

Assessing the potential toxicity of chemicals using human respiratory cell-based *in vitro* systems

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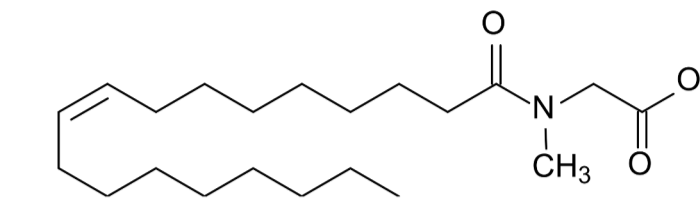
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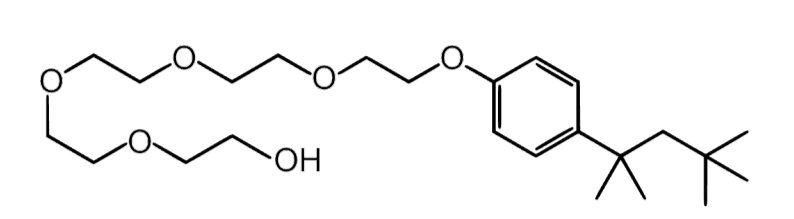
Surfactants are essential ingredients found in products such as household cleaners, personal care items, and medicines. As widely used chemicals, understanding the potential toxicity of surfactants is a key focus for regulatory agencies. Surfactants may interact with cell membranes, potentially compromising membrane integrity and leading to general cytotoxicity. To evaluate the potential respiratory toxicity of these chemicals, a human bronchial epithelial cell line (BEAS-2B) and a bronchial reconstructed human respiratory epithelium (RHRE; MucilAir bronchial, Epithelix, Switzerland) were exposed to two surfactants: Triton X-100 (non-ionic surfactant; CAS Number: 9036-19-5) and oleoyl sarcosine (anionic surfactant; CAS Number: 110-25-8). This work is a part of the INSPIRE (IN vitro System to Predict REspiratory toxicity) Initiative that aims to build scientific confidence in human cell-based methods to predict respiratory toxicity.

Oleoyl sarcosine



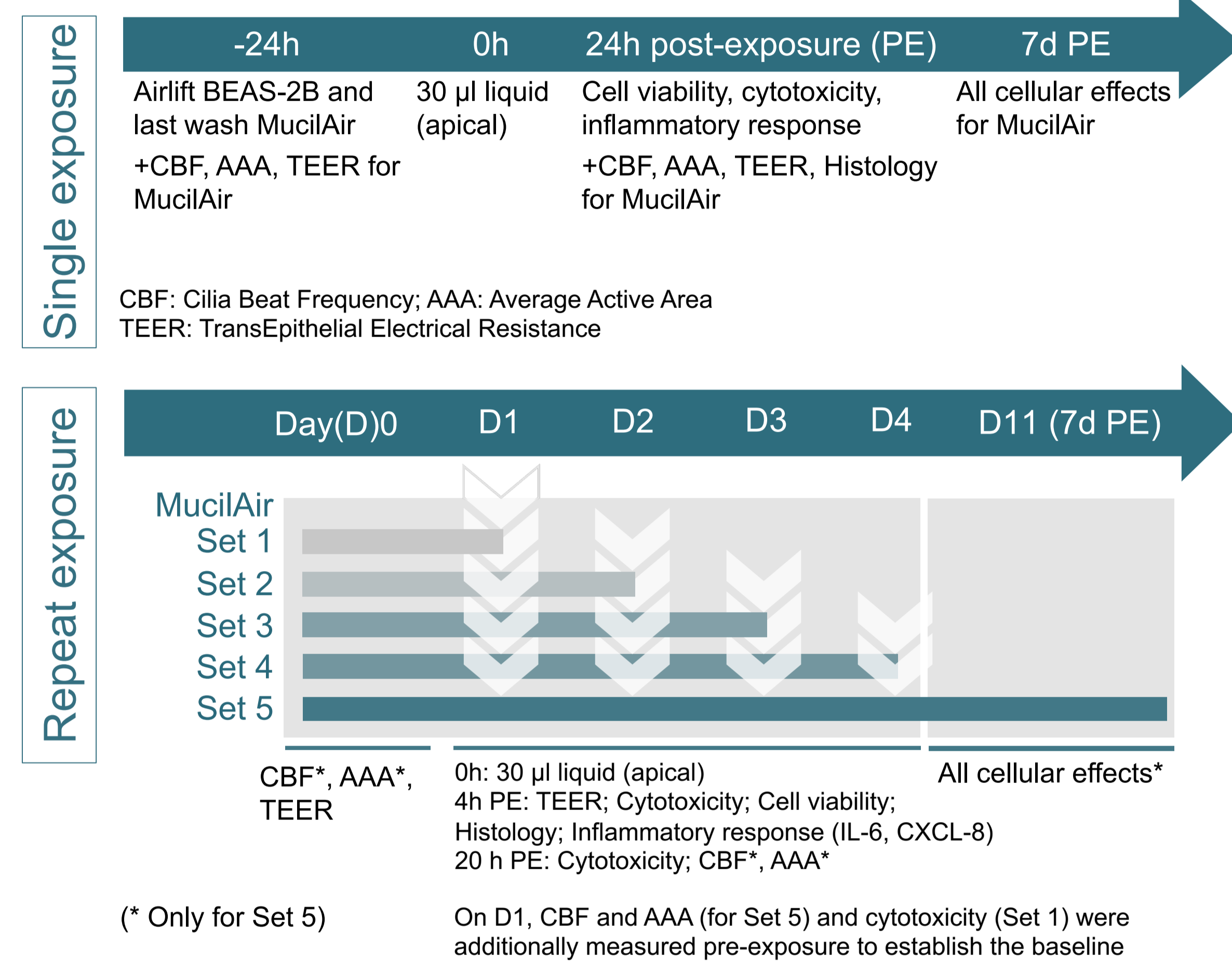
Anionic surfactant; Negatively charged
Insoluble in water
Critical micelle concentration: 0.026 g/L (74 µM)
Acute tox (inhalation): Cat. 4
Skin irritation: Cat. 2 / Eye Irritation: Cat. 2

