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Introduction:

- ❖ Cannabis smoke contains many combustion products that are detrimental to lung health
- ❖ Cannabis vaporizers heat the cannabis flower without burning, causing the release of cannabinoids such as tetrahydrocannabinol (THC) for subsequent inhalation without combustion products
- ❖ Current *in vitro* methods using aqueous solutions for inhaled cannabis product exposures are insufficient at capturing cannabinoid profiles

Air Liquid Interface (ALI):

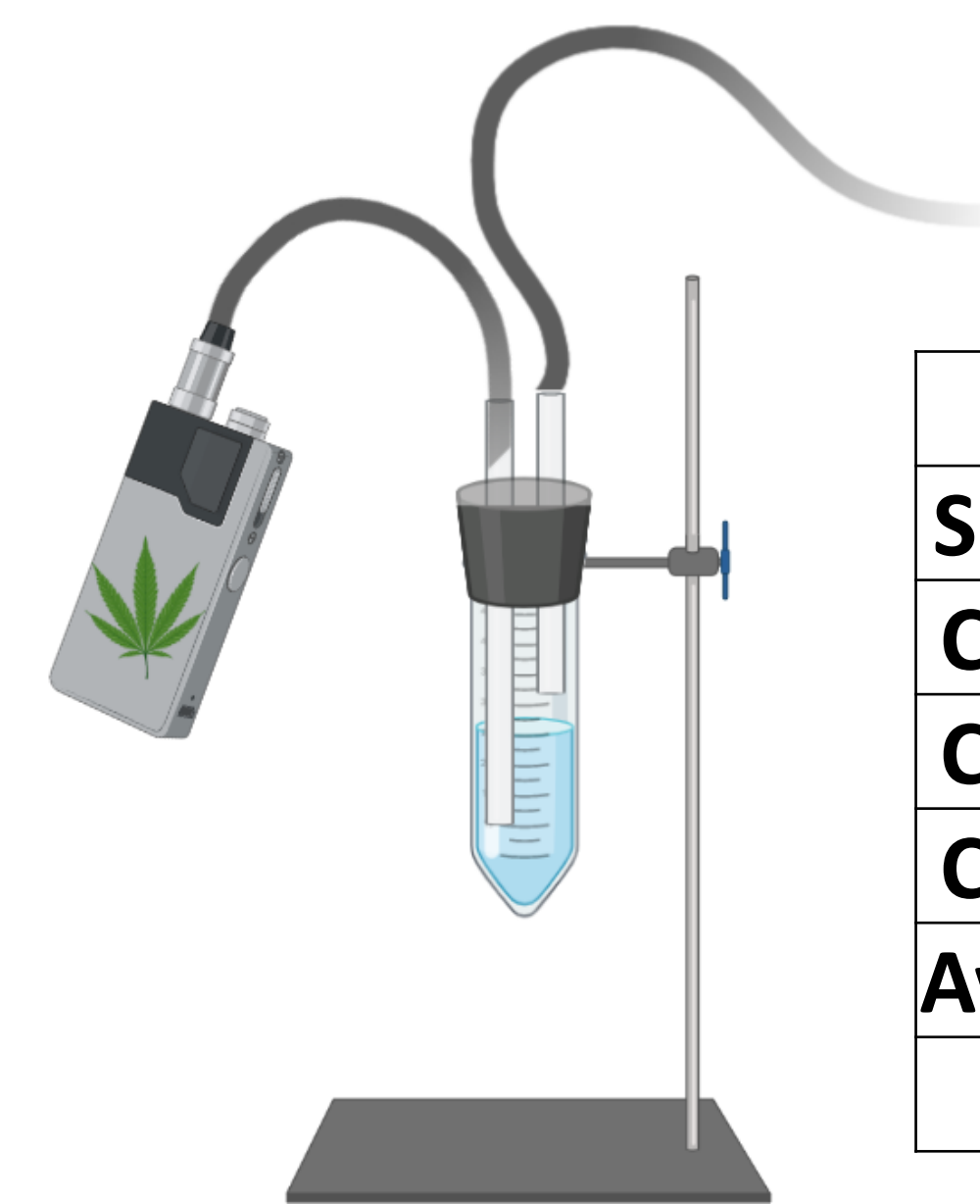
- Cells are exposed apically to air thereby more closely mimicking the lungs compared to submerged cultures
- Aerosol and vapour treatments deposit on the surface of cells compared to being delivered through media in traditional submerged cultures

Objectives:

1. Evaluate differences at the biological level (gene expression) between two exposure models.
2. Determine the consequences of cannabis vapor on the inflammatory response in lung epithelial cells.

