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Cause of tumour resistance to angiogenesis inhibitors identified

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A new study conducted by MedUni Vienna in collaboration with scientists from Hungary and Sweden has now shown for the first time that the success of specialised drugs to inhibit blood supply to tumours – so-called angiogenesis inhibitors – is compromised by the fact that these drugs do not effectively penetrate the tumour tissue and so do not reach the smallest blood vessels in the tumour.

Angiogenesis – the formation of new blood vessels from existing ones – significantly contributes to tumour growth, since tumours need oxygen and nutrients to progress. Several drugs are aimed at inhibiting angiogenesis. However, the benefit of this specialised cancer treatment does not always last long and certain types of cancer hardly respond to it, if at all. This resistance to angiogenesis inhibitors is a widespread problem in everyday clinical practice.

The scientists involved in the study have now shown that penetration of these angiogenesis inhibitors within the tumour tissue is quite variable. This means that only a few cancer cells are reached by an effective concentration of the drug.

In the international study, tumours were treated with five different angiogenesis inhibitors in a mouse model. Using a new imaging process (Matrix-Assisted Laser Desorption Ionization Mass Spectrometry Imaging; MALDI-MSI), the scientists were able to measure the concentration and distribution of the cancer drug in the tumour tissue and correlate them with the drug's efficacy.

Lead investigator Balazs Döme, Head of the Translational Thoracic Oncology programme at the Division of Thoracic Surgery at the Medical University of Vienna, says: "Previous research into the mechanisms of resistance to angiogenesis inhibitors predominantly focused on molecular factors. By focusing on the inhomogenous and therefore suboptimal distribution of the active agents in the tumour tissue, our team was able to identify an important mechanism that explains why angiogenesis inhibitors are sometimes ineffective in clinical use."

Joint lead investigator György Marko-Varga, Head of the Clinical Protein Research and Imaging research group at the Division of Biomedical Research of Lund University in Sweden adds: "The diminished efficacy of this cancer treatment is also probably due to the fact that it was previously impossible to reliably image the distribution of the drugs in the tumour tissue. Our new method therefore offers cancer researchers and oncologists the opportunity to gain a better understanding of how these drugs behave and how they are distributed in the body and the tumour tissue."

The results of this study, which have been published in the journal "Theranostics", should subsequently lead to the development of new treatment strategies to improve the distribution and efficacy of angiogenesis inhibitors in tumour tissue in the future.

More information: Szilvia Torok et al. Limited Tumor Tissue Drug Penetration Contributes to Primary Resistance against Angiogenesis Inhibitors, *Theranostics* (2017). DOI: 10.7150/thno.16767

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