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Aldehyde dehydrogenases as target for biomarker and drug discovery

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The human aldehyde dehydrogenases (ALDHs) play a major role in detoxifying highly reactive aldehydes into carboxylic acids. Deregulation of ALDHs have implications in a number of cancers. They play an important role as a cancer stem cell (CSC) marker due to high activity found in CSCs while high expression is also known to lead to resistance to chemotherapeutic drugs. Although the exact role of ALDH is not fully understood, emerging information indicates several isoforms from the ALDH1 family, ALDH3A1 and ALDH7A1 play key roles in many cancer types. To probe the role of ALDH functional activity, at this meeting we will present new data on small molecules that inhibits ALDH functional activity using cell free and cell-based assays; diethylbenzaldehyde (DEAB) was used as a control for inhibition while Aldefluor assay was used as an assay to demonstrate functional activity. Furthermore, our investigations in prostate cancer revealed that several ALDH-affinic probe compounds were able to reduce cell viability in both drug-resistant PC3 prostate cancer cells and patient-derived samples while synergistic effect was observed in combination treatment with docetaxel. Our early drug discovery approach will be presented at the meeting and include drug design to target ALDH7A1, an enzyme that is linked with oxidative stress, lysine metabolism and several diseases including cancer.

Biography

Klaus Pors is an Associate Professor of Chemical Biology at The Institute of Cancer Therapeutics, University of Bradford, UK. His research group is involved with discovery of novel biological and chemical tools to explore the importance of enzymes in different disease states. Particular focus is on exploiting abnormal cytochrome P450 (CYP), aldehyde dehydrogenase (ALDH) or aldo-keto reductase (AKR) expression in the tumour microenvironment as target for biomarker and drug discovery; he has published 35 papers on these topics. He is a RSC Chemical Biology and Bioorganic Group committee member and the European Editor of Journal of Cancer Metastasis and Treatment.

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