



**Information and Networking Event
Horizon Europe 2023 Calls
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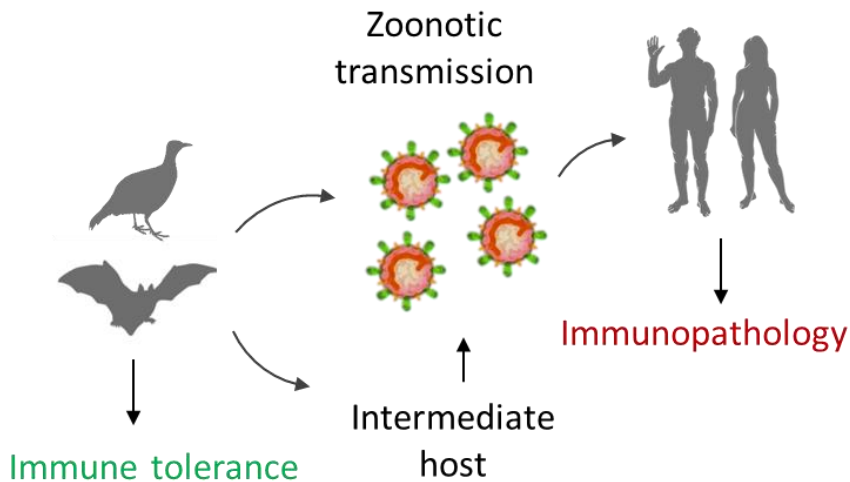


HORIZON-HLTH-2024-DISEASE-08-20: Pandemic preparedness and response: Host-pathogen interactions of infectious diseases with epidemic potential

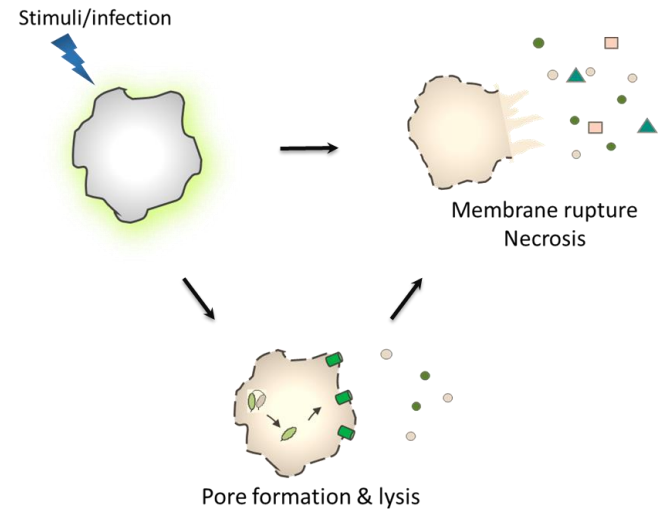
Friday, 13 October 2023

- TITLE of talk: [Pandemic preparedness: Novel mechanisms of bats in regulating pyroptosis, tissue damage and inflammation to tolerate pathogenic viruses](#)
- Name of presenter: **Kesavardana Sannula**
- Name of Organisation: [Indian Institute of Science \(IISc\)](#) (Academic institution)
- Country: [India](#)
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- Your web url: <https://kesavlab.wordpress.com/>

Decoding reservoir host mechanisms conferring dampened inflammation and virus tolerance: To reveal novel targets for mitigating pulmonary pathogenesis

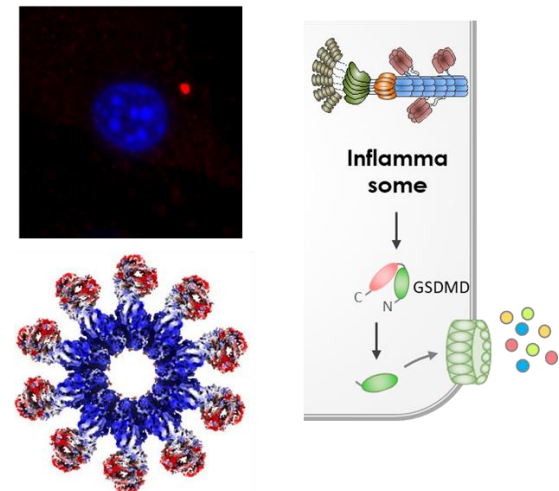


Programmed inflammatory cell death



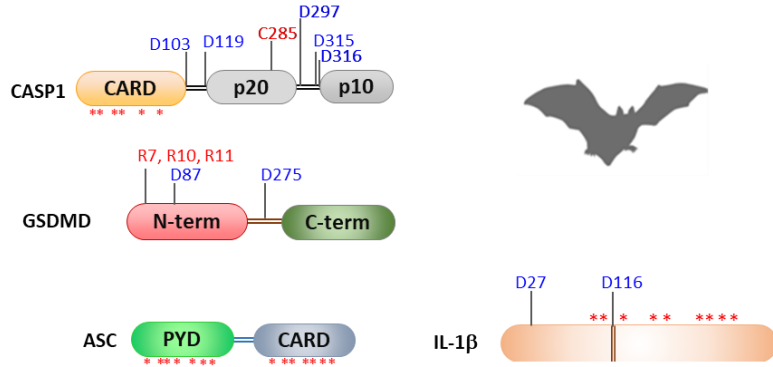
- Why zoonotic virus reservoirs tolerate viruses and elicit mild clinical symptoms?
- How zoonotic viruses acquire molecular mimicry to regulate host intracellular mechanisms?
- Identifying new targets by revealing key molecular determinants of zoonotic virus tolerance or immunopathology?

