The effect of Rapamycin on growth and productivity of an industrially-relevant recombinant CHO cell line and in relation to changes in mTOR signalling pathway

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Due to the high medical and commercial value of recombinant proteins for clinical and diagnostic purposes, the study of conditions that enhance the growth and productivity of host cell lines is a major research field in the biopharmaceutical industry. In this study, the cellular and molecular outcome of chemical manipulation of the mTOR complex 1 by Rapamycin was examined in a recombinant protein producing Chinese hamster ovary cell line during batch culture. Treatment with Rapamycin stalled the growth of the host cells only briefly and this effect was transient. The specific productivity increased in the beginning of batch culture and the longevity of culture and the final antibody yield were greater. Analysis of the downstream targets of mTORC1 in response to Rapamycin suggested that S6K1 regulation is crucial for cell growth in CHO cells. However, alternative pathways may counter-regulate the effect of inactivated S6K1 with long-term or continuous Rapamycin treatment. Since Rapamycin did not affect the phosphorylation of 4E-BP1 and the rate of global translation, we conclude that regulation of 4E-BP1 plays a more significant role than S6K1 in maintenance and control of recombinant protein synthesis.