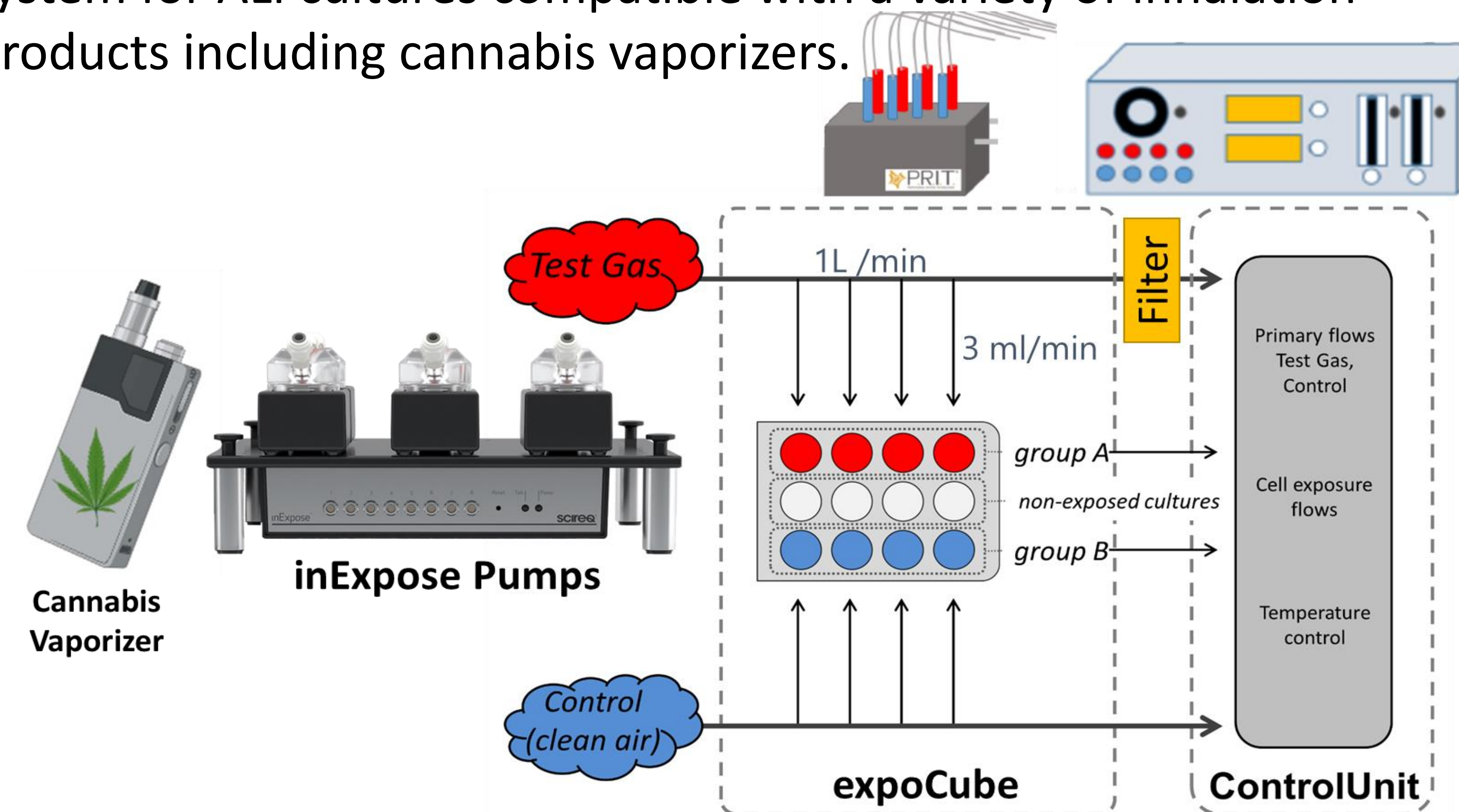
Methods: Treatments

Delivery Model 1: Cannabis vapor extract (CaVE) for submerged cultures is created by bubbling cannabis vapor through ethanol and captures major and minor cannabinoids.

