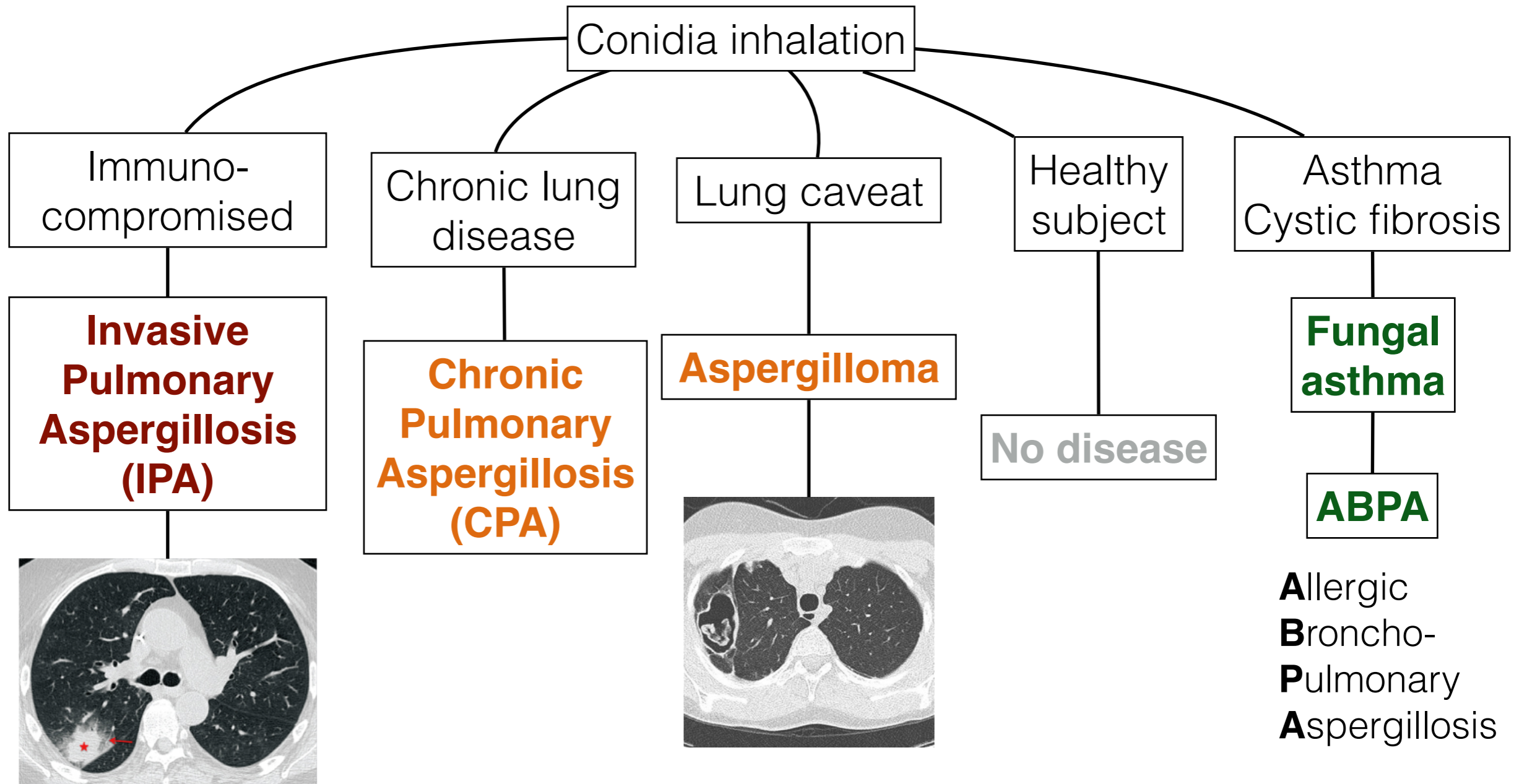


Role of humoral immunity against *Aspergillus fumigatus*

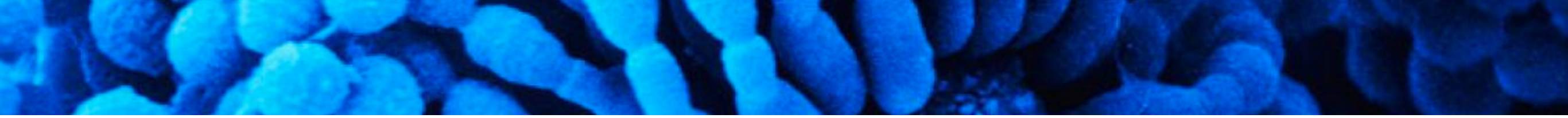
Sarah Dellière
Journée G2I
22/03/2024

Aspergillosis spectrum



Immune dysfunction - lung damage

Immune hyperactivity



Innate immune response



Humoral

Cellular

- Inflammation proteins
- Complement
- Antimicrobial peptides
- Immunoglobulines



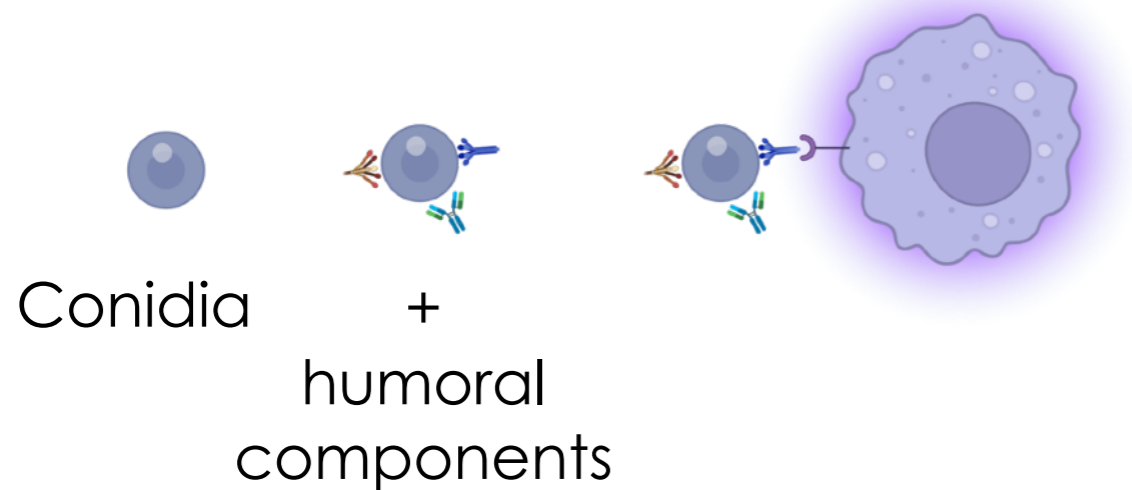


Multiple functions

Multiple functions

Liking pathogens and immune cells

Opsonisation and soluble mediators





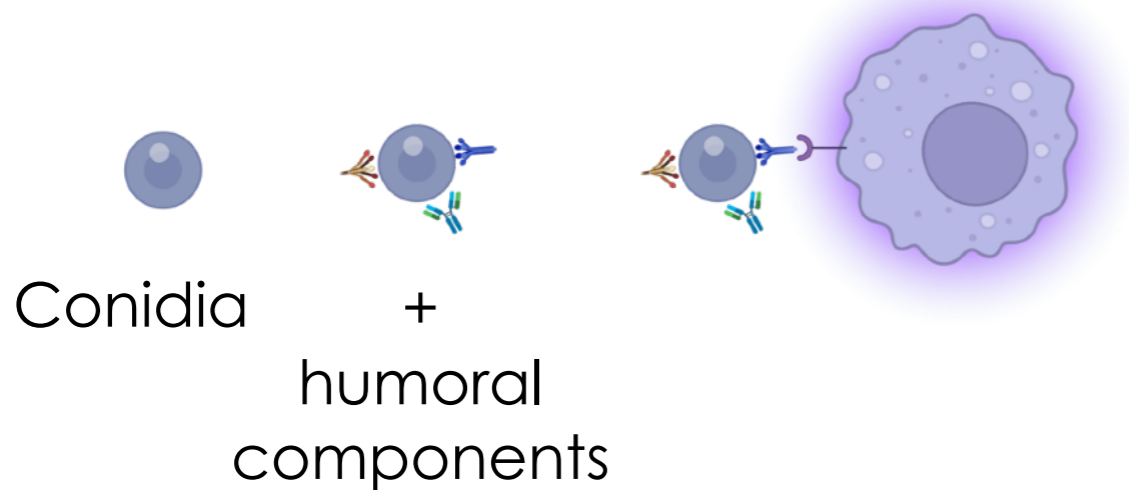
Multiple functions

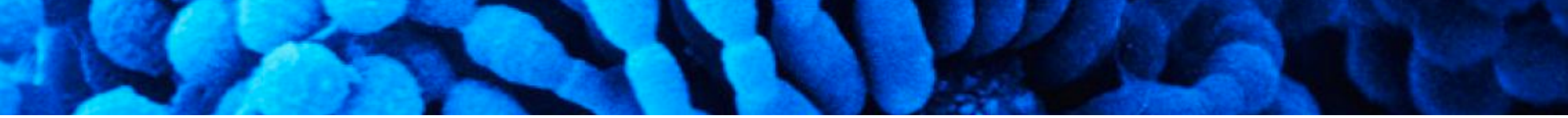
Direct
interaction



Liking pathogens and
immune cells

Opsonisation and soluble mediators





Multiple functions

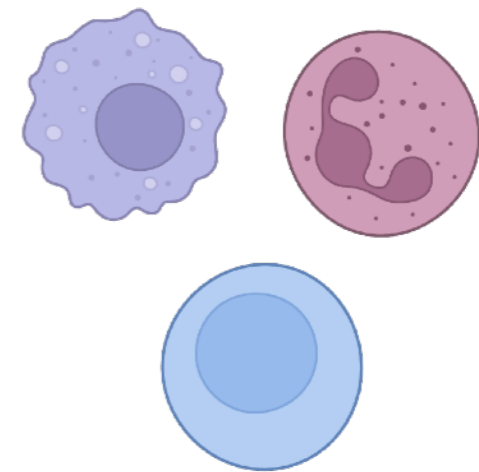
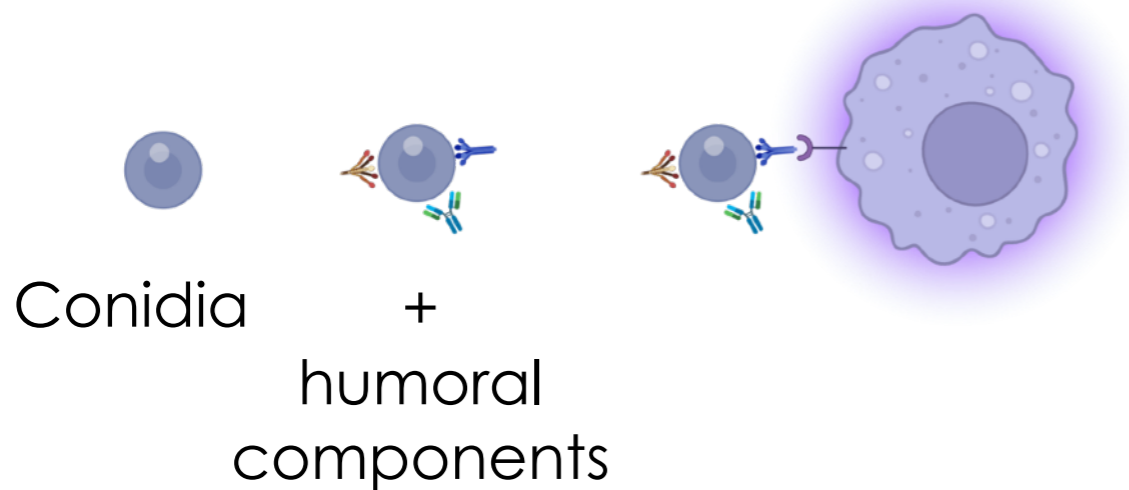
Direct interaction



