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

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Recent advances revealed unexpected capabilities of ribosome in controlling translation. The "specialized ribosome" concept proposes that depending on cellular and physiological contexts, ribosome variants are produced allowing differential translation of mRNAs subsets. Ribosomal RNA (rRNA) carry a ribozyme activity and are a source of ribosome heterogeneity. More than 200 chemical modifications, including 2'-O-ribose methylations have been identified so far that can be modulated individually thus opening up the possibility of numerous combinations and associated regulatory effects.

The potential role of rRNA heterogeneity in cancer will be discussed. The story starts with our discovery that modifications of rRNA methylation can occur during tumor initiation and progression (1,2). Modification of rRNA methylation pattern is associated with change in translational control of mRNAs encoding oncogenic proteins. We and others also revealed a novel facet of the tumor suppressor p53 protein, which can be now considered as a player of translational regulation through an unexpected mechanism involving the ribosome (3,4).

We developed approaches to decipher the role of rRNA methylation in controlling translation during tumorigenesis and during treatment with anti-cancer molecules such as 5-FU (5). Analyses of human samples series issued from different cancer types allowed identification of components involved in ribosome biogenesis and rRNA methylation as independent markers of poor prognosis (6-8). Interestingly, these components are involved either in the global or site-specific modulation of rRNA methylation pattern. Using bi-cistronic assays, *in vitro* translation and translatome analysis, we show that modulation of expression of rRNA methylation components associated with cancer patients' outcome affect translational fidelity and translation initiation of subsets of mRNAs promoting tumorigenesis and escape to anti-cancer treatments (9-12).

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