INTRODUCTION

Few effective medical treatment options are available for adrenocortical carcinoma (ACC). Intensive efforts are going on for exploring novel pathways and treatment targets. In our previous functional genomics study, retinoid signaling via the retinoid X receptor (RXR) was identified as a major pathogenic pathway in ACC and we have demonstrated the in vitro activity of 9-cis retinoic acid (9-cisRA) acting via the RXR on NCI-H295R cells. In this present study we have investigated the antitumoral effects of 9-cisRA and mitotane on ACC in vivo in a large-scale xenograft model.

METHODS

− 43 male H295R xenografted SCID mice in four groups (i. control, corn oil; ii. mitotane, 200 mg/kg; iii. 9 cisRA, 5 mg/kg; iv. combined, 200 mg/kg mitotane, 5mg/kg 9-cisRA)
− Protein isolation
− 3 protein sample/groups for LC-MSMS analysis
− Validation of one selected protein with Western-blot
− Pathway-analysis with David 6.7
− Western blot of 2-2-2 sample from physiologic, benign and malignant adrenal tissues

RESULTS

− 47 significant protein changes found with proteomics between the combined and control groups
− Protein SET was validated by Western-blot to be significantly underexpressed in the combined treated group relative to control
− Protein SET was found weekly expressed in human ACC tissue samples
− Proteins affected in p53- and Wnt-pathways were found
− Pathways linked to the ribosome and proteasome were identified

CONCLUSIONS

1. The SET protein might be a novel player in ACC biology, but its pathogenic relevance need to be confirmed
2. We have identified that combination of 9-cisRA and mitotane influences several pathways involved in ACC pathogenesis