Liking pathogens and immune cells

Anaphylotoxins

Opsonisation and soluble mediators

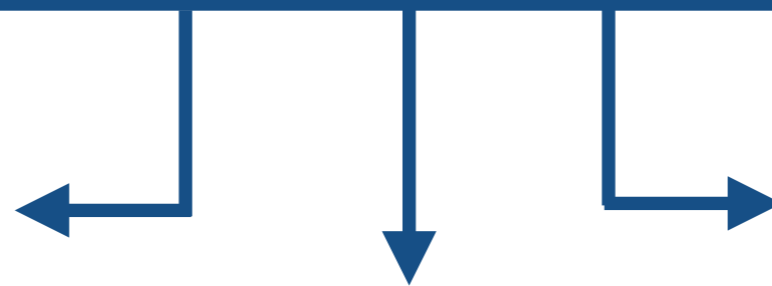


Recruitment

Aims

1. Identify major players of humoral immunity against *Aspergillus fumigatus* in BAL
2. Understand their interaction at molecular level and their impact on immune response

Identify candidate host markers of aspergillosis



Develop new therapeutic strategies

Identify new leads to understanding the pathogenesis



BAL

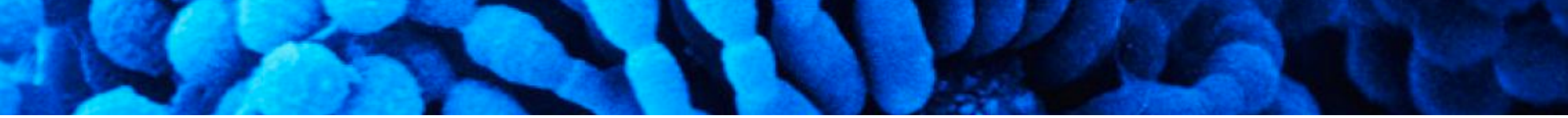
Aspergillus+ versus **control**

- 3 Invasive PA
- 3 Chronic PA
- 4 colonization



Proteomic
analysis





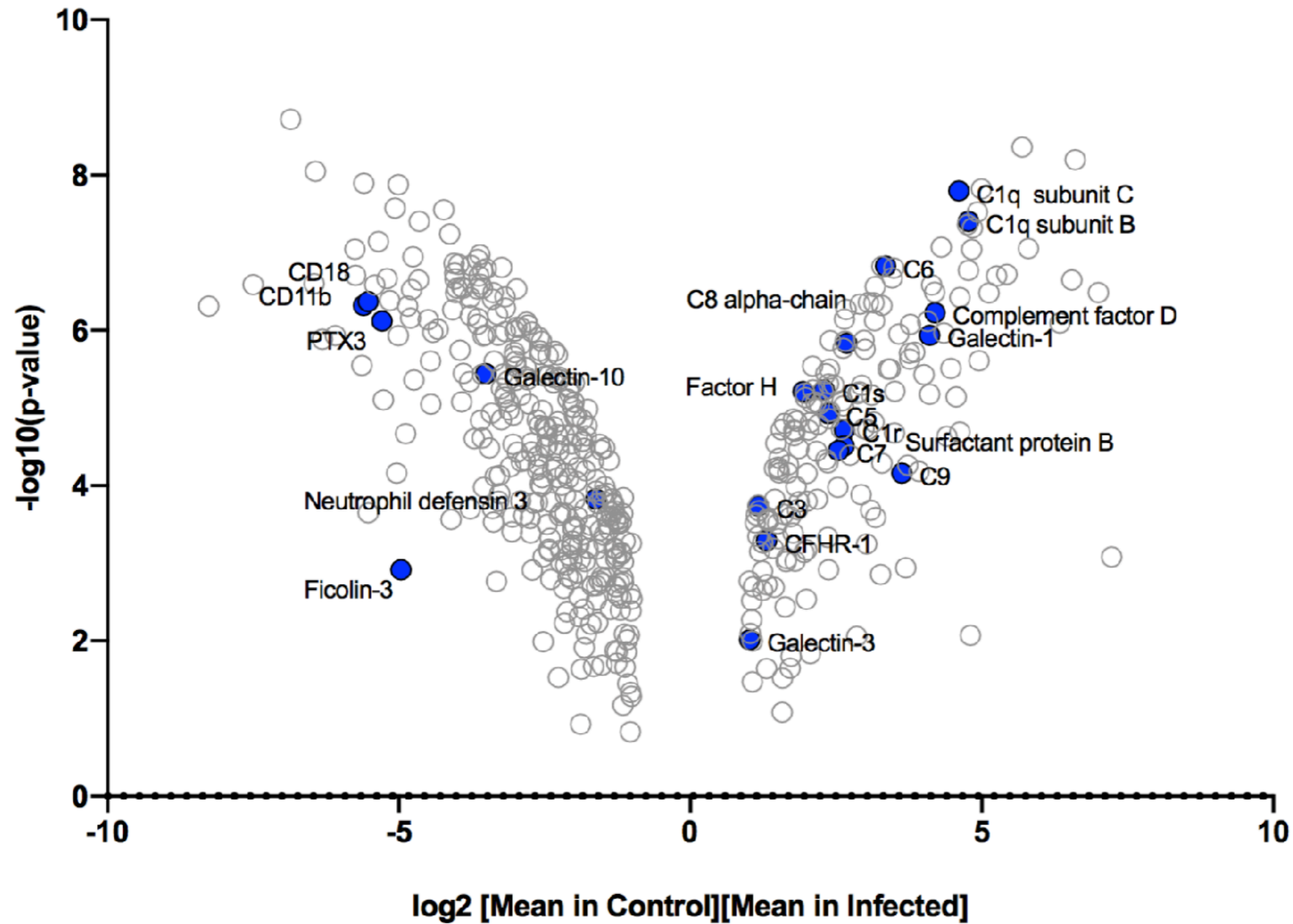
BAL

Aspergillus+ versus **control**

- 3 Invasive PA
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Proteomic analysis

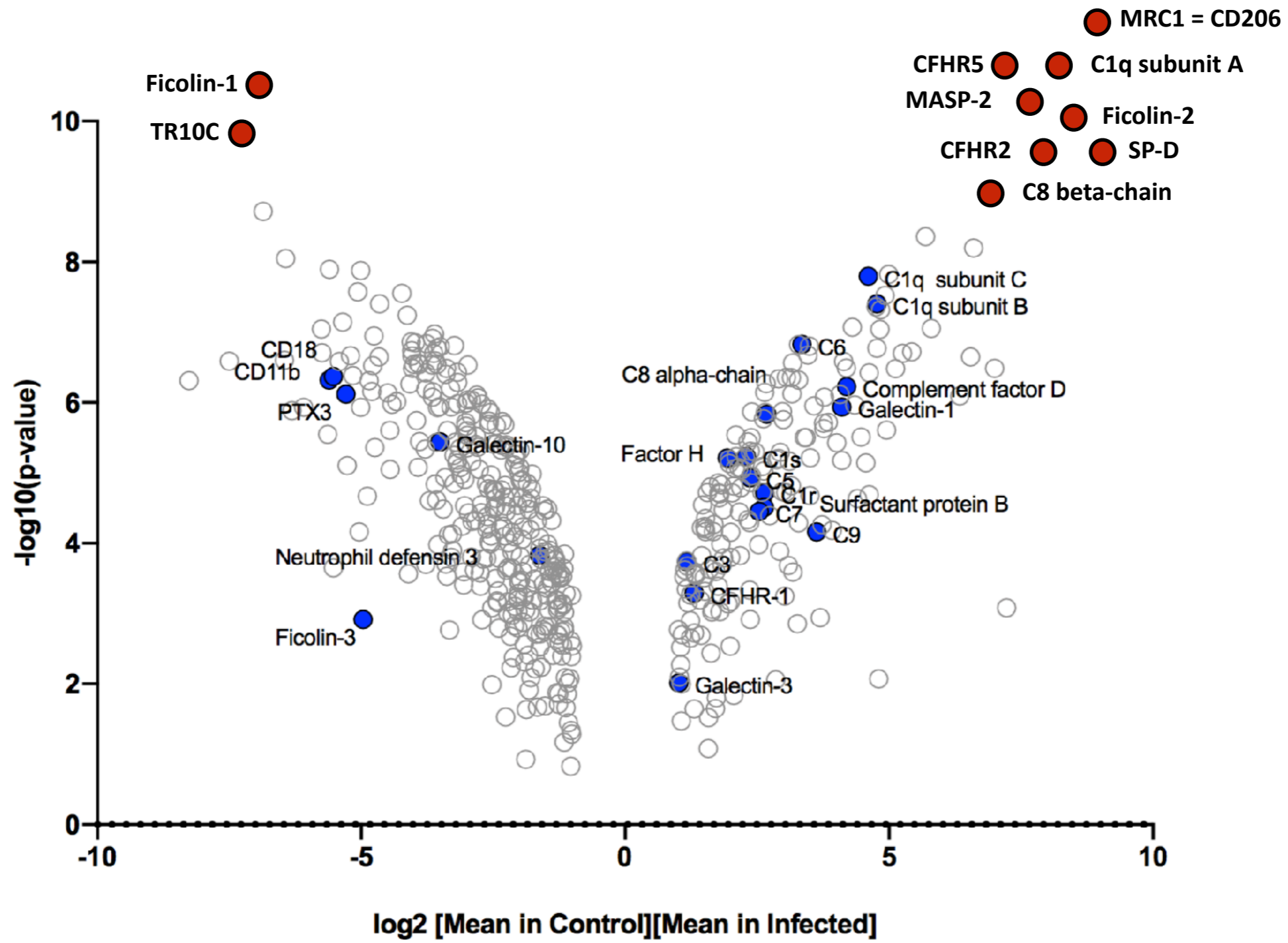
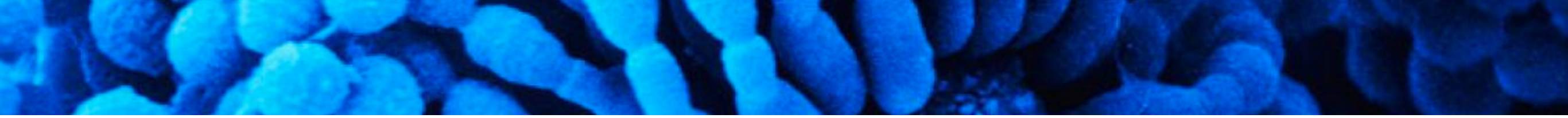


