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Submission of a revised manuscript (invited review)

Dear editors,

Many thanks for considering our manuscript for publication in *World Journal of Clinical Oncology*. We revised our article according to the reviewer's comments/suggestions. Here is a point to point response.:

- Summarizing section: we added a table (Table 1) that summarizes the main message of the review.
- Second sentence at the beginning of section 2.1: to clarify this paragraph we reorganized it as follows: "Knockdown of p53 in cellular models of breast and colon cancer resulted in the overexpression of Fibrillarin at both the mRNA and protein levels. It is suggested that tumorigenesis associated to mutated P53 promotes an increase in the methylation status of rRNAs, which alters their ribozyme activity, thus affecting their translation fidelity and rate."
- Second paragraph of section 2.1: We have revised this section by slightly modifying it: "Translation of these proteins relies on internal ribosome entry site (IRES) in the mRNA, which is a 5' cap-independent translation mechanism that may be used in specific conditions. The inhibition of rRNA methylation was shown to impair IRES translation initiation by perturbing the association of the 40S and 60S subunits (Basu et al., 2011). Therefore, it is conceivable that enhanced ribosomal methylation increases the translation of IRES-containing mRNAs"
- Page 10, we added the suggested reference by Penzo et al. after the sentence: "A recent review by Penzo et al. reports"



the functional roles of pseudouridines and related human pathologies.”

- Figures: We have fully redesigned Figure 1 and Figure 3. We also eliminated Figure 2 as its message is now in Table 1. We also adjusted the legends.

We hope that our revised manuscript will be accepted for publication in *World Journal of Clinical Oncology* and look forward to hearing from you.

Yours sincerely,

Steve Pascolo