Inflammatory Cell Death Mechanisms Against *Pseudomonas aerugonisa* in Cystic Fibrosis

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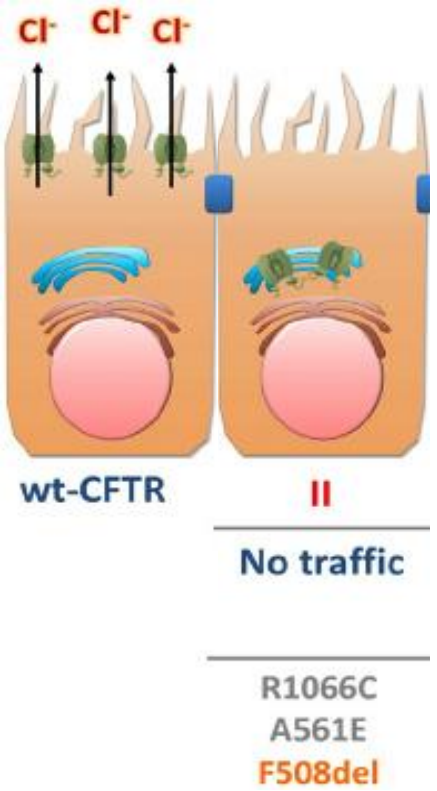
Cystic Fibrosis

- 1 in 3600 children born in Canada are affected
- Caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene
- Establishment of chronic bacterial infections
- Periods of stable disease and acute exacerbations



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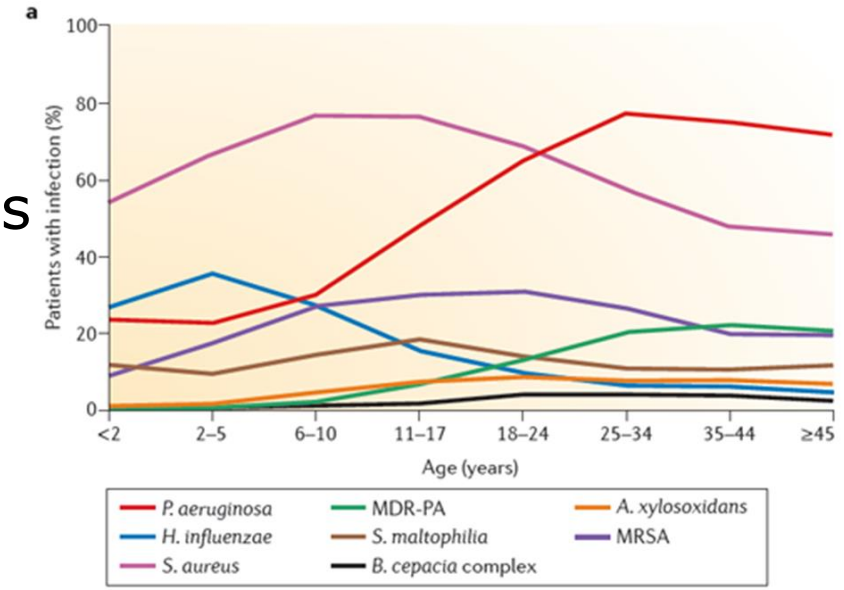
Adapted from Bell et al., 2015

Pseudomonas aeruginosa

- Opportunistic pathogen
  - Acute and chronic infections
- Most common bacterial pathogen in CF

