The impact of diesel exhaust particles on inflammatory and oxidative stress responses in a 3D *in vitro* epidermal model

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1. Background

- Diesel exhaust has detrimental effects on the pulmonary [1] and cardiovascular system [2].
- The skin functions as one of the main primary barriers to the outside environment. It protects against various environmental influences.
- Ambient air pollution is impacting the skin [3]. It is associated with premature aging, inflammatory and allergic skin conditions.

2. Research questions

- How to model the effect of diesel exhaust particles on the skin?
- What are the cellular and molecular pathways involved upon exposure of the skin to diesel exhaust particles?
- How is the skin's barrier function affected?

3. Methodology

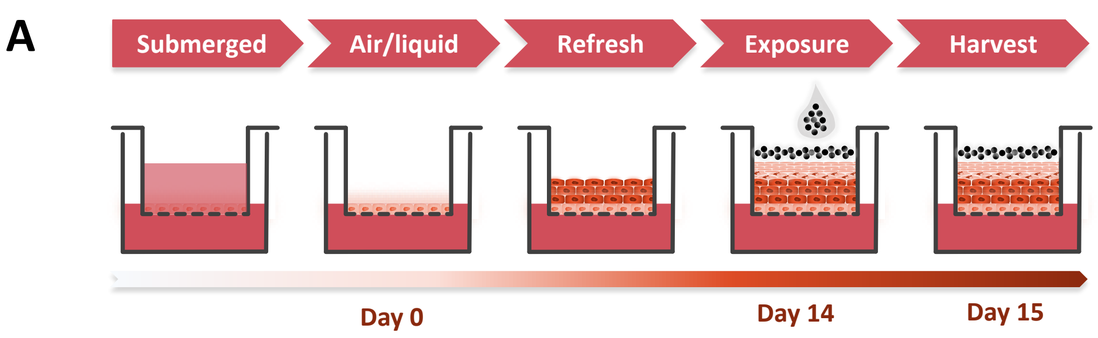

Figure 1A. Workflow of a 3D *in vitro* reconstructed human epidermal model for diesel exhaust particle (DEP) exposure. Skin model reconstructed from foreskin-derived neonatal human primary keratinocytes, cultured on a polycarbonate membrane. Topical application of DEP, SRM2975 at 1-100 µg/cm^2 in 30 µL/cm^2 PBS.

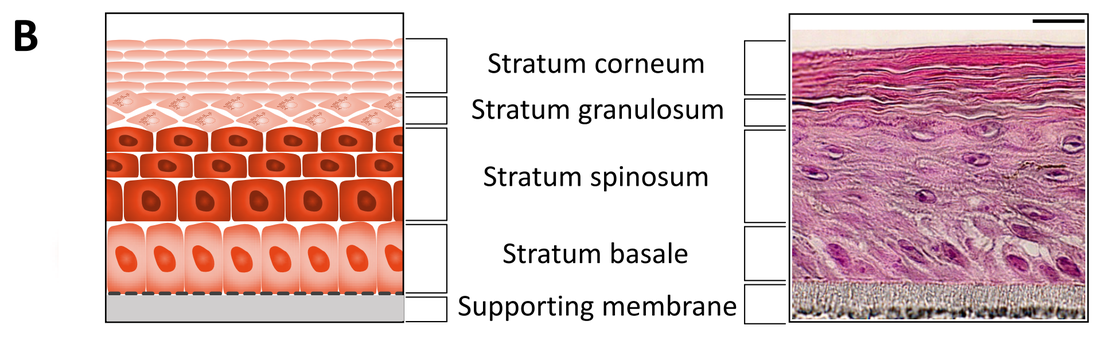

Figure 1B. Schematic representation of epidermal layers and morphology of 3D epidermal model. Paraffin embedded tissue sectioned at a 5 µm thickness and stained with Hematoxylin and Eosin. Scale bar represents 20 µm.