Increased in **Asp+** BAL

6



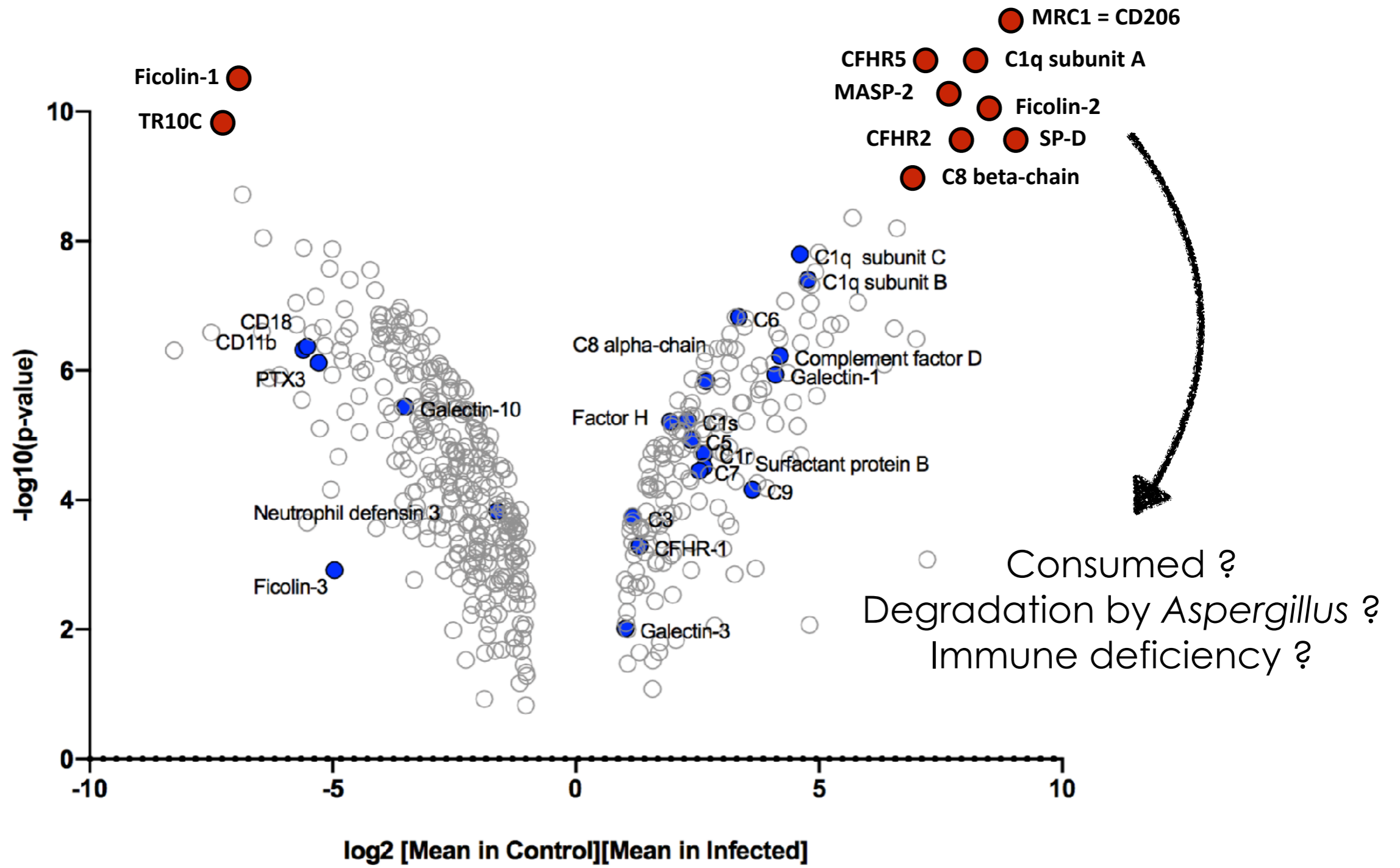
Decreased in **Asp+** BAL



←
Increased in Asp+ BAL

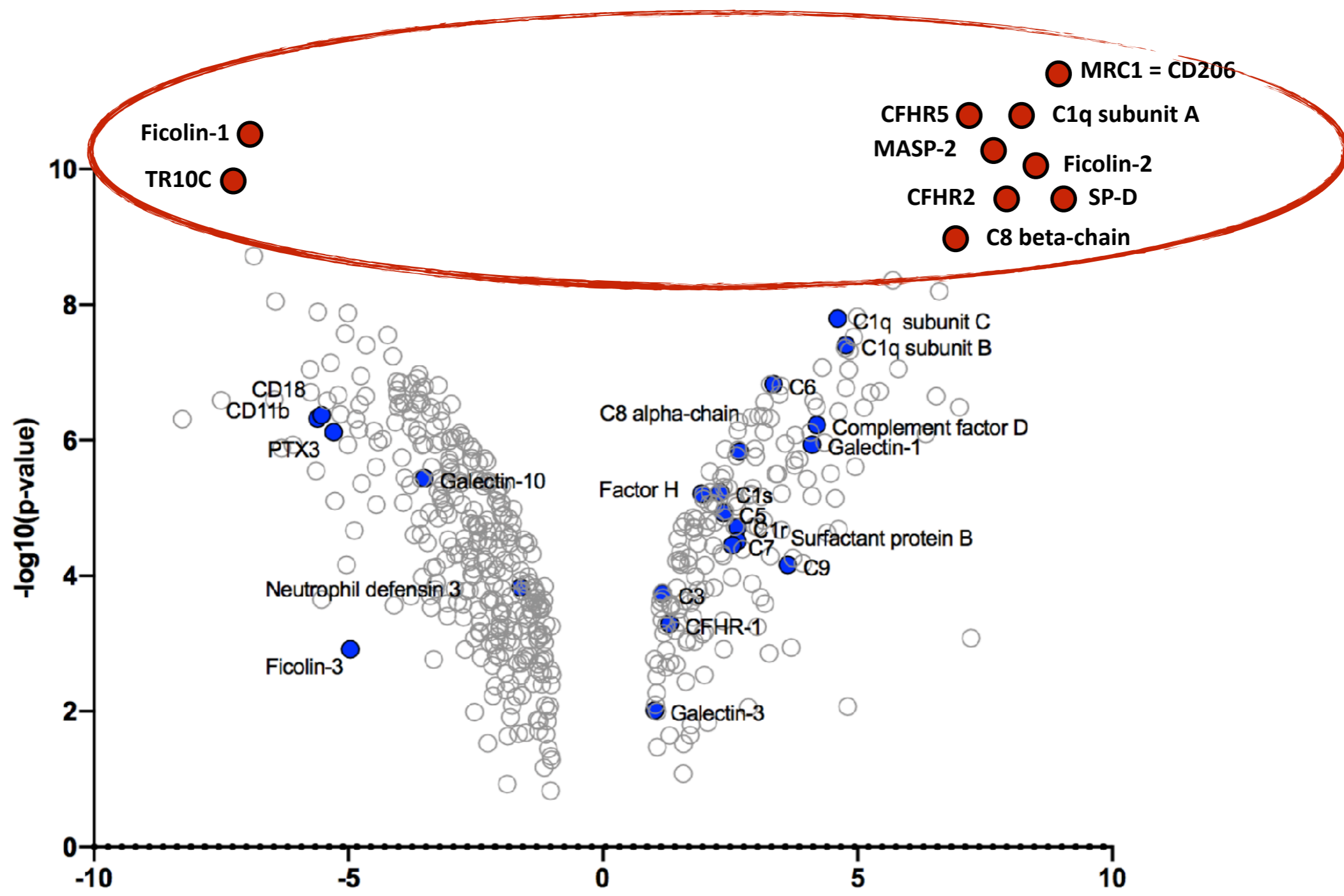
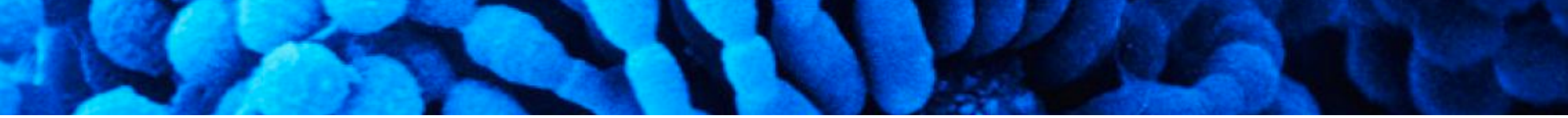
7

→
Decreased in Asp+ BAL

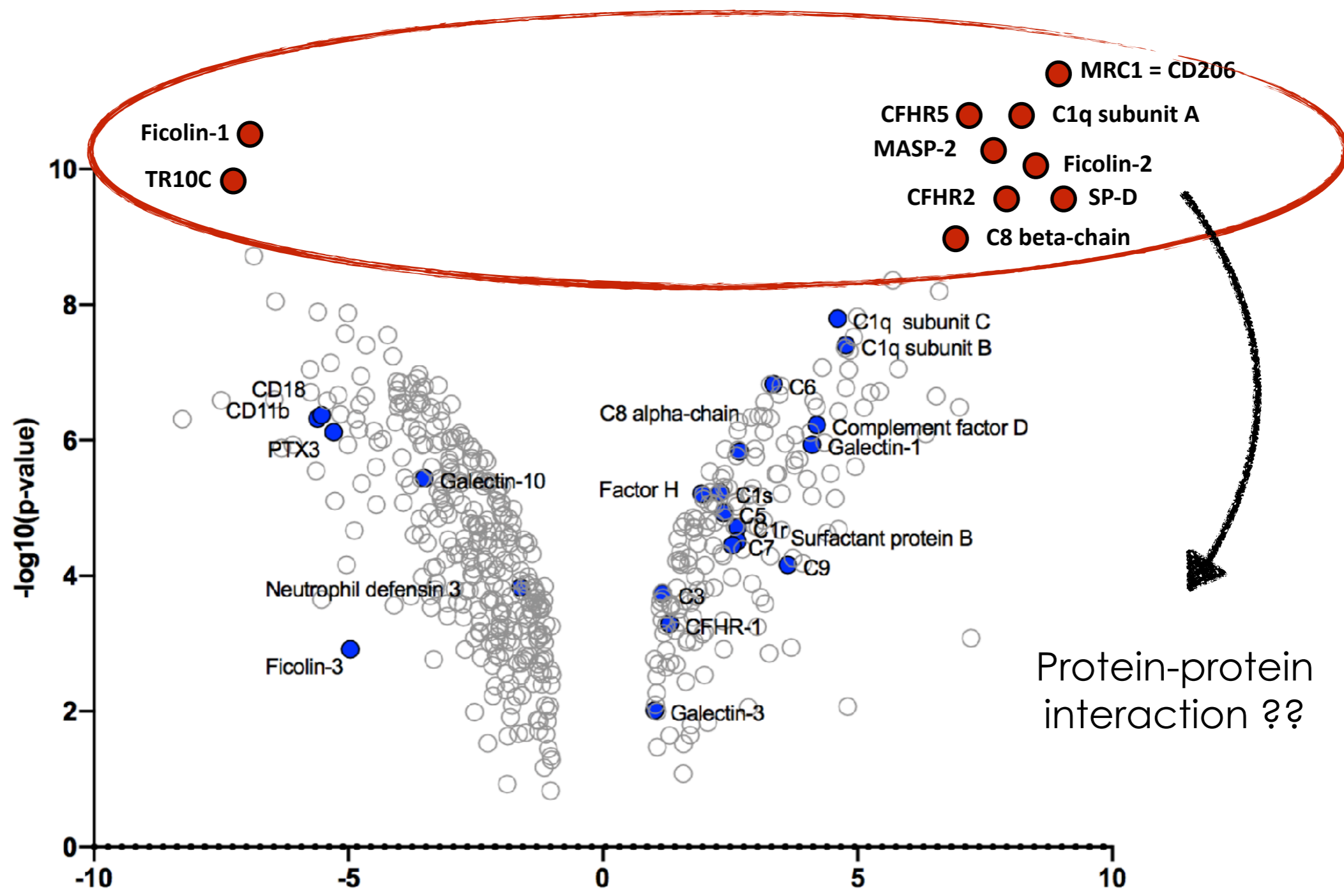
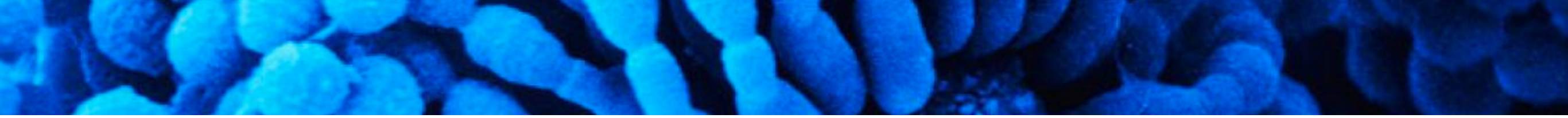


