Category: Keynote presentation

Title of Presentation: p90RSK as new molecular target in tumors with activated MAPK pathway

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In most human tumors, the MAPK pathway is constitutively activated due to several upstream oncogenic mutations. Since p90RSK is a downstream substrate of MAPK, it is often hyperactive and capable of phosphorylating substrates involved in tumorigenesis. We have previously demonstrated that in follicular thyroid carcinomas MDM2 is a substrate of p90RSK, this phosphorylation increases the stability of MDM2 and promotes p53 degradation. Therefore, the inhibition of p90RSK leads to an increase in the expression of p53 which, in turn, inhibits cell proliferation by transcriptionally upregulating the cell cycle inhibitor p21 and promotes apoptosis through modulation of Bax and Bcl-2. In the present study, by selecting p53wt melanoma, lung cancer, and medullary thyroid carcinoma cell lines with highly active p90RSK, we confirmed the role of the p90RSK/MDM2/p53 pathway in the regulation of the cell cycle and apoptosis. In conclusion, we demonstrated that p90RSK regulates cell proliferation and survival by controlling p53wt levels through phosphorylation of S166 of MDM2 in different tumors characterized by constitutive activation of the MAPK pathway, as occurs in p53wt follicular thyroid carcinomas.