AREG regulates expression of nucleolar proteins and stimulates growth of renal cancer

P-32-069

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Background: Clear cell renal cell cancer (ccRCC) is characterized by dysregulated nucleolar morphology that correlates with tumor malignancy. In our recent study we found that ccRCC cells of advanced tumors secrete amphiregulin (AREG) (Poplawski et al., 2023). Here, we hypothesized that AREG may contribute to the growth and nucleolar dysfunction of ccRCC tumors.

Methods: ccRCC cell line 786-O was stably transduced with GFP plasmid expressing AREG or empty vector. AREG expression was verified using qPCR and ELISA. Proteomic analysis was performed using LC-MS/MS. The cells were subcutaneously inoculated into the flanks of immunodeficient nude mice (approved by the local Ethics committee). Tumor growth was monitored weekly for at least 5 weeks. Following mice sacrifice, tumors were weighted and pulmonary metastasis was monitored.

Results: ELISA and LC-MS/MS confirmed increased secretion of AREG in the transfected cells. Tumors resulting from 786-0-GFP-AREG cells were statistically significantly bigger when compared with control cells. Proteomic analysis revealed that AREG overexpression altered expression of 343 proteins. Gene Ontology analysis revealed that the top enriched cellular compartment was the nucleolus. 77 out of the 343 altered proteins were confirmed as associated with nucleolar morphology/function.

Conclusion: AREG induces growth of ccRCC tumors in vivo and affects expression of nucleolar proteins.

Financed by National Science Centre grants 2018/29/B/NZ5/01211 and 2019/35/B/NZ5/00695.

References:

Popławski P et al (2023) Stem Cell Res Ther 2023, 14(1):200.