← Increased in Asp+ BAL

→ Decreased in Asp+ BAL

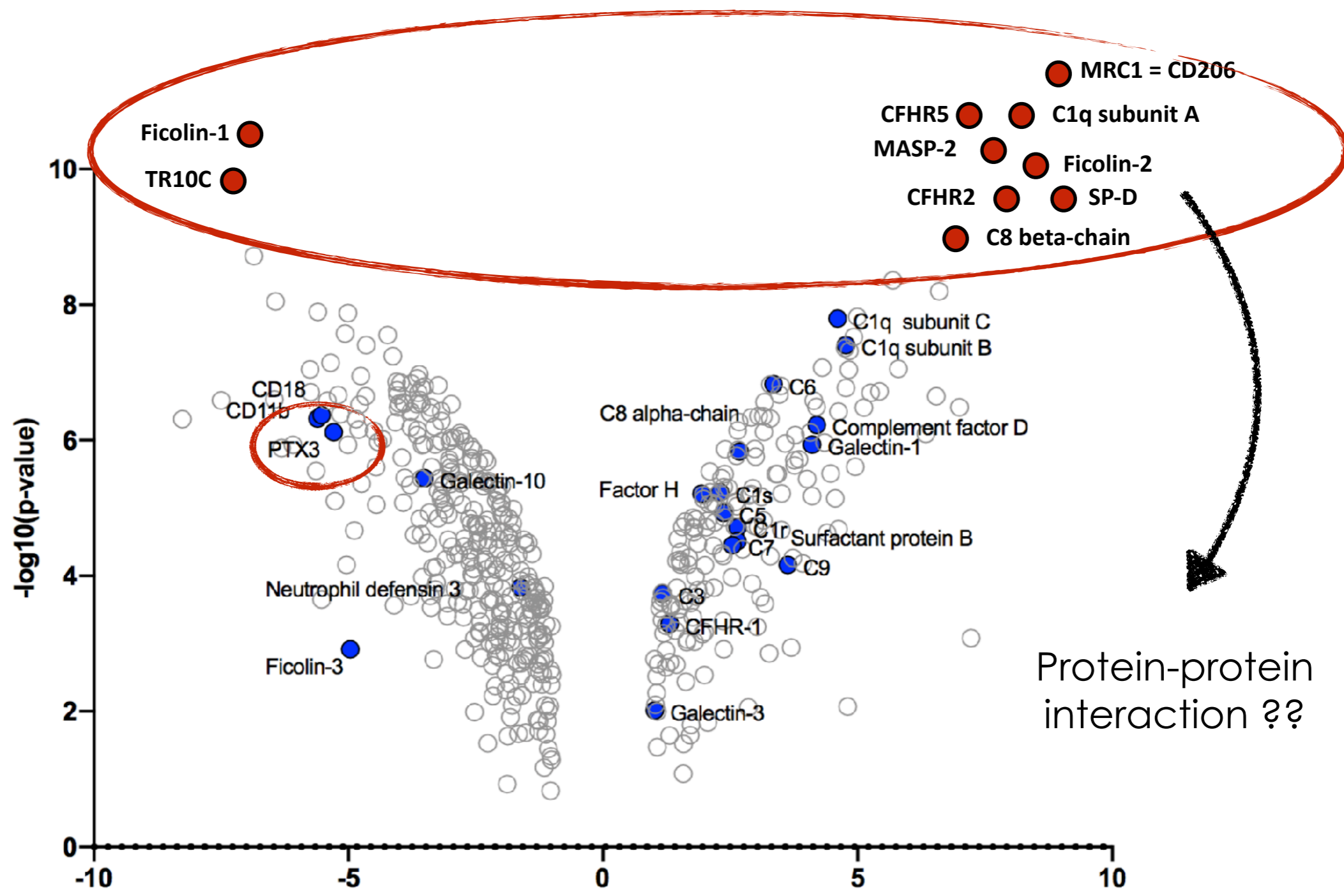


← Increased in Asp+ BAL 8 Decreased in Asp+ BAL →



← Increased in Asp+ BAL

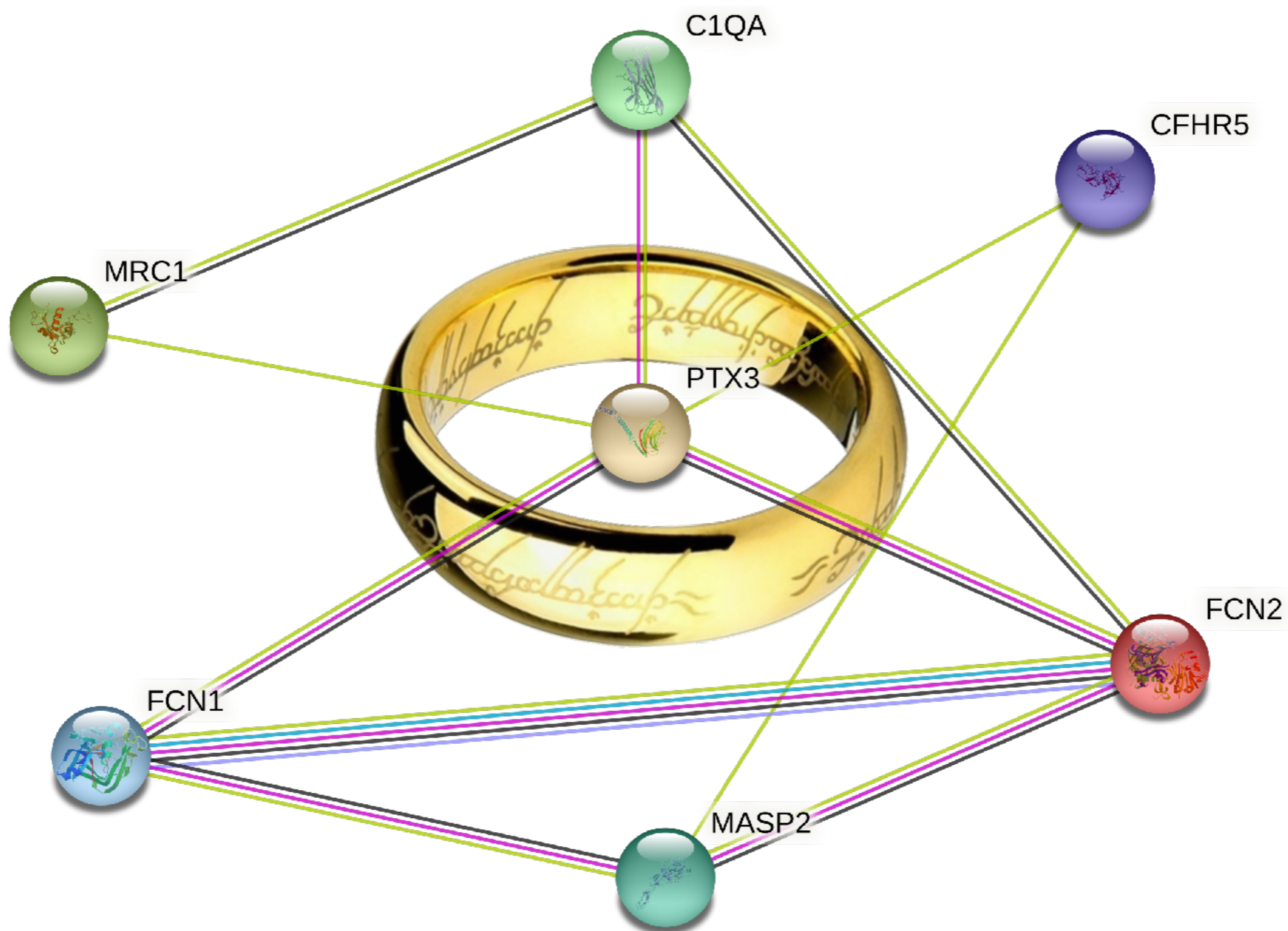
→ Decreased in Asp+ BAL



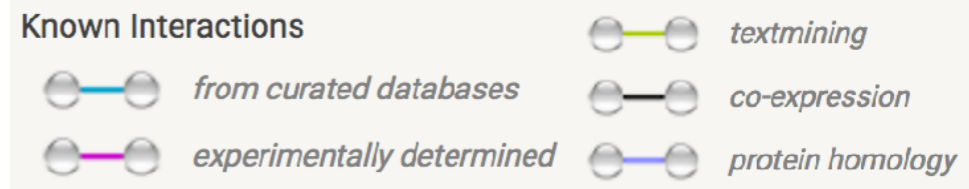
Protein-protein interaction ??

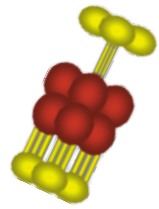
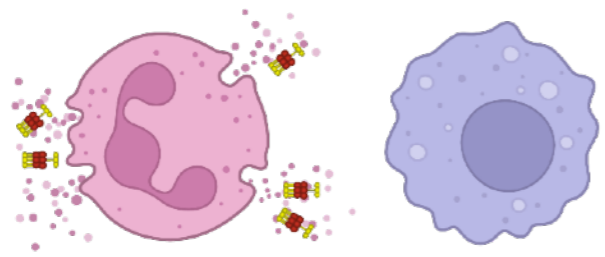
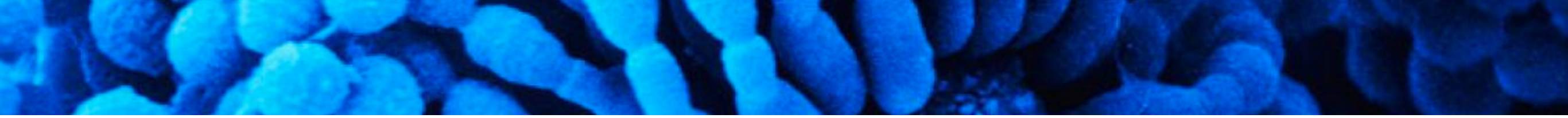
← Increased in Asp+ BAL 8 Decreased in Asp+ BAL →

One protein to bind them all ?



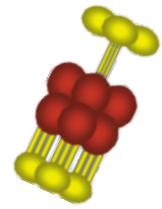
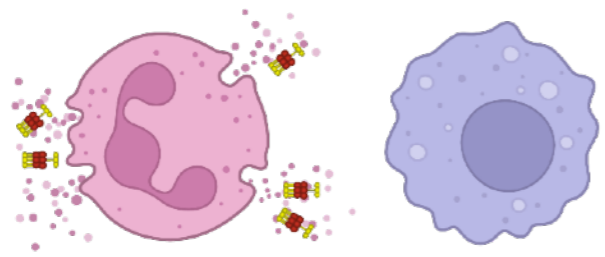
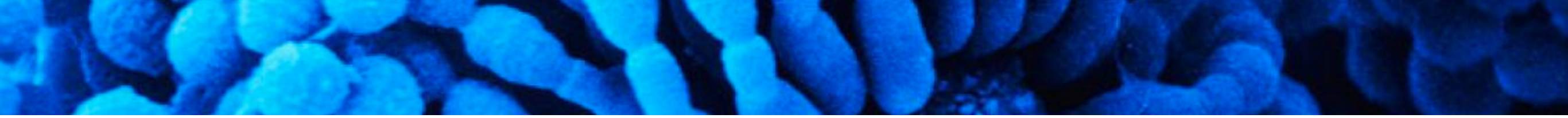
Immune crosstalk ?





Pentraxin-3

PTX3^{-/-} mice = ↑ ↑ ↑ susceptibility to IPA
Confirmed by human genetic variability
PRR

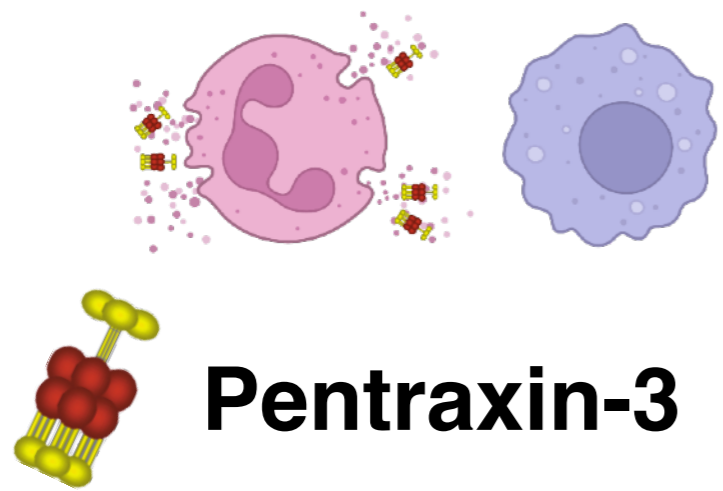


Pentraxin-3

PTX3^{-/-} mice = ↑ ↑ ↑ susceptibility to IPA
Confirmed by human genetic variability
PRR

Binding...