4. Results

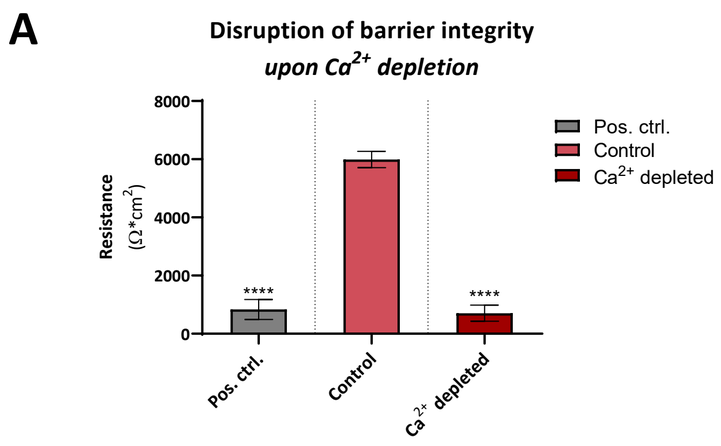

Figure 2A. Trans Epithelial Electrical Resistance (TEER) measured with MilliCell ERS-2 Volt-Ohm meter after 24 hours of calcium depletion. Positive control (Pos. ctrl.) is 0.08% Triton X-100 topically applied. n=4.

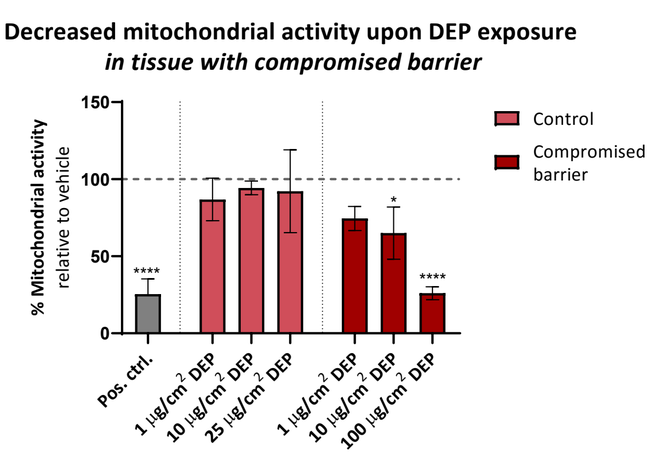

Figure 2B. Mitochondrial activity measured with MTT and MTS assays after 24 hours. Pos. ctrl. is 2.5 mM H_2O_2. n=2 for compromised barrier, n=3 for vehicle control and positive control.

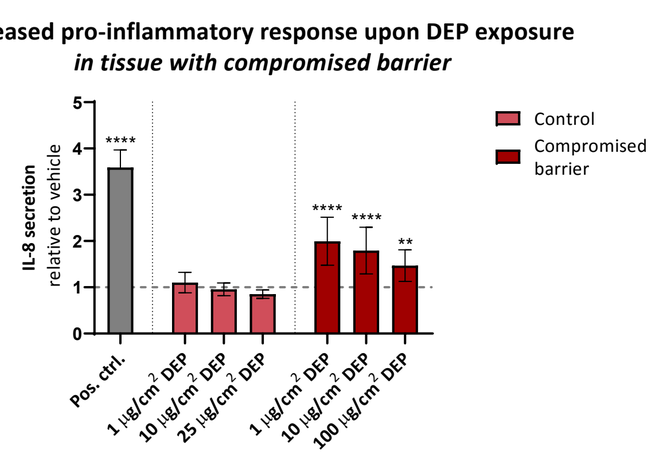

Figure 2C. Interleukin 8 (IL-8) secretion measured with enzyme-linked immunoabsorbent assay (ELISA) after 24 hours. Pos. ctrl. is 200 µg/mL lipopolysacharide. n=8 for compromised barrier, n=12 for vehicle control and positive control.

Bars represent mean of biological replicates. Error bars represent standard deviation. Grey dotted lines represent vehicle control. **Statistical analysis**: One-way ANOVA, Dunnett's multiple comparison test to vehicle control. * is adjusted P-value (* < 0.01; ** < 0.05; **** <0.0001).

5. Conclusions and outlook

- Calcium depletion disrupted the barrier integrity of the reconstructed human epidermal model, resulting in a compromised barrier function.
- DEP can trigger pro-inflammatory responses in an epidermal model with a compromised barrier function.
- Expanding research from exposure to diesel exhaust particles to complete diesel exhaust and ambient air.

6. References

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Funding

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 765602.

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