Inflammasome activation

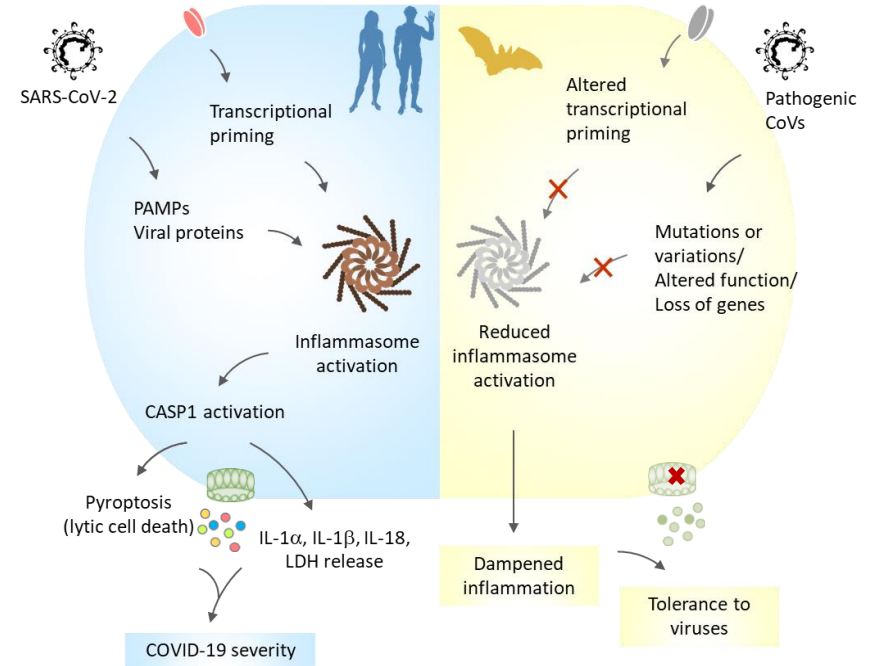


Pandemic preparedness:

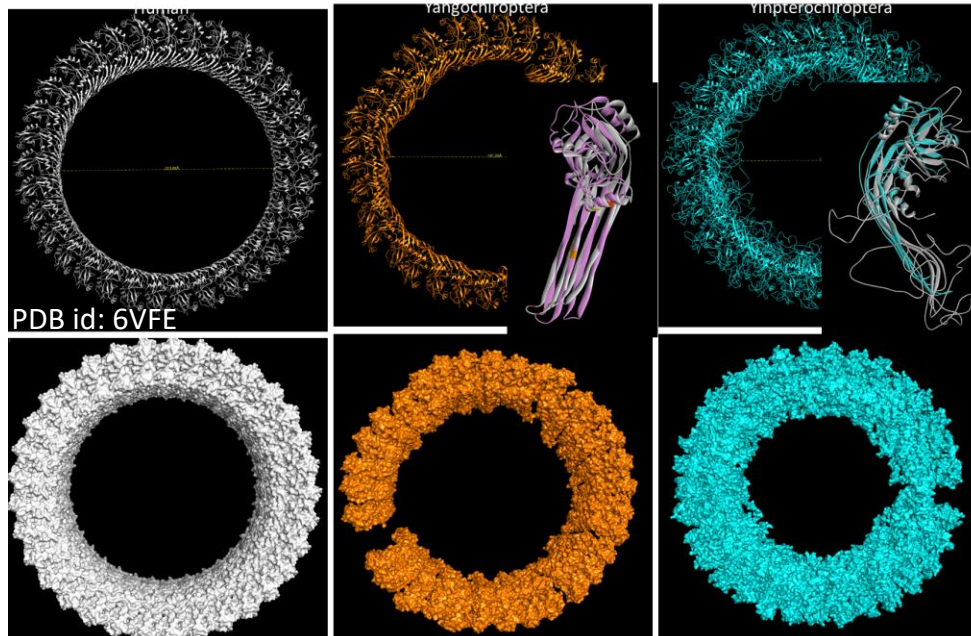
Novel mechanisms of bats in regulating pyroptosis, tissue damage and inflammation to tolerate pathogenic viruses



