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CpG Islands methylation alterations in cancer: Understanding the functional role of these security locks and their use as early tumour biomarkers

DNA methylation is an epigenetic modification consisting in the addition of a methyl group to a cytosine in a CpG context. In normal mammalian cells, CpG islands, mostly concentrated at promoter regions, are protected from DNA methylation, while intergenic and repetitive regions are normally hypermethylated. In cancer cells, a massive change in the global methylation pattern occurs. Intergenic and repetitive regions of the genome become hypomethylated leading to the reactivation of transposable elements and genomic instability. In contrast, a focal hypermethylation of CpG islands at promoter regions occurs and it is normally associated to gene expression downregulation. Thus, aberrant DNA methylation is one of the most striking features of cancer cells and several studies have demonstrated that cancer-specific methylation patterns exist. For this reason, DNA methylation represents an extremely useful biomarker for several applications, including cancer risk definition, prediction of clinical outcomes, treatment response and cancer relapse. From a functional point of view, the association between DNA methylation and gene expression, although notoriously recognized, is not yet fully known. In our laboratory we identified early DNA methylation alterations in colorectal cancer, localization-specific changes in low-grade gliomas, alterations that predict the risk of developing chronic lymphocytic leukemias years before diagnosis and correlating with the aggressiveness of the disease. A feature shared by almost all these alterations is that hypermethylation targets CpG islands associated with genes poorly expressed in the tissue where cancer occurs. We have undertaken an expression study for each gene associated with these alterations, showing further downregulation.

Biography

Patrizia Zavattari, received the MSc. degree in Biological Sciences at Pisa University (Italy) and the PhD at Cagliari University (Italy). She is Associate Professor of Experimental Biology and Genetics at Cagliari University, teaching in the Faculties of Biology, Pharmacy and Medicine. She is the Head of a Molecular Biology, Genomics and Epigenomics Laboratory. Her research interests are mainly focused on molecular oncology and complex traits. She worked both abroad (Paris, Oxford, Cambridge, Philadelphia) and in Italy (Milan, Novara). She is co-author of about forty publications. Since 2011 she is Review Editor of Frontiers and she reviews for various scientific journals.

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