To conidia at high concentration



Pentraxin-3

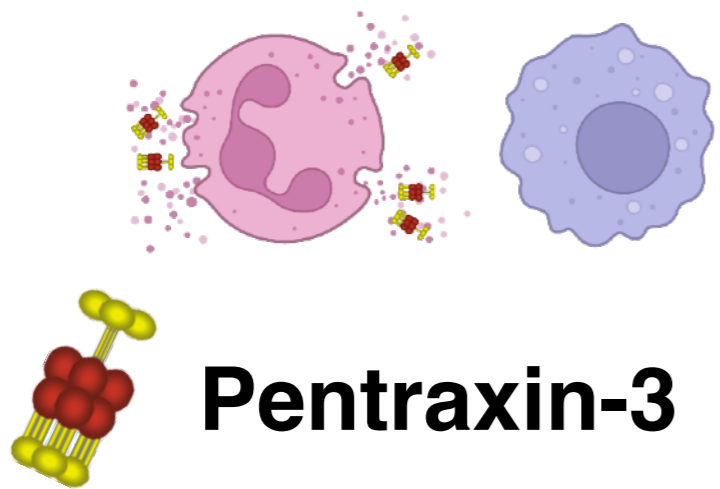
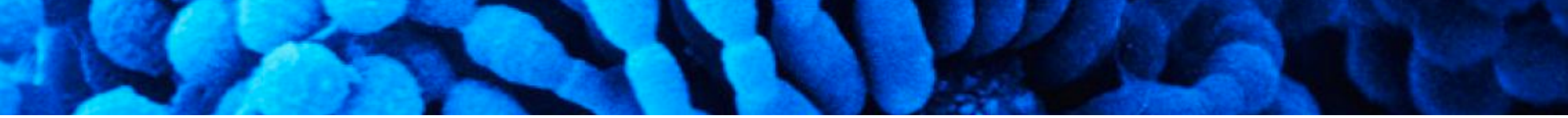
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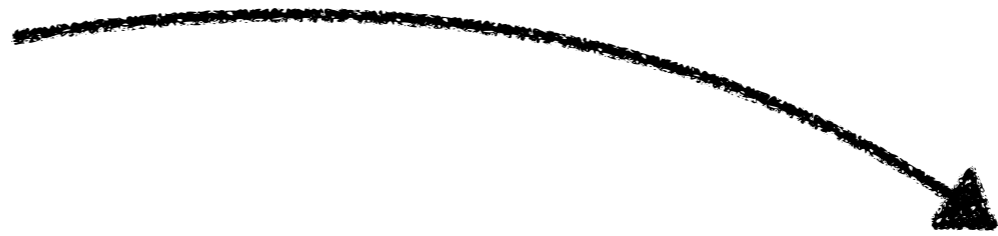


**Complement activation
Enhances Th1 response ?**



Pentraxin-3

PTX3^{-/-} mice = ↑ ↑ ↑ susceptibility to IPA
Confirmed by human genetic variability
PRR



Diagnosis marker ?
Therapy ?

To read list :
Kabbani et al. 2017
Biagi et al. 2008
Parente et al. 2020

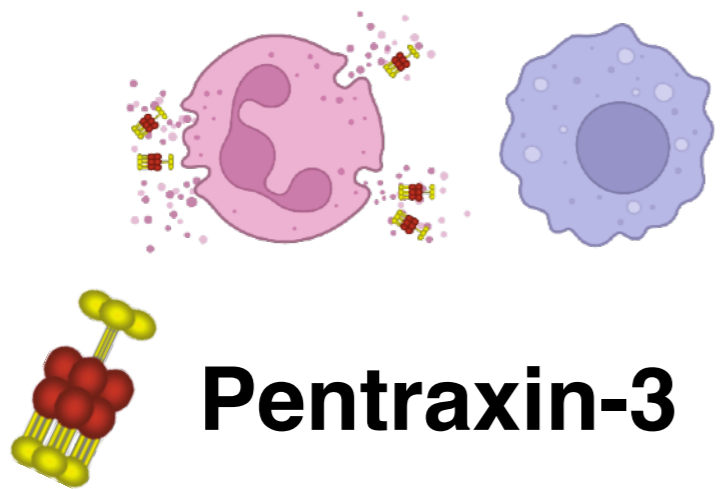
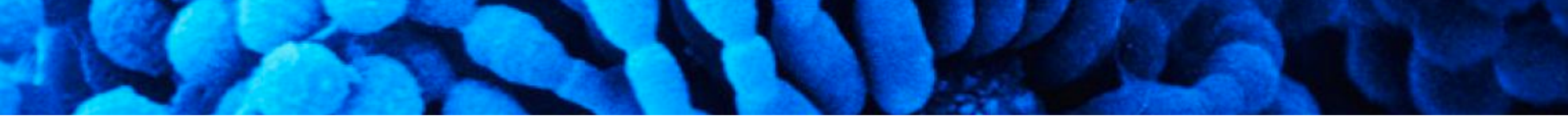
Binding...

To conidia at high concentration



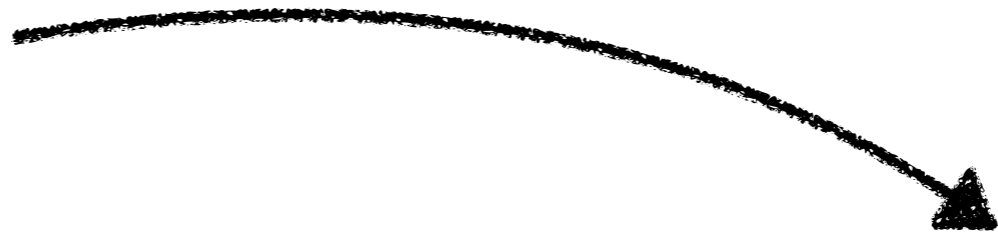
**Complement activation
Enhances Th1 response ?**

Parente et al. FEBS letters, 2020
Garlanda et al. Nature, 2001
Cunha et al. NEJM, 2014



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Binding...

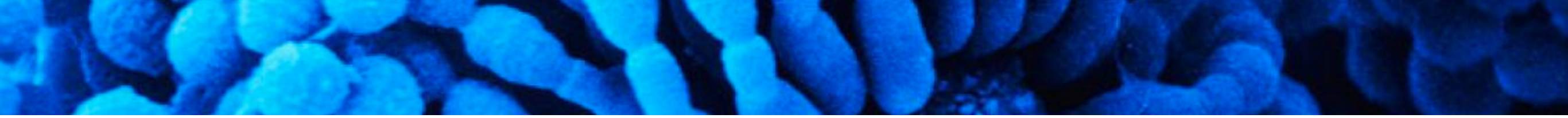
To conidia at high concentration

Ligand ?
Clear mechanism of action ?