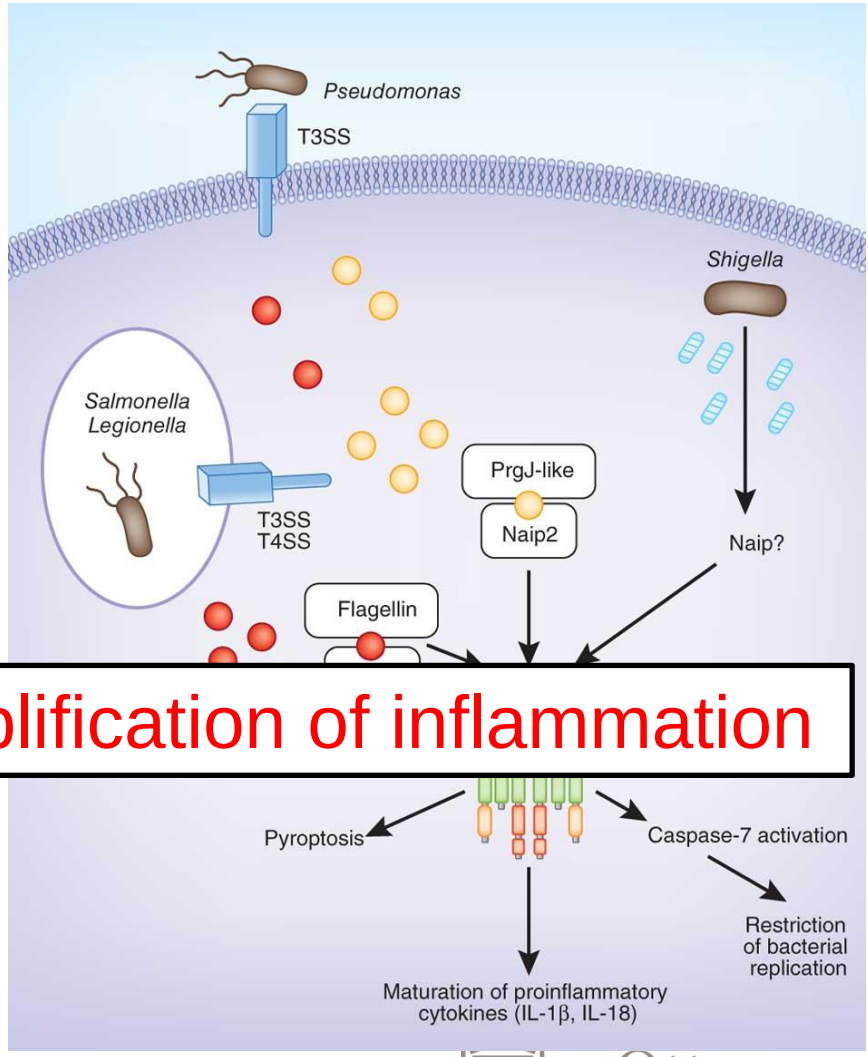


- Type III secretion system (T3SS)
  - Facilitates detection and infection of target cells
- Undergoes genetic and phenotypic adaptation

Adapted from Folkesson et al., 2012

Inflammatory cell death

- Inflammasome
  - Recruits and activates pro-caspase-1
  - Release of mature IL-1β and IL-18
  - Induction of pyroptosis



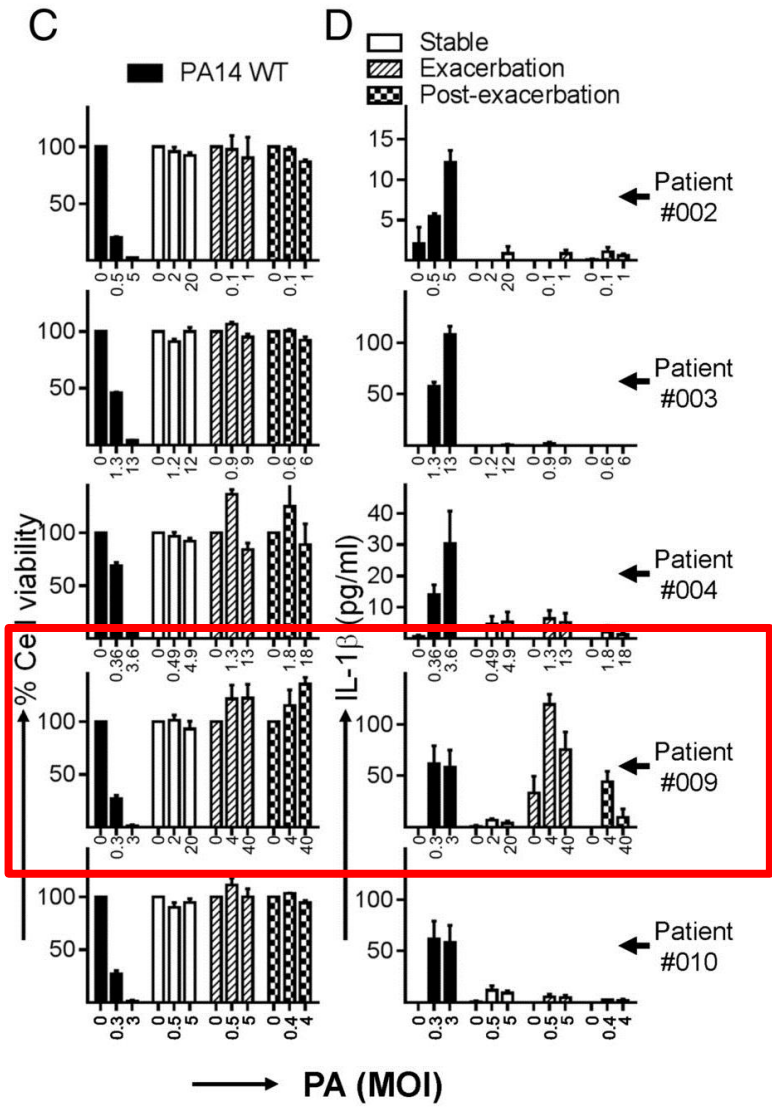
Inflammatory cell death → amplification of inflammation

Hypothesis

- During stable disease, *P. aeruginosa* fails to induce inflammasome signaling, however, during exacerbation periods, inflammasome signaling is reactivated.

Preliminary Results

- Stable isolates do not induce inflammasome activation
- Isolates from severe exacerbation events induce IL-1β production, but do not induce cell death



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Adapted from Huus et al., 2016

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