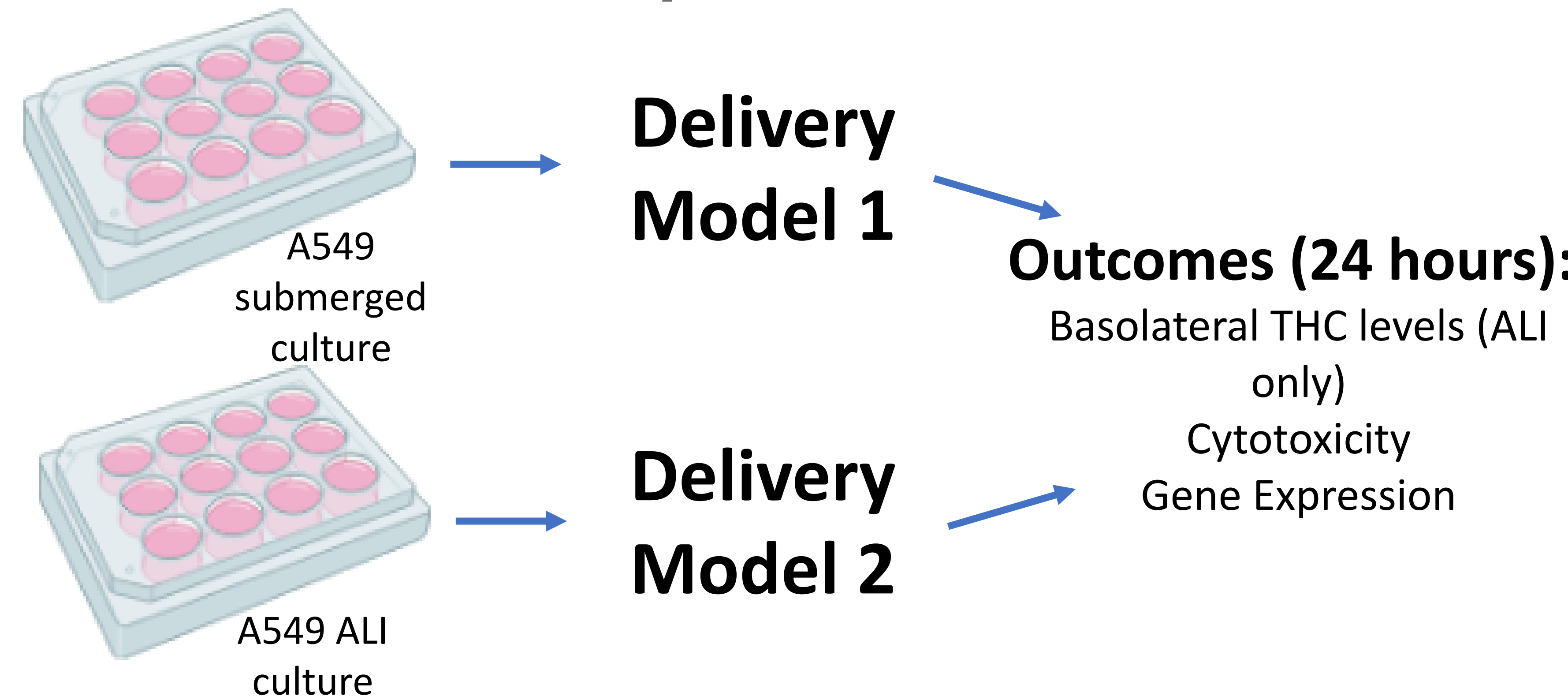


| Sample | Cannabinoid (ug/ml) | | | | |
|----------------|---------------------|-------------|-------------|--------------|--------------|
| | 9THC | CBD | CBG | CBC | CBN |
| CaVE-1 | 103.64 | 0.00 | 1.80 | 14.08 | 15.43 |
| CaVE-2 | 102.89 | 0.00 | 1.80 | 13.92 | 15.39 |
| CaVE-3 | 103.96 | 0.00 | 1.81 | 14.16 | 15.51 |
| Average | 103.50 | 0.00 | 1.80 | 14.06 | 15.44 |
| SD | 0.55 | 0.00 | 0.00 | 0.12 | 0.06 |

