Combining TEER and high-resolution spatial impedance mapping on porous MEA for improved *in vitro* barrier measurements

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Accurate assessment of barrier integrity is vital for evaluating tissue barriers *in vitro*. While transepithelial and transendothelial electrical resistance (TEER) enable real-time, non-destructive quantification of barrier tightness on porous supports (Figure 1a), it only provides a single value of barrier tightness per time point. These single-value measurements mask cellular heterogeneity and may miss localized disruptions. To address this shortcoming, microelectrode arrays (MEAs) offer high spatial resolution impedance measurements [1] (Figure 1b). However, their conventional fabrication on solid, non-porous substrates restricts their integration in multi-compartment organ-on-chip models.

To overcome this issue, we developed a novel silicon-based porous microelectrode array (pMEA) comprising an 11 x 11 grid of titanium nitride (40µm diameter) electrodes. The pMEA is integrated into a Transwell-like setup and includes an additional large electrode in the top and bottom compartments, enabling simultaneous TEER measurements (Figure 1c).

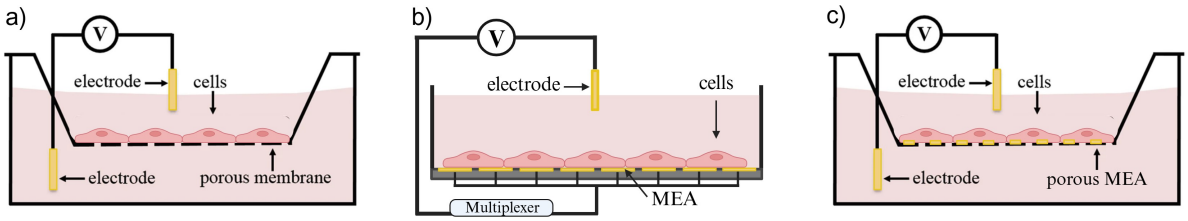

Figure 1: Conventional Transwell setup for measuring TEER (a). MEA for measuring cellular impedance (b). In-house developed Transwell setup with integrated porous MEA (pMEA) for simultaneous measurements of TEER and cellular impedance (c).

Endothelial cells (HUVECs) were cultured directly on the pMEA to monitor barrier formation. TEER gradually increased to 8.5 ± 1.8 Ω·cm^2, while the average pMEA impedance at 1 kHz increased from (1.5 ± 0.02) × 10^4 Ω to (9.1 ± 1.2) × 10^4 Ω. The spatial variability, defined as the coefficient of variation for the pMEA impedance across electrodes, decreased from 34 ± 11 % to 22 ± 2 % after 6 days, indicating that HUVECs remain heterogeneous even after maturation. Upon barrier disruption with biological agents such as tumor necrosis factor alpha (TNF-α), both TEER and pMEA impedance decreased. More interestingly, the pMEA spatial variability increased from 17 % to 33 %, revealing uneven barrier disruption, a feature not captured by TEER measurements alone.

Our results underscore the ability of the pMEA to capture barrier spatial heterogeneity in multicompartment setups, a critical feature for understanding disease mechanisms and one that is beyond the capabilities of traditional Transwell and TEER-based technology. In conclusion, the novel pMEA offers a powerful platform for investigating vascular and gut barrier function, enabling detailed study of dynamic processes such as pathogen translocation, immune cell migration and cancer cell metastasis.

References:

[1] Venz A., Duckert B., Lagae L., Takalloo S.E., Braeken D. *Sci Rep* 15, 1592 (2025). https://doi.org/10.1038/s41598-025-85783-9