Phenotyping mitochondrial metabolism in oral and oesophageal cancer: respiratory capacity in cancer cell lines and human oesophagus biopsies

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In 2018, 18 million people worldwide were diagnosed with cancer, with an incidence of 5.5% and a 5-year survival rate of 18-30% for oral and oesophageal cancer (OOC).[1] Two of the main causes for the devastating influence of OOC are the lack of convenient biological markers for its diagnose and effective treatment options. Metabolism of cancer cells is highly adaptable with great plasticity of metabolic pathways, providing key characteristics for survival and spreading.[2] In the last decade, alterations of the pH in the cancer microenvironment and its intracellular regulation emerged as a modulator of cell metabolism.[3] Therefore, we want to address the influence of extracellular and intracellular pH (pH_e and pH_i) on the metabolism of human oral cell lines (HOK/NOK; DOK and UPCI-SCC090) using High-Resolution FluoRespirometry (O2k, Oroboros Instruments). The contribution of the glycerol 3-phosphate pathway to mitochondrial respiration was compromised at high pH_i in UPCI-SCC090 cells.

Glycerol 3-phosphate is a crosslink between penthose phosphate and glycolytic pathways. Therefore, pH_i and glycerophosphate dehydrogenase presents a possible target for cancer treatment.

In addition, we study the mitochondrial metabolic fingerprint of human biopsies obtained during diagnostic endoscopy in patients suspected for Barrett‘s oesophagus to correlate it with pathohistological reports. This blinded study is ongoing, aimed at finding metabolic biomarkers for the different stages of cancer development such as inflammation, metaplasia, dysplasia and adenocarcinoma.

Key words: oral cancer, mitochondrial physiology, ROS, pH, oesophagus, human tissue

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