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Investigate the effect of rapamycin in senescence and chromatin remodelling

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Cellular senescence is an irreversible state of proliferation arrest characterized by a number of markers, such as changes in cell morphology, increased senescence-associated β-galactosidase activity (SA-β-gal), altered chromatin and nuclear structure and production of Senescence-Associated Secretory Phenotype (SASP). Cellular senescence is considered as a tumor suppressor mechanism and it could also play an important role in ageing process. The mammalian TOR protein (mTOR) has been found to promote cellular senescence by different pathways and rapamycin (the inhibitor of TORC1) shows potential in delaying this processes, and hence ageing. In this research, we investigated the role of rapamycin in the onset of senescence. Our findings showed some potential for rapamycin in reversing some senescence markers, for example, the reduction of SA-β-gal, IL-6, p16 and p21. In terms of the effects of rapamycin on histone modifications, the results showed that rapamycin did not reverse histone modifications that are caused by senescence (H4K20me3, H4K16ac). On the other hand, some epigenetic regulator genes showed an increase of expression when treated with rapamycin (CHRAC1) and some showed no obvious changes (EZH2). SIRT1 (a histone deacetylase) was downregulated after rapamycin treatment at the protein level, whereas the RNA data showed a slight increase. These findings might suggest and support the idea that rapamycin could have the effect in delaying or decelerating specific features of cellular senescence, including SASP. These effects might be mediated independent of chromatin regulation. Alternatively, they might be controlled by chromatin, but these mechanisms are not targeted by rapamycin.

Biography

Buthaina Al Shueili graduated in Biotechnology from Sultan Qaboos University. She completed her Master's degree in Biomedical Science (Cell Engineering) from University of Glasgow. She currently works as an Academic Lecturer in Biology department, Sultan Qaboos University, Oman.

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