Triton X-100

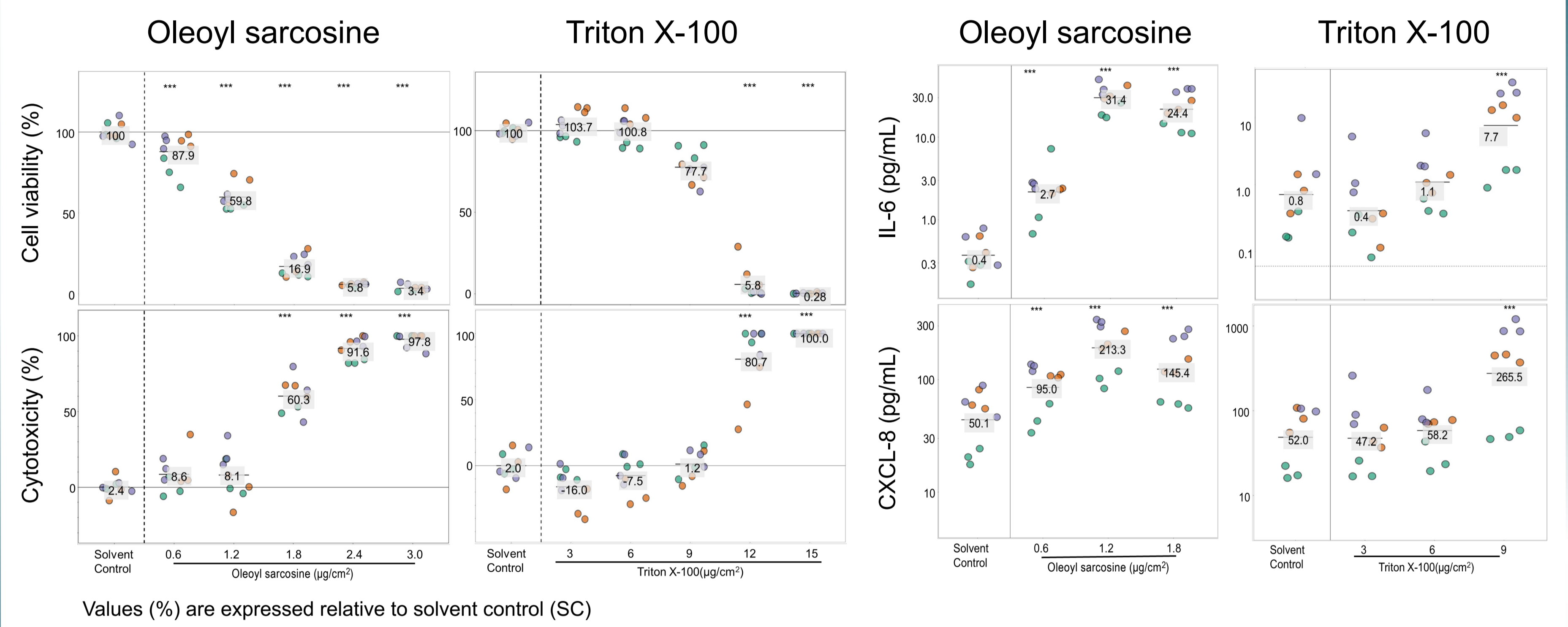


Non-ionic surfactant; Not charged
Soluble in water
Critical micelle concentration: 0.17 g/L (260 µM)
Acute tox (inhalation): No cat.
Skin irritation: Cat. 2 / Eye Irritation: Cat. 1

Study design



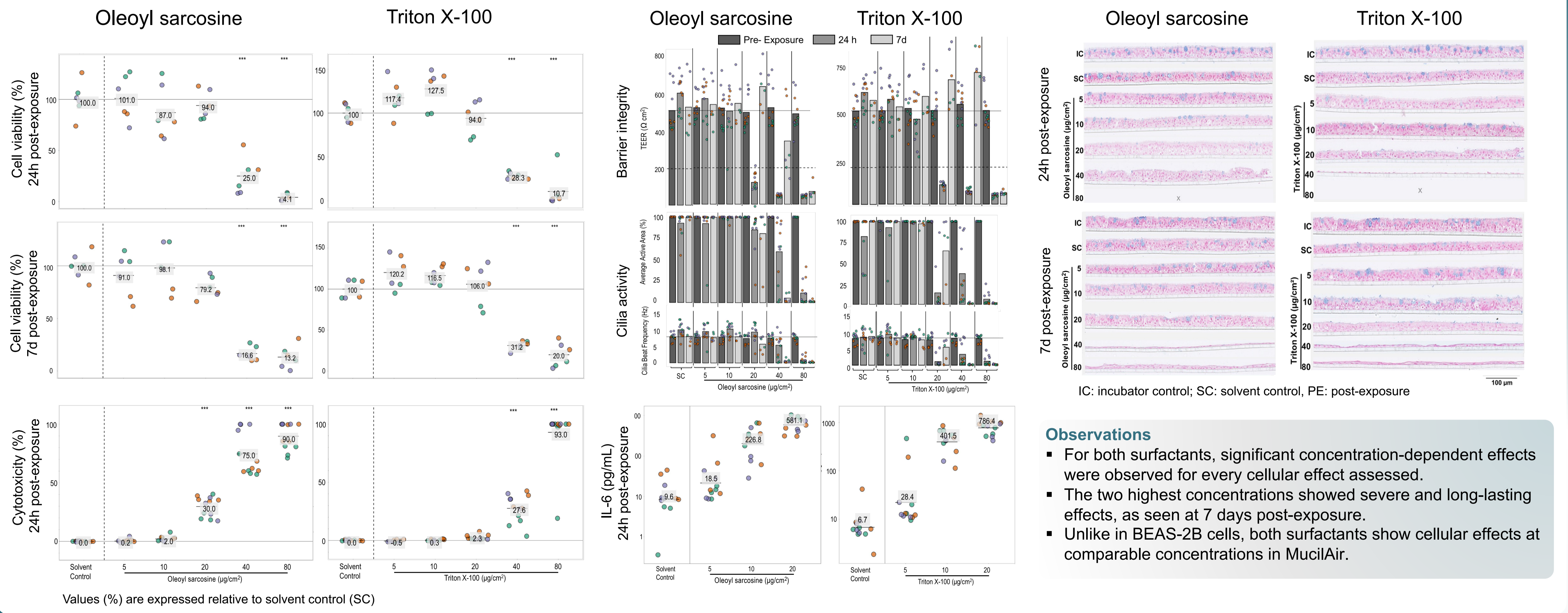
Results BEAS-2B (single exposure)



Observations

- For both surfactants, significant concentration-dependent cellular effects were observed for every cellular effect assessed.
- Oleoyl sarcosine exposures showed cellular effects at lower concentrations than Triton X-100.

