among the most malignant tumors reflects the smaller contribution of this suppressor compared to other genetic alterations, such as EGFR amplification. In meningiomas, *BRCA1* methylation seems to leave the meningothelial cells mercy to the mitogenic effects of estrogen, especially in low hormonal rate condition. Additionally, the absence of *BRCA1* for DNA repair could contribute to the accumulation of more genetic disorders that lead to the oncogenesis.



Functional meaning of BRCA1 in various cellular regulatory pathways, with emphasis on the activation of tumor suppressor p53.

Conclusions

We concluded that BRCA1 methylation represents a frequent epigenetic phenomenon in gliomas and meningiomas, notably occurring inversely proportional to the tumor grade. Moreover, BRCA1 methylation appears to be a key point in the appearance of meningiomas in males. Further research should better characterize this molecular alteration, as well as assess its functional meaning in tumorigenesis.