Delivery Model 2: The ExpoCube is an advanced toxicant exposure system for ALI cultures compatible with a variety of inhalation products including cannabis vaporizers.



Methods: Experimental Outline



Results:

Figure 1: CaVE treatment of A549 cells causes significant cytotoxicity starting at a concentration of 2500ng of THC/ml. Whole cannabis vapour causes significant cytotoxicity at 30 minutes but not 10 minutes exposure time at ALI.

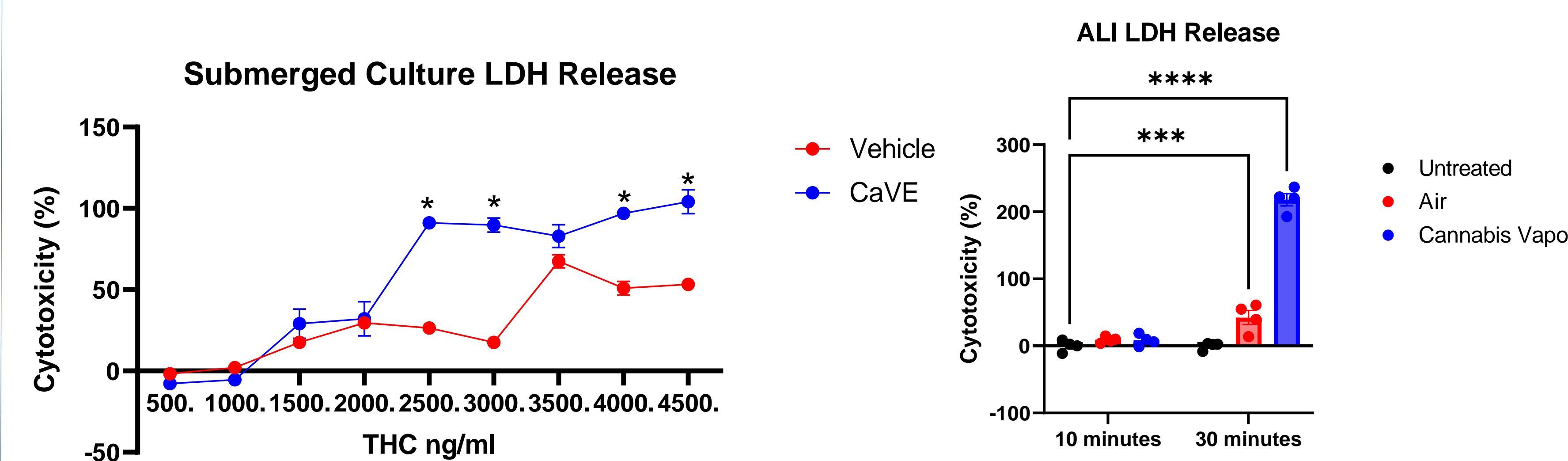


Figure 2: THC concentration of the ALI basolateral compartment increases with exposure time and is reproducible between plates.

