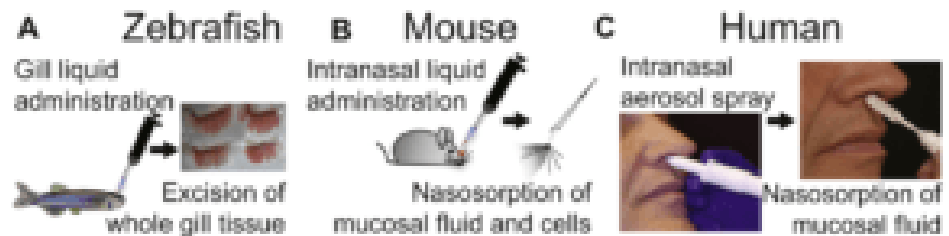
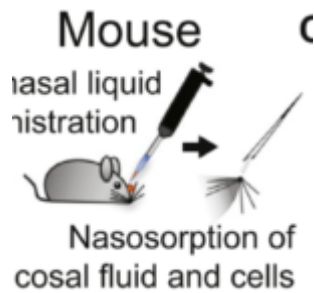


Animal models to measure mucosal innate immunity: zebrafish vs mice.



Kinetic profile of mucosal pro-inflammatory cytokine responses after zebrafish gill, mouse, and human nasal stimulation with R848. A-C (Source: Progatzy *et al.*, 2019 JACI).

The nasal mucosal site is the main entry point for respiratory viral pathogens that are responsible for a high burden of global morbidity. Studying early innate immune responses could lead to improved understanding of immune mechanisms against viral pathogens, as well as lead to the development of improved therapeutics. Animal models are very useful tools to study immunological mechanisms of diseases and conduct pre-clinical testing prior to human trials. However, the use of an inappropriate animal model that is not similar to human pathology or disease progression can slow the development of new therapeutics.

Progatzy *et al.*, aimed to compare respiratory mucosal innate

immune responses in parallel zebrafish, murine and human viral TLR agonist challenge models. They compared innate immune responses to the toll-like receptor (TLR)-3 agonist polyinosinic:polycytidylic acid (poly[I:C]) and TLR-7/8 agonist resiquimod (R848). poly[I:C] and R848, mimic double-stranded and single-stranded RNA respectively, thus are suitable agonists to measure anti-viral innate immune responses.

Mucosal poly[I:C] challenge in zebrafish and humans did not result in induction of innate immune responses, measured by expression of TNF- α , IL-1 β , IL-6, IFN- α and IFN- γ at serial timepoints (1-8hrs) post challenge. However, challenge in mice significantly induced expression of TNF- α , IL-6 and IFN- γ . This finding suggests zebrafish but not mice are an appropriate model to study innate mucosal immune responses to poly[I:C], as they have similar response kinetics as humans.

Mucosal R848 challenge of zebrafish, mice and humans lead to very similar innate immune responses and kinetics, where TNF- α production was observed during early timepoints, while IFN- γ levels increased at later timepoints. Additionally, similar expression kinetics of IL-1 β and IL-6 responses were observed in all 3 models. Indicating that both zebrafish and mice, are appropriate models to study immune mechanisms of R848 challenge.

In summary, Progoatzky *et al.*, demonstrated that zebrafish are a more appropriate model than mice to study mucosal innate immune responses to viral pathogens, as they have similar immune responses and kinetics as human in response to viral-TLR-agonists.

Journal Article: Progoatzky *et al.*, 2019. [Induction of innate cytokine responses by respiratory mucosal challenge with R848 in zebrafish, mice, and humans.](#) JACI

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