AB054. SOH23ABS_054. Under-expression of serine-arginine protein kinase 1 (SRPK1) in mucinous colorectal cancer, mediates resistance to oxaliplatin

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Background: Approximately 10% of all colorectal cancers (CRCs) are mucinous. Mucinous CRCs are resistant to multiple chemotherapy agents, including oxaliplatin. Serine-arginine protein kinase 1 (SRPK1) is an enzyme, which modulates the activity of multiple splicing factors. The objectives of this study were to evaluate SRPK1 expression in mucinous CRC and investigate its potential role in oxaliplatin resistance.

Methods: Immunofluorescence staining with SRPK1 of tumour microarrays (TMAs) were performed to compare expression between mucinous and non-mucinous rectal cancers. Levels of SRPK1 protein expression were analysed in LS174T (mucinous CRC) and HCT116 (non-mucinous CRC) cell lines by western blot. Cell death was investigated by flow cytometry. LS174T cells underwent transfection with an SRPK1 lentivirus activation plasmid.

Results: Our TMA cohort included 15 mucinous and 40 non-mucinous rectal cancers. SRPK1 was found to be under-expressed in our mucinous group compared to the non-mucinous cohort (P=0.014). Similarly in our cell line model, SRPK1 was found to be under-expressed in our mucinous CRC cell line (P=0.007). Treatment with oxaliplatin resulted in a significant increase in cell death in non-mucinous CRC cells (P=0.007), but not in mucinous cells. Following transfection of the mucinous CRC cells with an SRPK1 activation plasmid; mucinous cells demonstrated a significant increase in sensitivity to oxaliplatin (P=0.029). Pathway analysis found the AKT/mTOR axis to be differentially activated in mucinous cells, as compared to non-mucinous cells or SRPK1 up-regulated mucinous CRC cells.

Conclusions: Under-expression of SRPK1 in mucinous CRC results in resistance to oxaliplatin, which may be mediated via the AKT/mTOR pathway.

Keywords: Mucinous; colorectal cancer (CRC); serine-arginine protein kinase 1 (SRPK1); oxaliplatin resistance; AKT/mTOR

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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