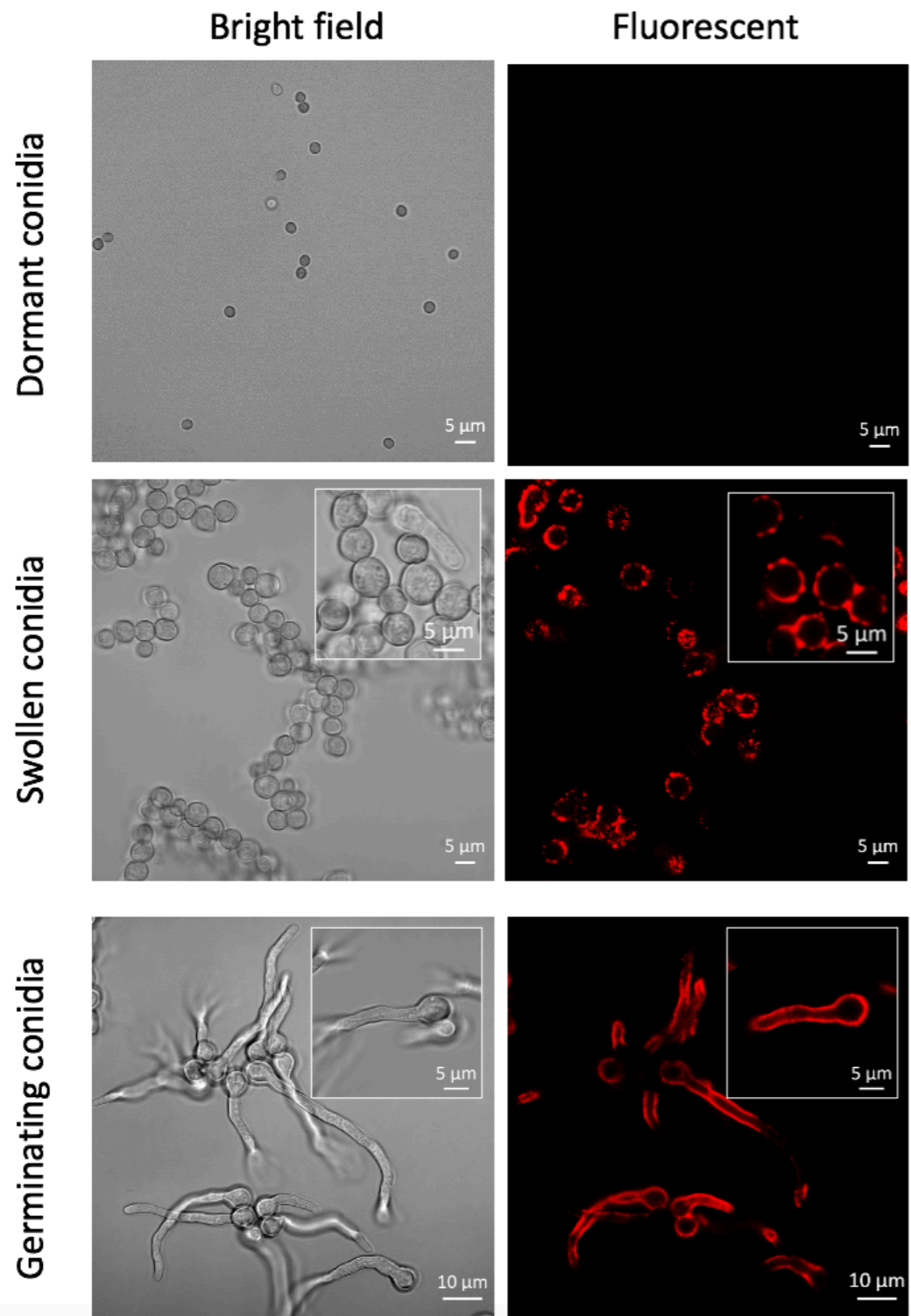


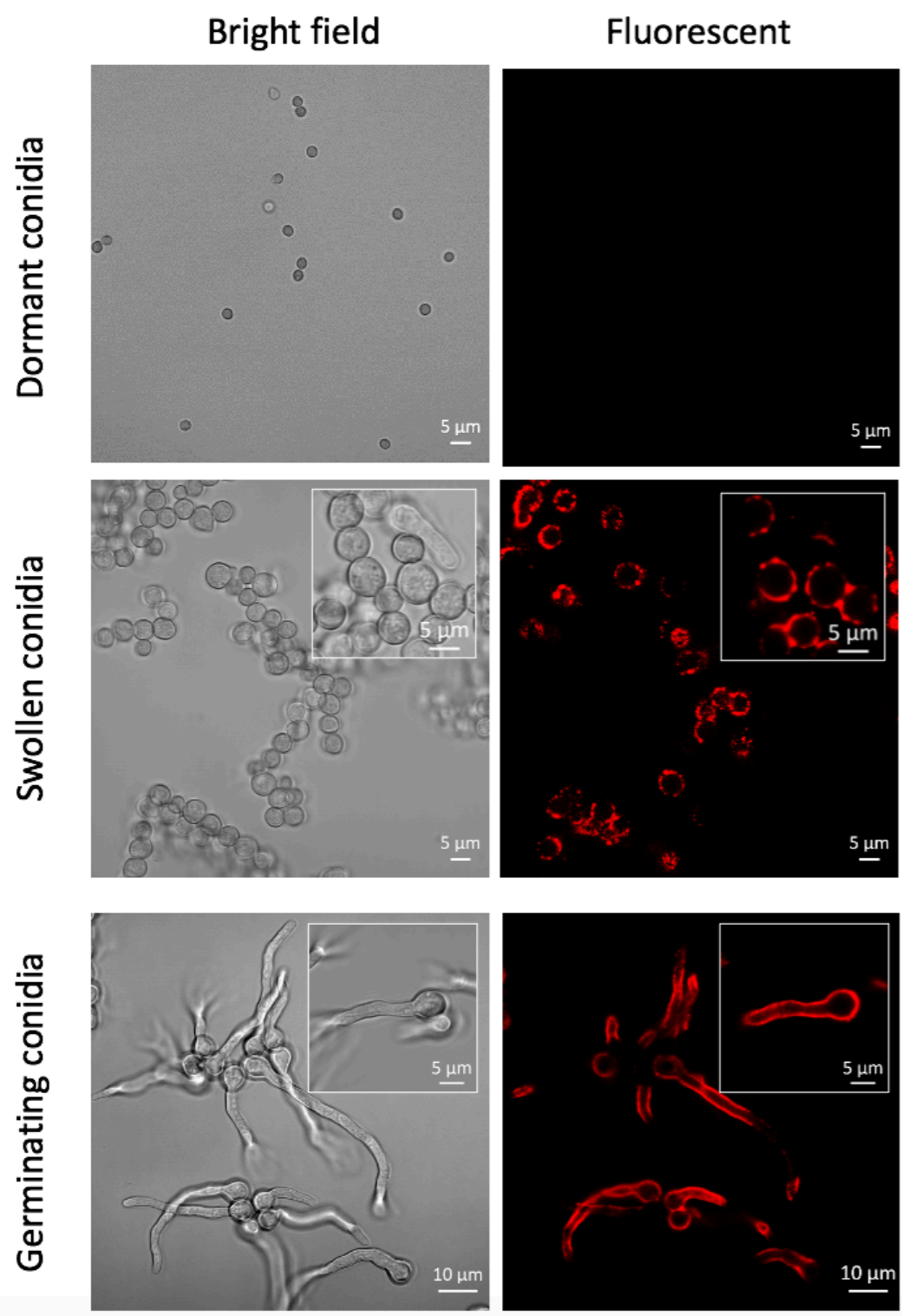
Complement activation
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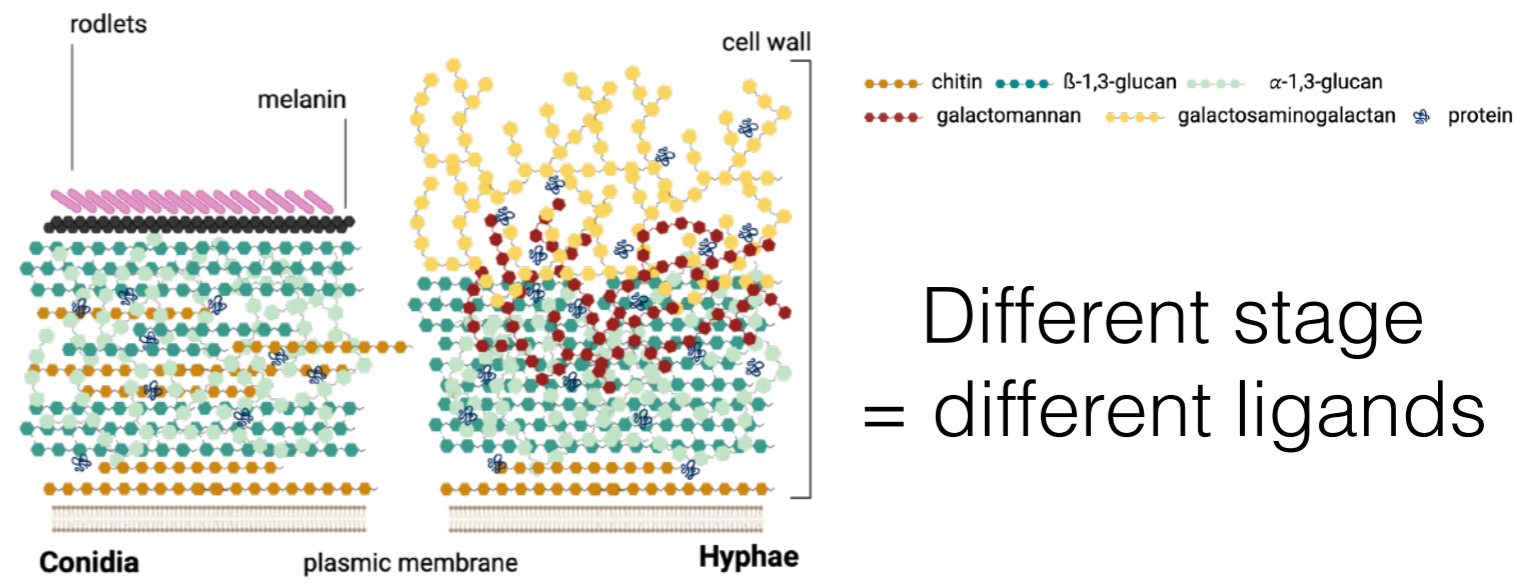


No binding to dormant conidia
(Poor binding observed by flow cytometry)
Binding to swollen and germinated conidia

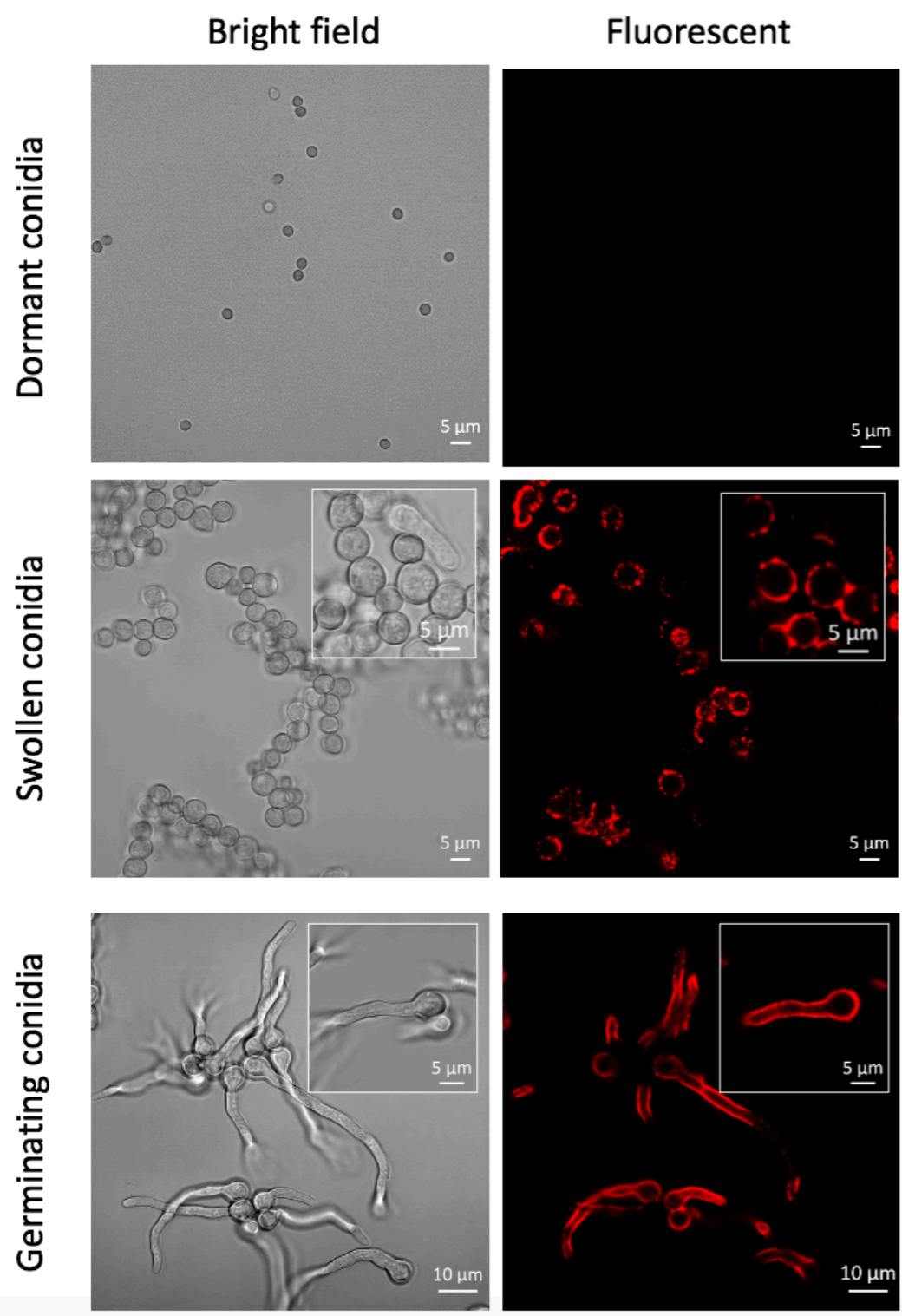
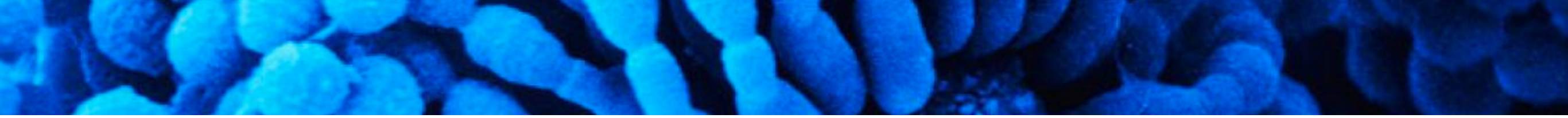




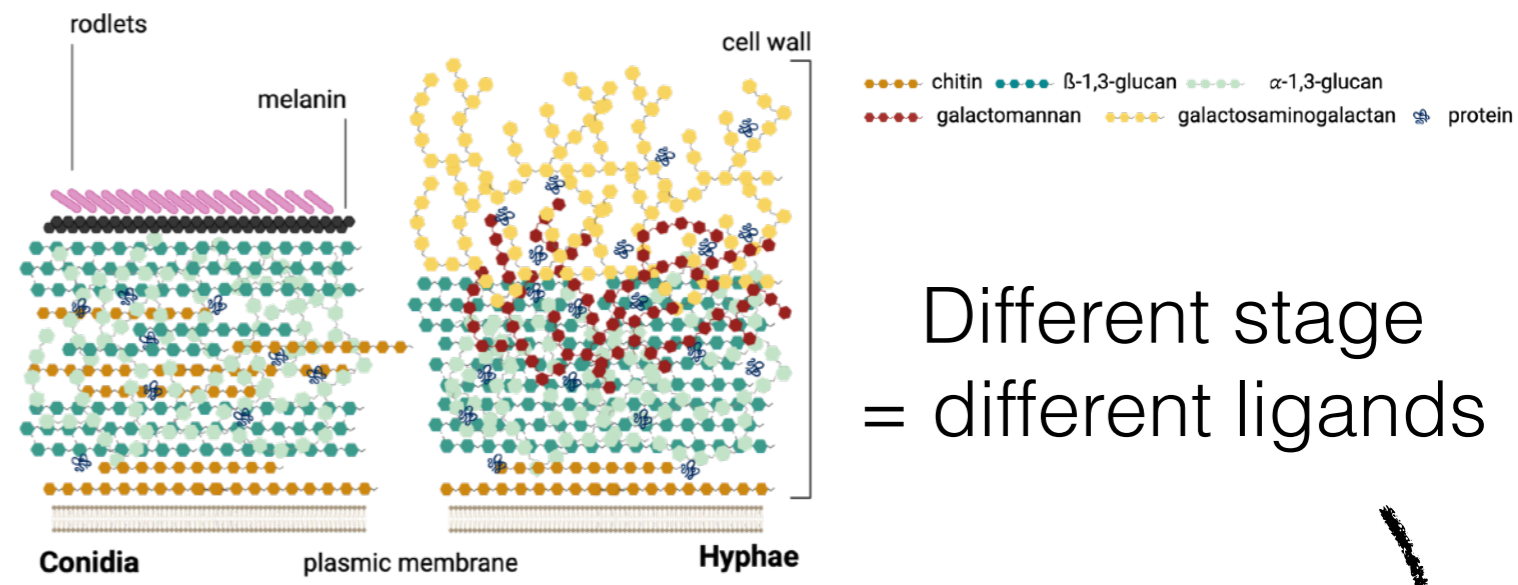
No binding to dormant conidia
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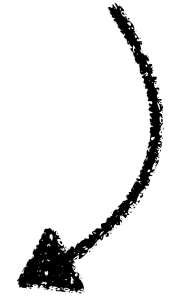
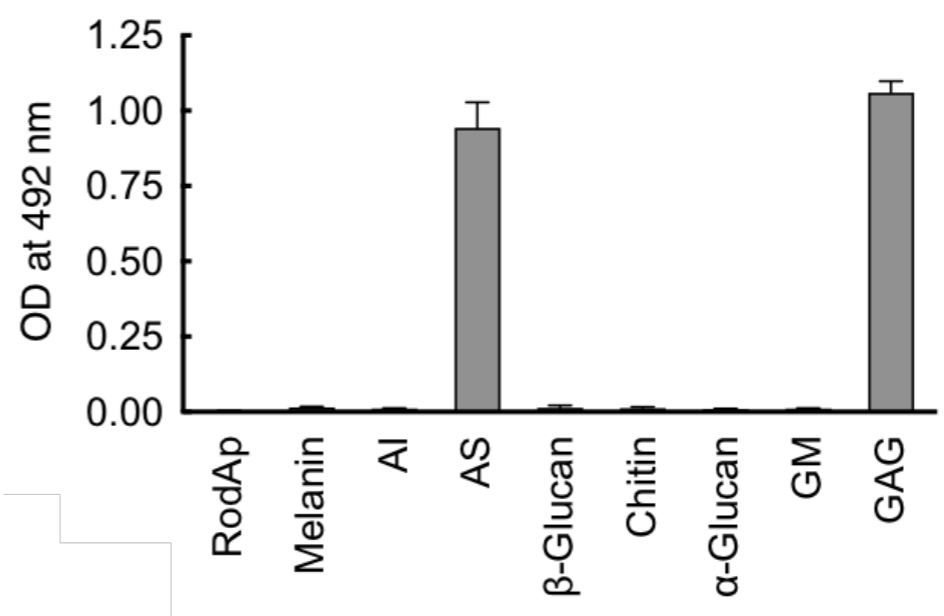
Different stage
= different ligands