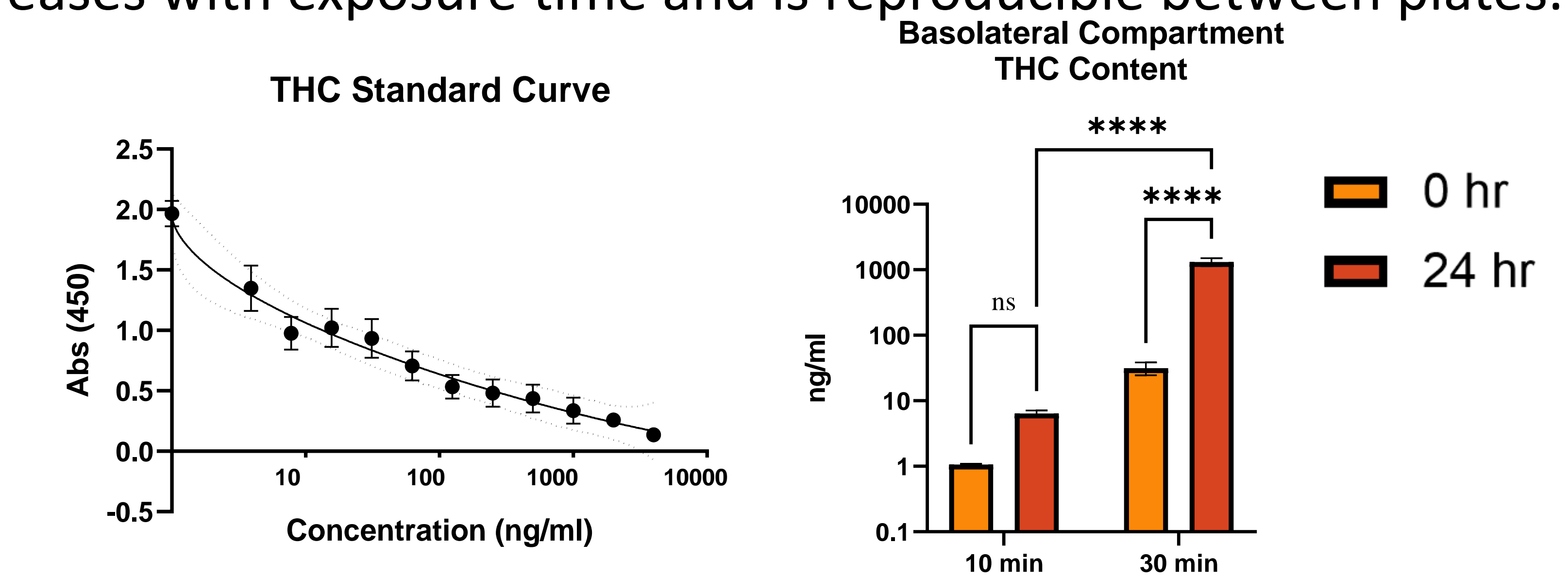


Figure 3: Genes relating to alveolar epithelial cell type 1 (AQP5), alveolar epithelial cell type 2 (SFTPC), and tight junction formation (TJP1) were unchanged between cell culture model and cannabis vapor treatment.