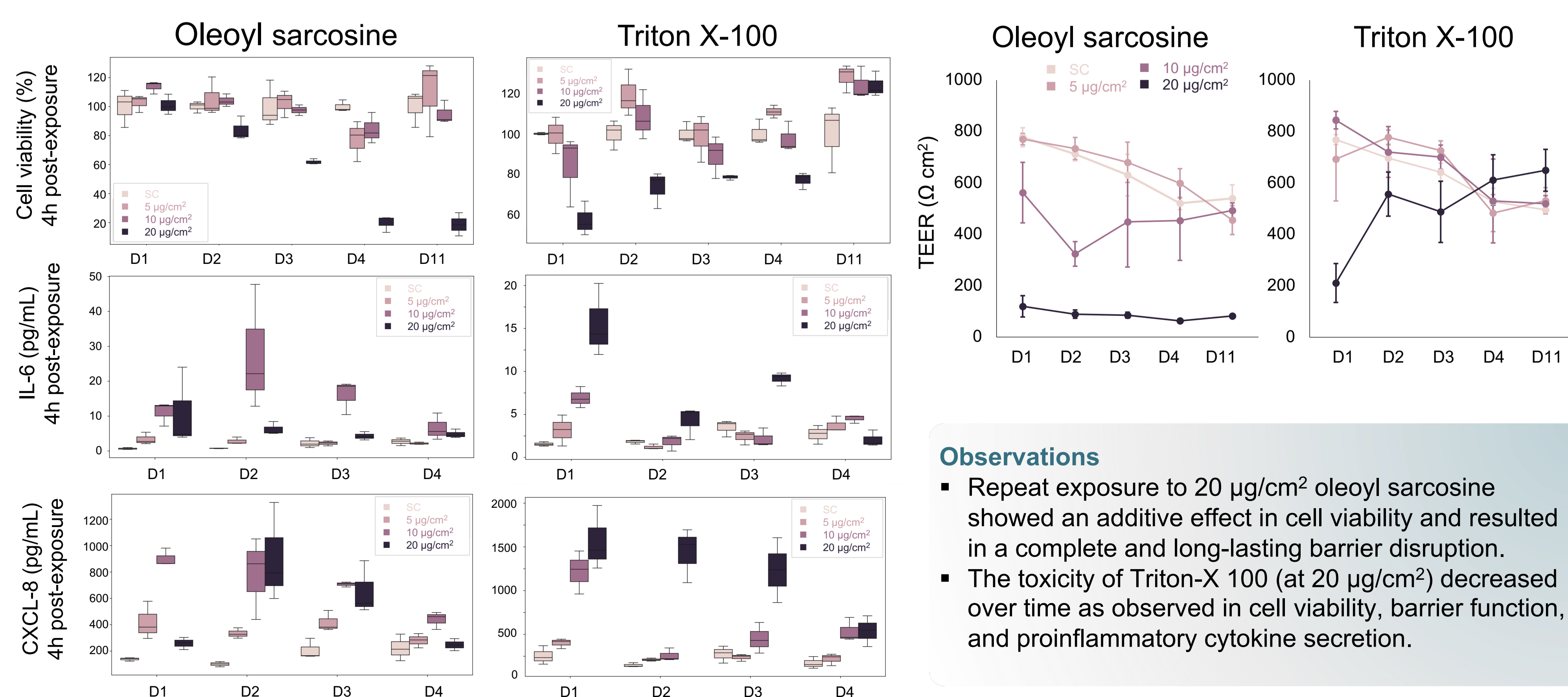
Results MucilAir (single exposure)



Observations

- For both surfactants, significant concentration-dependent effects were observed for every cellular effect assessed.
- The two highest concentrations showed severe and long-lasting effects, as seen at 7 days post-exposure.
- Unlike in BEAS-2B cells, both surfactants show cellular effects at comparable concentrations in MucilAir.

Results MucilAir (repeat exposure)



Observations

- Repeat exposure to 20 µg/cm² oleoyl sarcosine showed an additive effect in cell viability and resulted in a complete and long-lasting barrier disruption.
- The toxicity of Triton-X 100 (at 20 µg/cm²) decreased over time as observed in cell viability, barrier function, and proinflammatory cytokine secretion.

Conclusions & next steps

- Concentration-dependent cellular effects were observed for both surfactants in all experimental settings.
- BEAS-2B cells seem to be more sensitive than MucilAir tissues, which may be attributed to the lack of mucus and the overall lower tissue thickness of BEAS-2B cells.
- Preliminary repeat exposure results may indicate an additive effect in oleoyl sarcosine (only at the highest concentration) that is not observed for Triton X-100 exposures.
- These surfactants are currently being tested in an alveolar cell model, and testing of 13 additional surfactants in MucilAir is planned. These results will further inform an ongoing multi-laboratory study testing ~20 chemicals in MucilAir.