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Differential expression of *GSPT1* GGC_n alleles in cancer

- Joana Malta-Vacas[a],
- Paula Ferreira[a],
- Carolino Monteiro[b],
- Miguel Brito[a],

- [a] Higher School of Health Technology of Lisbon, Polytechnic Institute of Lisbon, Av. D. João II, Lote 4.69.01, 1990-096 Lisbon, Portugal
- [b] Faculty of Pharmacy, University of Lisbon, Av. Prof. Gama Pinto, 1649-003 Lisbon, Portugal

Abstract

The human eukaryotic release factor 3a (eRF3a), encoded by the G1 to S phase transition 1 gene (*GSPT1*; alias *eRF3a*), is upregulated in various human cancers. *GSPT1* contains a GGC_n polymorphism in exon 1, encoding a polyglycine expansion in the N-terminal of the protein. The longer allele, GGC_{12}, was previously shown to be associated to cancer. The GGC_{12} allele was present in 2.2% of colorectal cancer patients but was absent in Crohn disease patients and in the control group. Real-time quantitative RT-PCR analysis showed that the GGC_{12} allele was present at up to 10-fold higher transcription levels than the GGC_{10} allele ($P < 0.001$). No *GSPT1* amplifications were detected, and there was no correlation between the length of the alleles and methylation levels of the CpG sites inside the GGC expansion. Using flow cytometry, we compared the levels of apoptosis and proliferation rates between cell lines with different genotypes, but detected no significant differences. Finally, we used a cytokinesis-block micronucleus assay to evaluate the frequency of micronuclei in the same cell lines. Cell lines with the longer alleles had higher frequencies of micronuclei in binucleated cells, which is probably a result of defects in mitotic spindle formation. Altogether, these findings indicate that *GSPT1* should be considered a potential proto-oncogene.

Corresponding author. Tel: +351-218980400; fax: +351-218980460.