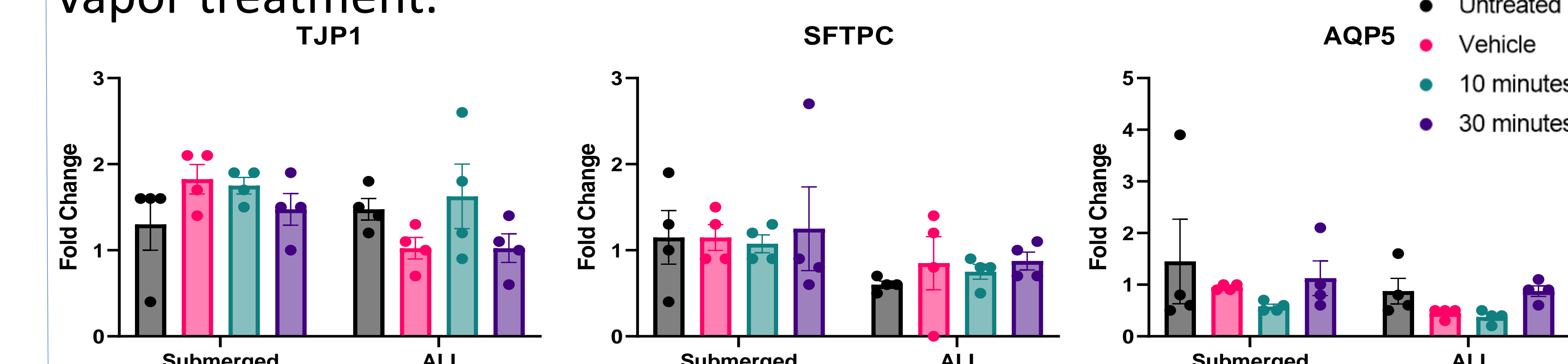
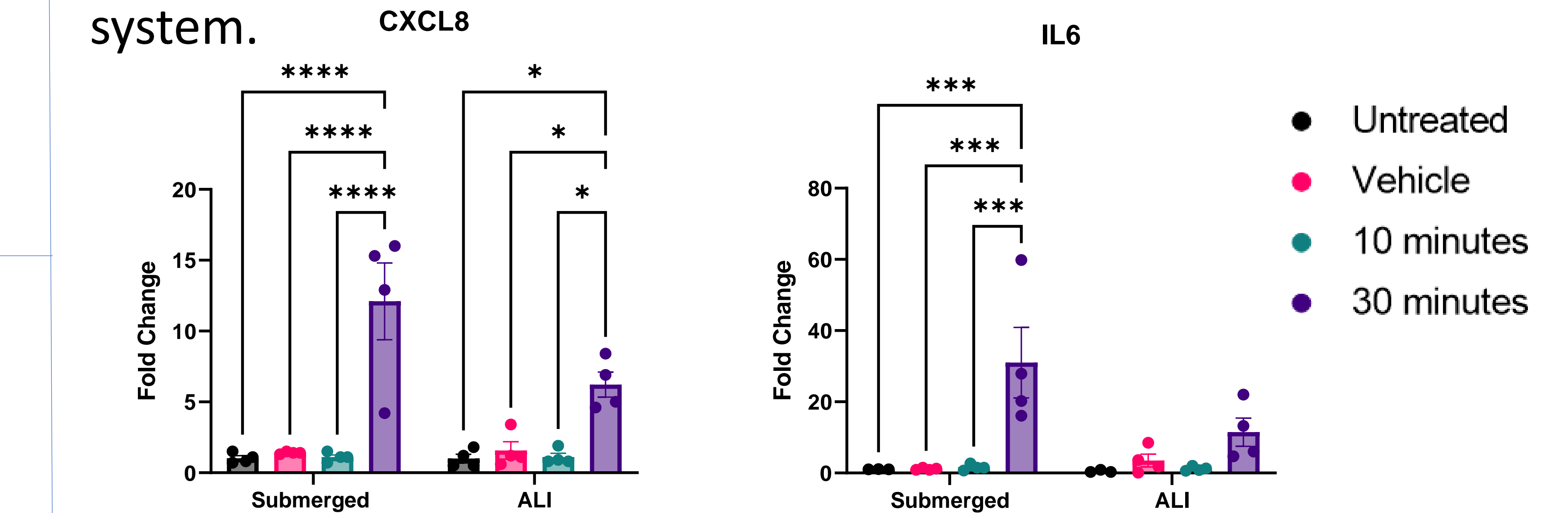


Figure 4: Proinflammatory gene CXCL8 is increased significantly after cannabis vapor exposure in both submerged and ALI cultures. IL6 is increased significantly only in the submerged cell culture system.



Conclusions:

- ❖ CaVE successfully captures the cannabinoid profiles of cannabis vapor
- ❖ The ExpoCube delivers cannabis vapor to cells at ALI in a reproducible and controllable manner
- ❖ Cannabis vapor shows potential to induce a proinflammatory response causing increases in CXCL8 and IL6
- ❖ This is the first study to investigate the impact of vaporized cannabis products on the structural cells of the lungs.

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