Aurora Kinases Mediate Wnt/β-catenin Pathway in Adrenocortical Tumor Cells

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INTRODUCTION: Adrenocortical cancer (ACC) are tumors with low incidence and there is no effective therapy for patients with advanced or metastatic disease. Therefore, discovery of new therapeutic targets is of great importance for ACCs treatment. Dysregulation of Aurora kinases showed to be associated with tumorigenesis and drugs that inhibit Aurora kinase activity are available showing great efficacy in tumor growth control. Studies reveal a crosstalk between Aurora kinase A and SMAD5, a protein that promotes epithelial-mesenchymal transition (EMT) and invasion in cancer cells. Molecular markers for EMT include decreased expression of E-Cadherin, nuclear localization of β-catenin and up-regulation of genes related to the Wnt/β-catenin pathway, such as Cyclin D1 and c-myc. To date, overexpression of beta-catenin in ACCs has been correlated with worse prognosis. **OBJECTVES:** To study whether the pan Aurora kinase inhibitor, AMG 900, has a role in the Wnt/β-catenin pathway and in the β-catenin nuclear translocation. **MATERIAL AND METHODS:** H295A cells were synchronized in mitosis with colchicine and treated with AMG 900 for 6, 24 and 48 hours. Total and enriched nucleus and cytosol proteins were obtained by different centrifugation grades and detergents. Western blotting was performed for protein expression and subcellular localization. **RESULTS AND DISCUSSION:** Treatment of H295A cells with AMG 900 for 48 hours showed decreased expression of β-catenin. After 6 hours of treatment, there is no difference in the β-catenin expression levels in the nucleus and cytosol; however, we found decreased expression of Cyclin D1, one of the main products of β-catenin nuclear translocation and we found 2 folds increased expression of E-cadherin after 24 hours of treatment with AMG 900, suggesting that Aurora kinases may play an important role in the EMT process. **CONCLUSION:** Our results suggest that Aurora kinases might be involved in EMT process during tumor development acting through the β-catenin pathway.

Key words: Adrenocortical Tumor, Aurora kinase, β-catenin
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