INTERPLAY BETWEEN MITOCHONDRIAL RIBOSOMAL PROTEIN S18-2 AND RETINOBLASTOMA ASSOCIATED PROTEIN IN REGULATION OF CELL STEMNESS AND DIFFERENTIATION

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Background: We have found that S18-2 is involved in regulation of the RB-dependent pathway. It binds to both hypo- and hyperphosphorylated RB. The binding between RB and S18-2 is promoted when cytoplasmic S18-2 is targeted to the nucleus, and this disrupts the association of E2F1 with RB, as indicated by the increased level of free E2F1 in the nucleus. This presumably lifts the RB-dependent block to S-phase entry in the cell cycle. We have also found that overexpression of the human S18-2 immortalized primary rat embryonic fibroblasts (REFs) that showed properties of embryonic stem cells. Elevated expression of S18-2 in stem cells (our findings and analysis of published microarray data) raises the question of whether this protein co-operates with the RB protein in differentiation and cancerogenesis. **The aim:** We wanted to seek a connection between the expression of RB and S18-2 in -/-Rb1 MEFs and stemness. We hypothesized that simultaneous expression of both proteins at the high levels might support stemness. **Methods:** Transfections, inoculation into SCID mice, directed differentiation, q-PCR, immunostaining, immunohistochemistry, western blotting. **Results:** We showed that S18-2 protein, together with RB, plays a crucial role in cell de-differentiation. We have found that overexpression of S18-2 and RB is needed for maintenance of cell stemness. Such cells can differentiate into various cell lineages under certain conditions. **Conclusion:** The presence of RB and simultaneous expression of S18-2 at high levels are required for the cell stemness.

[1] *Mushtaq M, et al. Oncotarget. 2016, in press, PMID: 27489352.*
[2] *Mints M, et al. Oncotarget. 2016, 7(16):22150-8.*
[3] *Darekar SD, et al. Oncotarget. 2015, 6(25):21016-28.*

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