No binding to dormant conidia
(Poor binding observed by flow cytometry)
Binding to swollen and germinated conidia



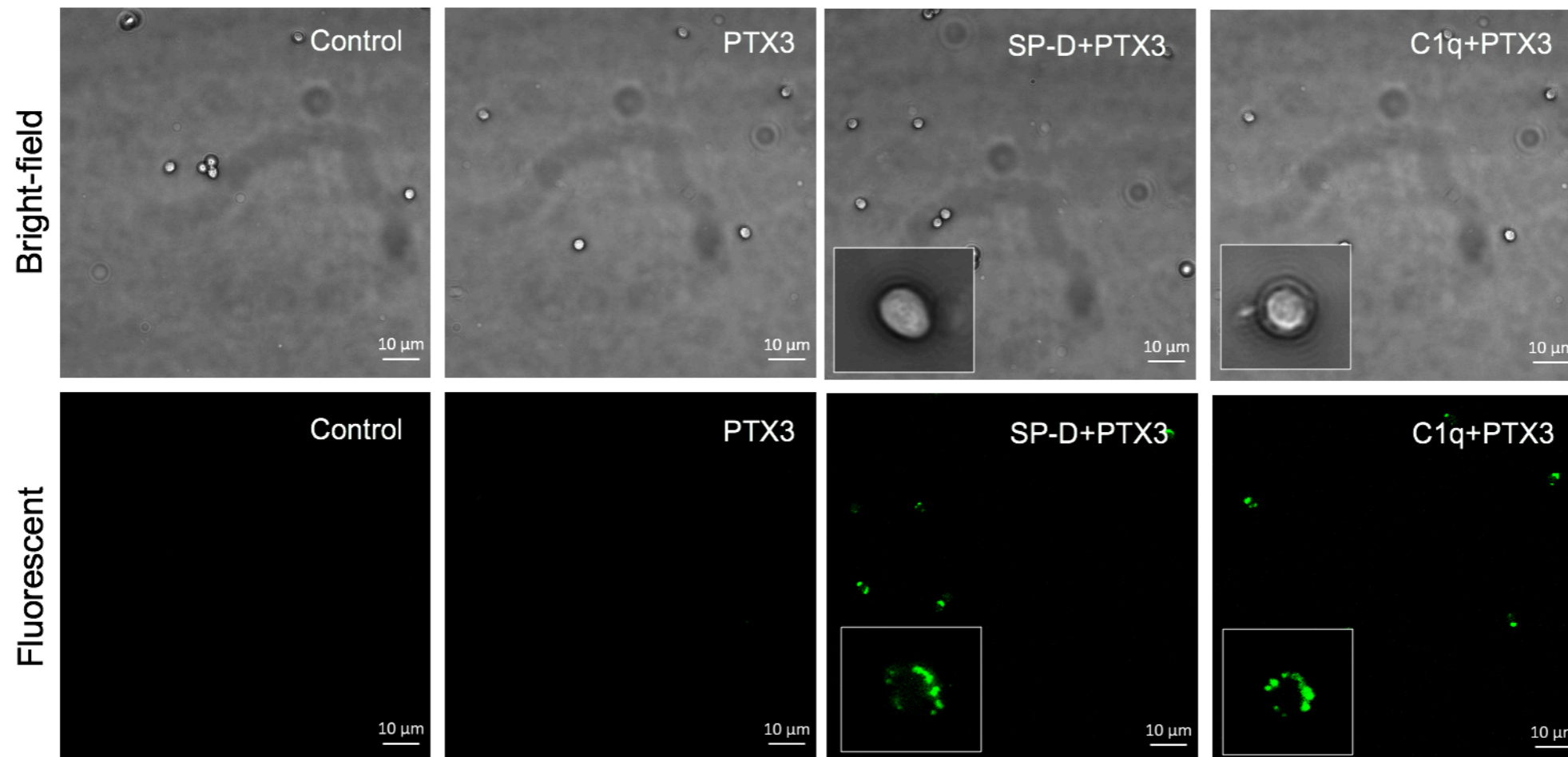
Different stage
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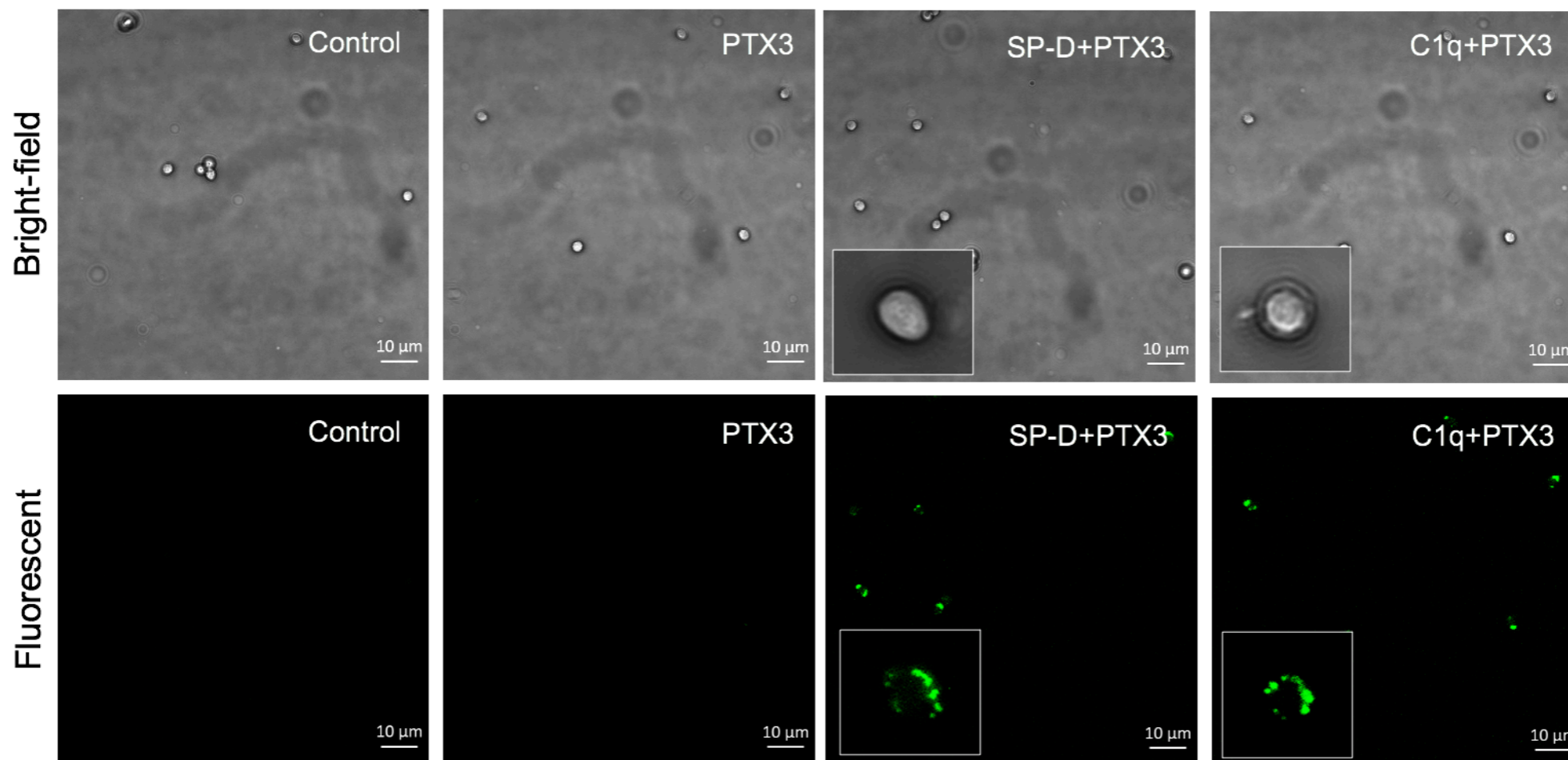
PTX3 binds galactosaminogalactan

AI: Alkali-Insoluble
AS: Alkali-Soluble

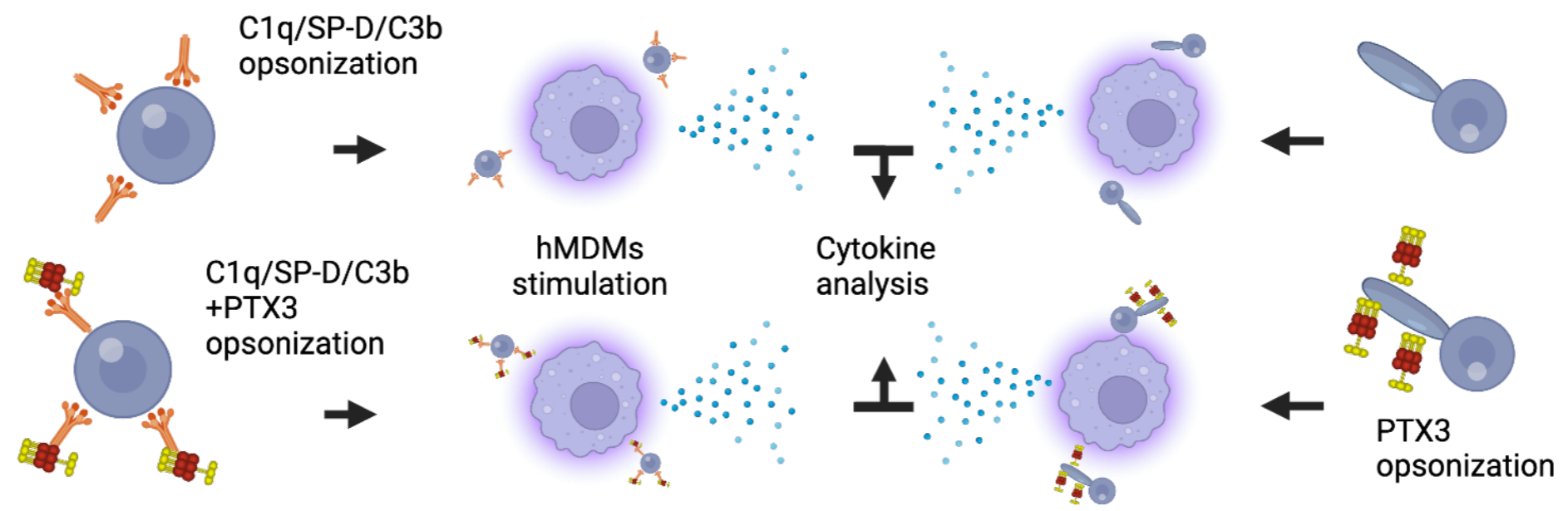
Confirmed increased binding of PTX3 to conidia through SP-D, C1q and C3b

