

03 February 2009

Expert Opinion on the Doctoral Thesis of Lenka Horalkova with the title:

“Characterisation of Rat Alveolar cell line R3/1”

The alveolar epithelium is the major biological barrier in determining the disposition of drugs administered to the lung. Alveolar epithelial cells are responsible for the maintenance of lung haemostasis and clearance of xenobiotic substances from the airways. The doctoral thesis of Lenka Horalkova reports an evaluation of an *in vitro* cell culture model of the alveolar epithelium. The ability of a promising cell line, R3/1, to model alveolar epithelial permeability and the metabolic potential of the lung was studied via the application of cell and molecular biology. A variety of cell culture approaches were used in an attempt to induce the formation of functional tight junctions leading to a tight epithelial barrier suitable for drug transport studies. The culmination of the work was an evaluation of the peptidase expression by R3/1 cells.

The results described within this doctoral thesis are an advance towards the much needed *in vitro* model of the alveolar epithelium to facilitate studies in biomedical research and inhaled drug delivery. A thorough investigation has established the advantages and limitations of the cell model. Although the cells were unable to provide a suitable epithelial barrier for drug permeability screening, the cells were verified to possess many alveolar type I cell features, especially with regard to peptidase expression. In this context, this thesis provides valuable data about the methodology, applicability and suitability of R3/1 cell line for biopharmaceutical applications. The thesis is written in English and is clearly structured. Parts of the work are already published in European Journal of Pharmaceutical Sciences, demonstrating the novelty and importance for the scientific community.

In summary, the doctoral thesis of Lenka Horalkova reports novel investigations and I recommend that Lenka Horalkova is admitted to her defense.



Ben Forbes
London, 03 February