ALDH<sup>+</sup>/CD44<sup>+</sup> Putative cancer stem cell population as therapeutic target in malignant pleural mesothelioma

Lourdes Cortes-Dericks
University of Hamburg, Germany

Malignant pleural mesothelioma (MPM) is a lethal cancer of the mesothelium with high chemotherapeutic resistance via unknown mechanisms. The cancer stem cell (CSC) theory proposes that a rare cell subpopulation exists in tumors causing relapse after chemotherapy, thus, rendering these cells as critical targets responsible for tumor recurrence. We sought to identify a sub-population of chemoresistant cells by using putative CSC markers, aldehyde dehydrogenase (ALDH) and CD44 in three MPM cell lines; H28, H2052 and Meso4. We found that both ALDH<sup>high</sup> - and ALDH<sup>low</sup>-sorted fractions were able to generate phenotypic heterogeneity and sphere formation, the latter being less efficient, and both contained ALDH<sup>+</sup>/CD44<sup>+</sup> subpopulations. Cis- diamminedichloroplatinum(II) (cisplatin) treatment failed to reduce ALDH activity and conveyed only a short-term inhibition of sphere formation in both ALDH<sup>+</sup> and ALDH<sup>-</sup> fractions of the three MPM cell lines. Modulation of drug sensitivity by an ALDH inhibitor, diethylaminobenzaldehyde (DEAB) resulted in significant reductions in cell viability but not a complete eradication of the sphere-forming cells, suggestive of the presence of a drug-tolerant subpopulation. At the transcript level, the cisplatin + DEAB-resistant cells demonstrated an upregulated mRNA levels for ALDH1A2, ALDH1A3 isozymes and CD44 indicating the involvement of these markers in conferring drug resiliency in both ALDH<sup>+</sup> and ALDH<sup>-</sup>- fractions of the three MPM cell lines. Our study shows that ALDH<sup>high</sup> CD44<sup>+</sup> cells are implicated in conveying chemoresistance to cisplatin in the three MPM cell lines, and may therefore, serve as therapeutic targets to improve the current treatment modalities in mesothelioma. Importantly, the double expression of CD44 and ALDH rather than ALDH alone better delineates a drug-tolerant, sphere-forming cell population in the tested MPM cell lines.

Biography
Lourdes Cortes-Dericks completed her PhD in Biological Sciences from the University of Hamburg, Germany. Her Postdoctoral studies at the University Hospital Berne, Division of General Thoracic Surgery were focused on the identification and characterization of normal resident stem cells in healthy lung, and tumour-initiating cells in lung cancers. One of her major projects led to the identification of a chemoresistant putative cancer stem cell population using established cancer stem cell biomarkers in malignant pleural mesothelioma. She is now a freelance editorial assistant and has been a reviewer for peer-reviewed articles in reputed journals for biological sciences.

cortes-dericks@gmx.de