Using exogenous volatile organic compound (EVOC) probes to target tumour-associated aldo-keto reductase activity: a potential tool to detect lung cancer

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Aims

Evaluate the expression of ALKs associated with aldol/retroaldol metabolism in lung cancer and non-neoplastic cancer samples.

• Detecting ALK-associated alcohols and aldehydes from in vivo breathspace using gas chromatography-mass spectrometry (GC-MS) techniques as a tool to detect breath samples.

• Assessing the impact of ALK inhibition on VOC levels in in vivo samples.

1. Background and Objectives

Cancer metabolism represents a promising and largely untapped area in cancer research. Rapid growth, poor blood flow and persistent genetic errors in neoplastic tissue expose cells to hypoxia, leading to the generation of reactive oxygen species (ROS) through aerobic glycolysis. These ROS drive cellular proliferation, inflammation, and genomic instability. ALKs are an enzyme family that is upregulated in some cancers as an adaptation to hypoxic conditions. ALKs can be targeted for the development of therapeutic agents (‘alkyl-selective agents’).

Our hypothesis is that a similar approach can be used in lung cancer. AKRs are involved in the metabolism of aldehydes to alcohols and play a role in generating ROS, therefore targeting these enzymes could lead to improved cancer detection.

2. Method

2.1. Preclinical samples were analysed using the same GC-MS workflow used for the detection of VOCs in clinical breath samples (Breath Biopsy). We are seeking to investigate whether AKRs can be targeted as early detection of cancer sensitive markers. This can be measured in breath using Breath Biopsy.

2.2. Microarray analysis of AKR1B10 gene expression in lung cancer cell lines H460 and A549 cells. A) Western blot analysis showing that two different levels of inhibitions are observed with this compound treatment depending on the cell line used.

3. Results and Discussion

3.1. AKR1B10 knockouts. The clone without reduced expression of AKR1B10 gene

3.2. AKR1B10 and AKR1B15 knockouts. (A) Monitoring AKR activity in lung cancer cells using microarray analysis. (B) Western blot analysis showing that two different levels of inhibitions are observed with this compound treatment depending on the cell line used. EVC Probes targeting AKR metabolic activity as a tool for early detection of lung cancer.


4. Conclusions

• AKR enzymes are potential targets for EVOC probes to detect lung cancer.

The data collected is consistent with our hypothesis that ALKs can be used as early detection of cancer markers. This can be measured in breath using Breath Biopsy. We are seeking to investigate whether AKRs can be targeted as early detection of cancer sensitive markers. This can be measured in breath using Breath Biopsy.