# Precision-cut Lung Slices (PCLS)



#### Holger P. Behrsing, Ph.D. Principal Scientist Respiratory Toxicology Program



## Topics to be Covered

## **Precision-cut Lung Slices (PCLS)**

- Isolation and Culture Methods
- PCLS Test System:
  - What does it represent? How is it used?
- Established Utility
  - Datasets demonstrating performance
- Current Results: Various Products Tested
- References & Contact Information



# **PCLS: Isolation and Culture**



1. Inflate lung tissue and section periphery



2. Create tissue cores



3. Slice cores with slicer









9

0 0

4. Mounted in vials





5. Roller culture

# In Vitro/Ex vivo Models: PCLS



### Adverse Respiratory Events & Choice of System



## Human PCLS: Acute Parenchymal Damage



#### **Aminoflavone Damage**

Concentration-depend. IL-1β increases

- Control tissue shows alveoli lined by mostly viable cells
- Exposure of human PCLS to 10  $\mu M$  Aminoflavone causes cytokine increases in < 24 hr
- Days later, severe tissue damage was noted: AF-induced, decreased cellularity and nuclear changes reflecting toxicity



### PCLS: Long Term Culture (e.g. rat PCLS)



### PCLS: Compound-induced Macrophage Activation



BCNU (carmustine) exposure shows numerous macrophages, many of which have infiltrated alveolar walls mimicking interstitial pneumonitis

ED-1 Immunostain

Large areas of parenchyma exhibit extensive deposition of collagen fibers, especially at slice margins

Masson's Trichrome

### HuPCLS: Long Term Culture (IIVS)



### 500 µg/mL Min-U-sil 5 Exposure to HuPCLS







Note: values above the highest standard were extrapolated by Luminex xPonent software

### **Exposure Methods: Solubles & Aerosols**



## **Testing Application: High Content**

- PI requires evaluation of pulmonary risk
- Study focus is on respiratory changes/function endpoints
- Study design can be acute or chronic exposure



# Acknowledgements & References



- Behrsing, H. P., M. J. Furniss, et al. (2013). "In vitro exposure of precision-cut lung slices to 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole lysylamide dihydrochloride (NSC 710305, Phortress) increases inflammatory cytokine content and tissue damage." Toxicol Sci 131(2): 470-9.
- Furniss, M. J., R. E. Parchment, et al. (2010). "The Influence of Phortress on Cytokine Levels and Tissue Viability in Precision-cut Rat Lung Tissue." The Toxicologist 114: 108.
- Behrsing, H. P., C. Ip, et al. (2006). "Demonstration of Differential Toxicity Induced by Aminoflavone Prodrug in Human and Rat Precision-cut Lung Slices." The Toxicologist 90: 403.
- Tyson, C. A., K. Amin, et al. (2005). "Comparison of BCNU and SarCNU Toxicity in Long-Term Cultures of Precision-cut Lung Slices." The Toxicologist 84: 240.
- Behrsing, H. P., K. Amin, et al. (2004). "Induction of Fibrosis by Bleomycin and Carmustine in Rat Lung Slices." The Toxicologist 78: 52.

Questions? Posters available upon request www.iivs.org Holger Behrsing, Ph.D. <u>hbehrsing@iivs.org</u>

