CHARACTERIZATION OF S6KS ISOFORMS IN A MODEL OF PROSTATE CANCER

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Introduction and objectives: Cancer is one of the major current causes of mortality worldwide and therefore a very important public health issue. Over the last years, mTOR signaling pathway have been shown to be deregulated in a variety of human cancers, which is not entirely unexpected, since it is a critical regulator of cell growth and metabolism. Aiming to better understand the biochemical and metabolic processes related to cancer, we explored the molecular functions of a family of proteins activated by mTOR, the ribosomal S6 kinases (S6Ks), in a model of prostate cancer.

Materials and methods: In vitro, we investigated the role of S6Ks isoforms (p70-S6K1, p85-S6K1 and p54-S6K2) in cell proliferation, viability, migration and resistance to chemotherapy by overexpressing S6Ks genes and by knocking them down with shRNA delivered by lentivirus in PC3 prostate cancer cell line. Experiments were also performed in vivo, using prostate cancer cell line PC3-luc expressing the luciferase reporter gene, by injecting these cells into Nude mice and measuring tumor growth. Results: So far, our results showed that the knockdown of all S6Ks isoforms, but mainly p54-S6K2, significantly reduced cell migration, colony formation and resistance to docetaxel in PC3-luc cells. In vivo preliminary results showed that the injection of PC3-luc cells overexpressing S6Ks isoforms caused increased tumor growth in Nude mice when compared to control. Conclusions: These data suggest that S6Ks play a relevant role in tumor growth and resistance to chemotherapy in prostate cancer and might be a potential target for future anticancer therapies.

Key words: S6K, cancer, prostate