Infectious disease models 3.0

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The growing spread of emerging infectious diseases, such as COVID-19, or resistant pathogens indicates the need to speed up research on repurposing already approved drugs or testing novel innovative compounds. Since effective drugs or vaccines must induce both humoral and cellular responses against pathogenic challenges, novel alternative human approaches are needed – thus Infectious Disease Models 3.0 - and improved methods for delivery have to be tested.

Rapid developments in high content screening as well as organotypic cultures provide groundbreaking new tools to study pathogen transfer at entry sites or to test novel treatment strategies. Therefore, we design optimized intelligent human barrier models combined with infection-relevant immune cells and humoral components in order to characterize and hinder overshooting host responses, pathogen entry and initial transmission steps within a 3D system. These human systems offer improved power to test delivery methods, adjuvants, repurposing of drugs or novel vaccination approaches in high throughput and will be an important challenge with broad interest. Using these models, we could demonstrate that:

(i) C5aR inhibition of nonimmune epithelial cells suppressed inflammation as assessed by local complement production, anaphylatoxin and pro-inflammatory cytokine released and maintained epithelial integrity in SARS-CoV-2-infected primary human airway epithelia (1),
(ii) antiviral sprays effectively shielded airway epithelia from infection with different SARS-CoV-2 variants of concern (2), influenza A and B (3), and
(iii) corticosteroids created a suppressive microenvironment and promoted fungal invasion in epithelial/immune respiratory models (3).

Crucially, these human systems offer the opportunity to evaluate novel therapeutic intervention strategies or test drugs or vaccination efficiency in a personalized manner.

References

1. Posch, W., Vosper, J., Noureen, A., et al. (2021), J Allergy Clin Immunol.; 147(6):2083-2097.e6. doi: 10.1016/j.jaci.2021.03.038
2. Zaderer, V., Dichtl, S., Posch, W., et al. (2023), Respir Res;24(1):88. doi: 10.1186/s12931-023-02397-3
3. Zaderer V, Diem G, Posch W, et al. (2024), Respir Res; 25(1):102. doi: 10.1186/s12931-024-02718-0.
4. Luvanda, M.K., Posch, W., Noureen, A., et al. (2021), J Fungi (Basel);7(3):221. doi: 10.3390/jof7030221