Sahana N, Jain D & Kesavardhana S. *J Leuko Biol.* 2022
 Mishra S.....Kesavardhana S.. *Biorxiv.* 2023



- The differential regulation of inflammasome and pyroptosis activation in bats and humans, which determine zoonotic viral tolerance or immunopathology



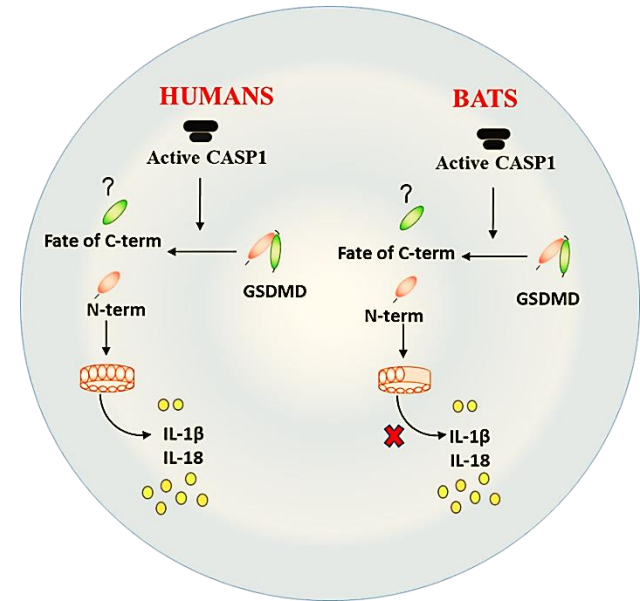
Hypothesis:

Bats have evolved to regulate pyroptosis machinery to mitigate virus-induced tissue damage and cytokine storm.

This may be a potential mechanism for bats to tolerate pathogenic viruses without clinical symptoms

Aims:

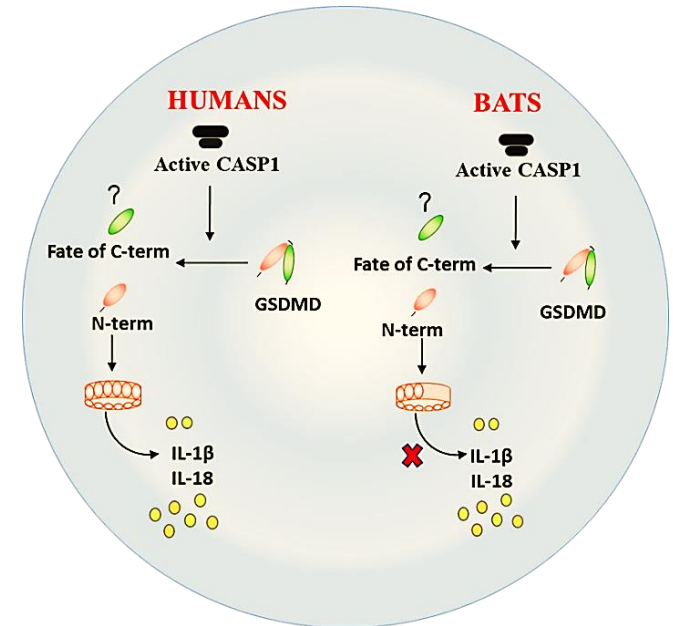
1. Comprehensive characterization of bat GSDMD mutations in GSDMD function, pyroptosis activation and release of IL-1a, IL-1b and IL-8
2. Mechanism of bat mutations mediated restriction of GSDMD pore-forming activity to suppress inflammation
3. Functional validation of bat GSDMD mutations in mitigating pathogen-mediated pyroptosis and inflammation (including in vivo studies)
4. Possible approaches to target GSDMD pore activation in pulmonary virus infections.



The proposed mechanism of bat GSDMD mutations mediated alleviation of pore formation, pyroptosis activation and release of proinflammatory cytokines (IL-1b and IL-18)

Hypothesis:

1. Proof of concept: Bats (reservoir hosts for pathogenic viruses) have evolved to operate unique mechanisms for alleviating virus-mediated pathogenesis
2. Establishing novel bat mechanisms in regulating Gasdermin-mediated pyroptosis and cytokine storm and how these mechanisms facilitate virus infections in bats without causing pathogenesis.



The proposed mechanism of bat GSDMD mutations mediated alleviation of pore formation, pyroptosis activation and release of proinflammatory cytokines (IL-1b and IL-18)

Molecular cues of pathogenic traits



Predicting pathogenic potential of zoonotic viruses



Possible prediction of pandemic potential

Profile of the partners sought (type, skills, role, etc.)

Expertise:

1. Protein structure based analysis
2. Zoonotic viruses and Comparative Biology
3. Inflammasomes, pyroptosis and necroptosis
4. Virus induced inflammation and pulmonary pathogenesis
5. Nucleic acid sensing: ZBP1, viral Z-RNA sensing, inflammation and necroptosis