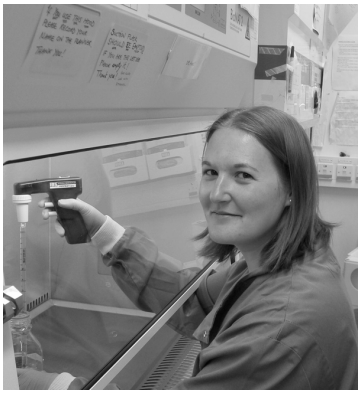
Institut Européen de Chimie et Biologie

I E C B

Ribosome alterations in cancer: impact on translational control and tumorigenesis.



Virginie MARCEL
Cancer Research Center of Lyon (CRCL), FRANCE

Ribosomes are specialized entities that participate in regulation of gene expression during the translation of mRNA into protein through their ribozyme activity carried by ribosomal RNAs (rRNA). In cancer cells, ribosome biogenesis is overactivated inducing a global increase in protein synthesis. In addition, few studies reported that protein composition of ribosome is modified by genetic mutations leading to increased cancer susceptibility. We recently reported that rRNA composition is altered during cancer progression using human mammary epithelial cell lacking p53 expression. We observed that rRNA methylation pattern is modified at some given sites, located within catalytic domains of ribosome. Indeed, we showed that p53 represses expression of the rRNA methyl-transferase fibrillarin (FBL) by binding directly to FBL. Alteration of rRNA methylation induce by p53 inactivation is accompanied by impairment of translational fidelity and an increase of internal ribosome entry site (IRES)-dependent translation initiation of key cancer genes. Moreover, FBL overexpression contributes to tumorigenesis and is associated with poor survival in patients with breast cancer. Thus, p53 acts as a safeguard of protein synthesis by regulating FBL and the subsequent quality and intrinsic activity of ribosomes.

Institut Européen de Chimie et Biologie
2, rue Robert Escarpit - 33607 Pessac, France
Tél. : +33(0)5 40 00 30 38 - Fax. : +33(0)5 40 00 22 15
www.iecb.u-bordeaux.fr