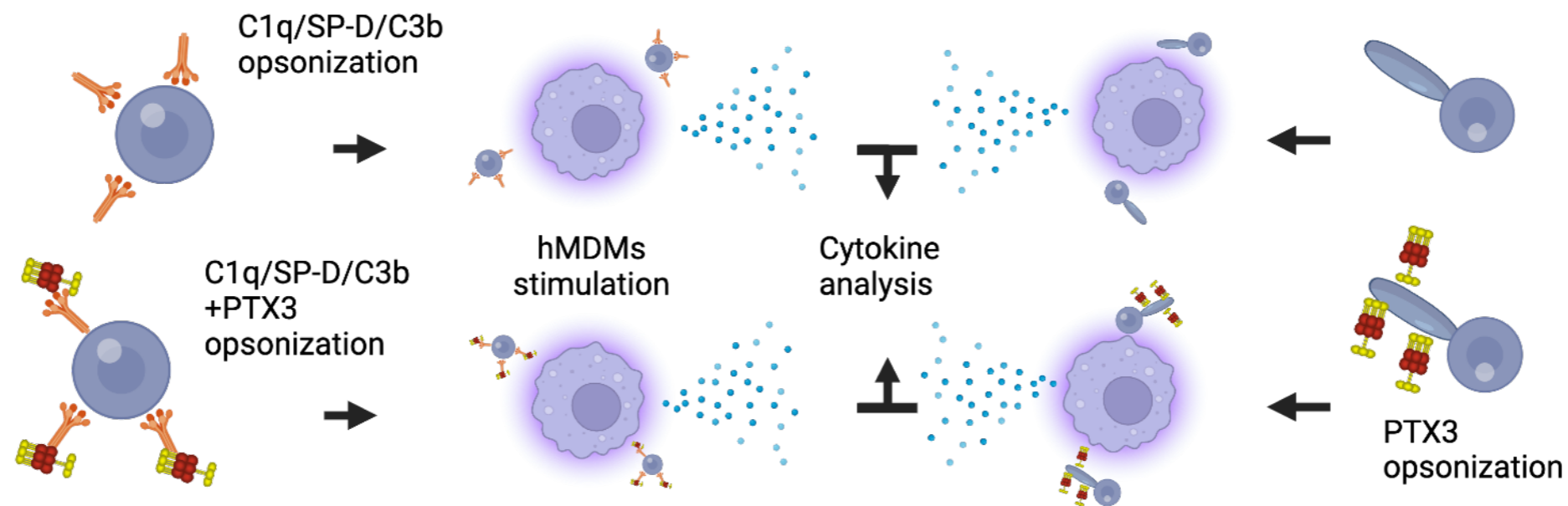
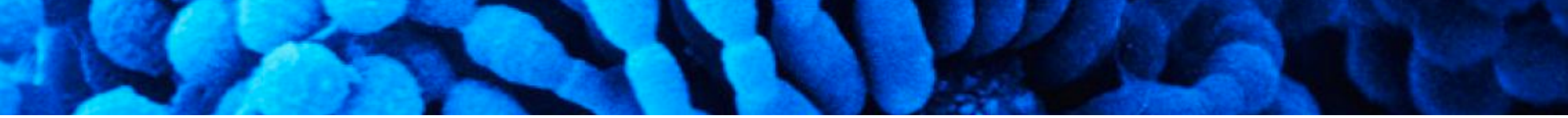


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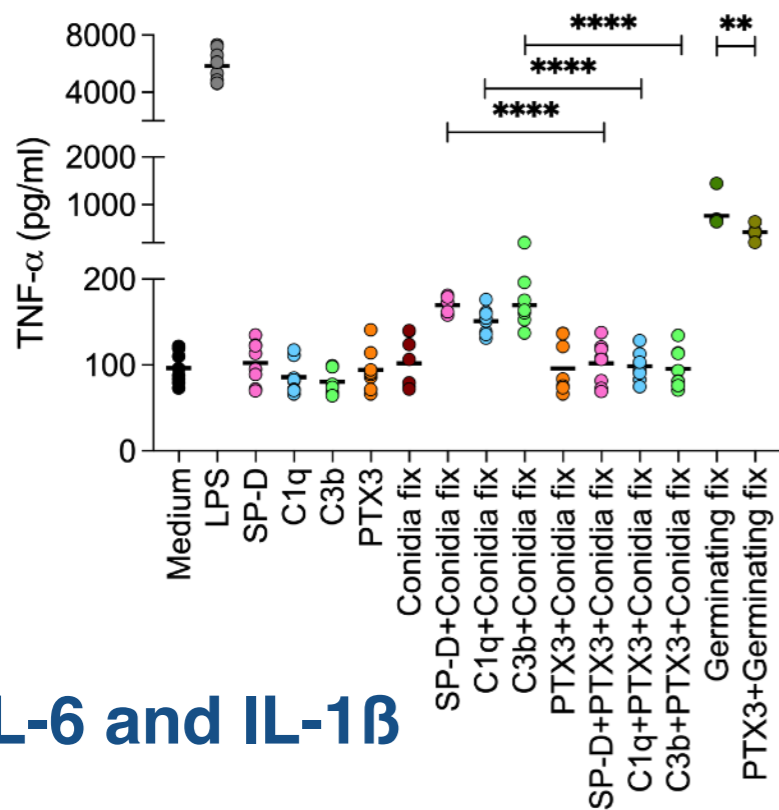


What is the impact of this indirect (conidia) or direct (hyphae) binding of PTX3 on the immune response ?

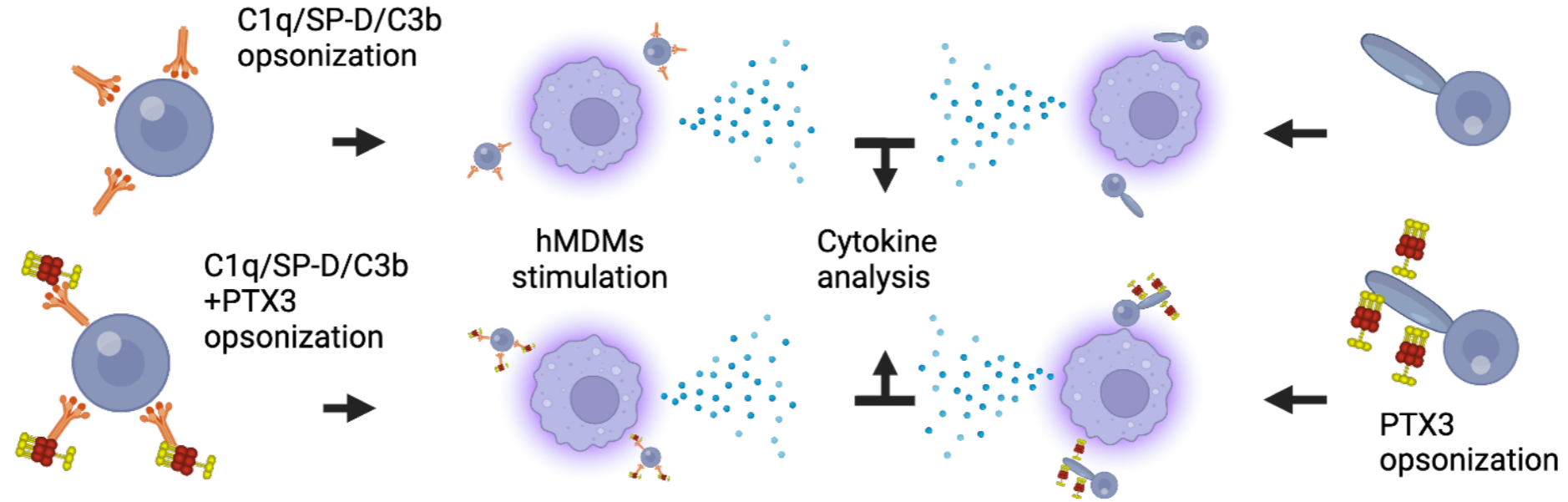
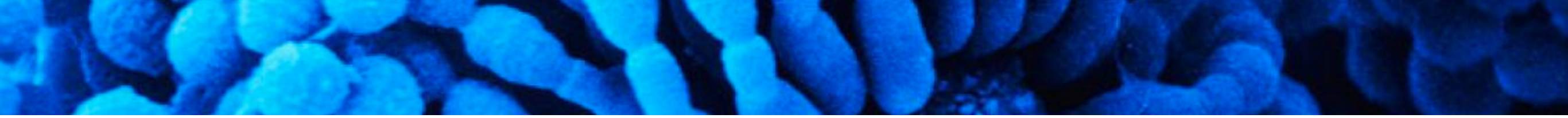




↓ pro-inflammatory cytokines

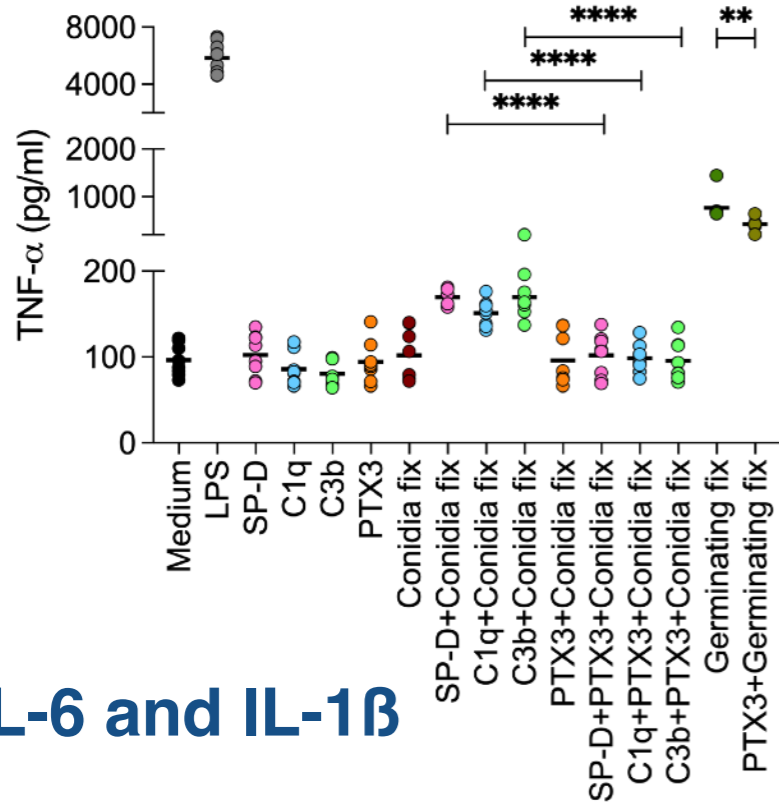


= IL-6 and IL-1 β

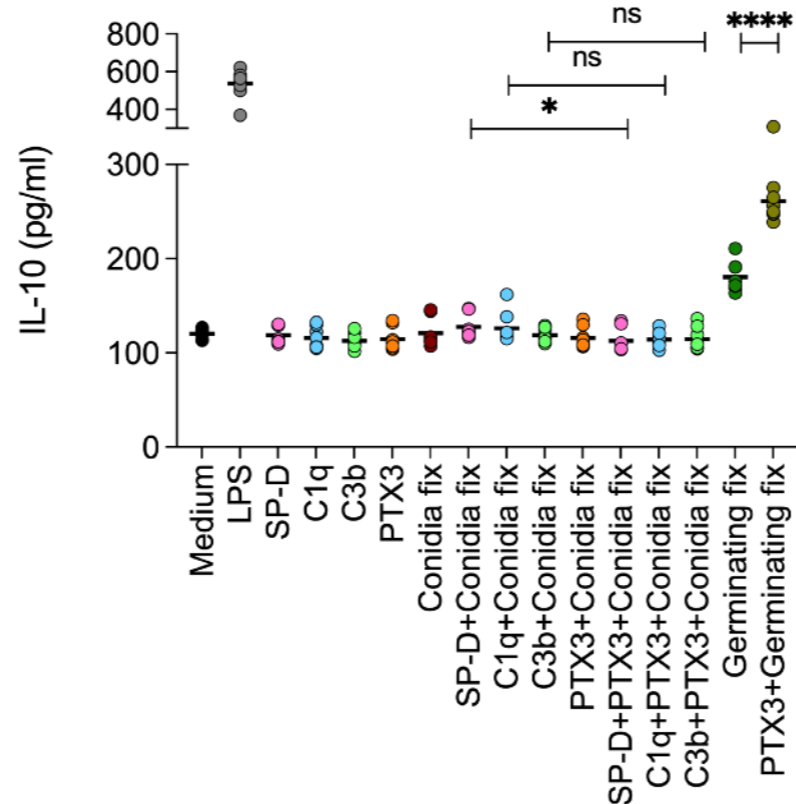


↓ pro-inflammatory cytokines

↑ anti-inflammatory cytokines

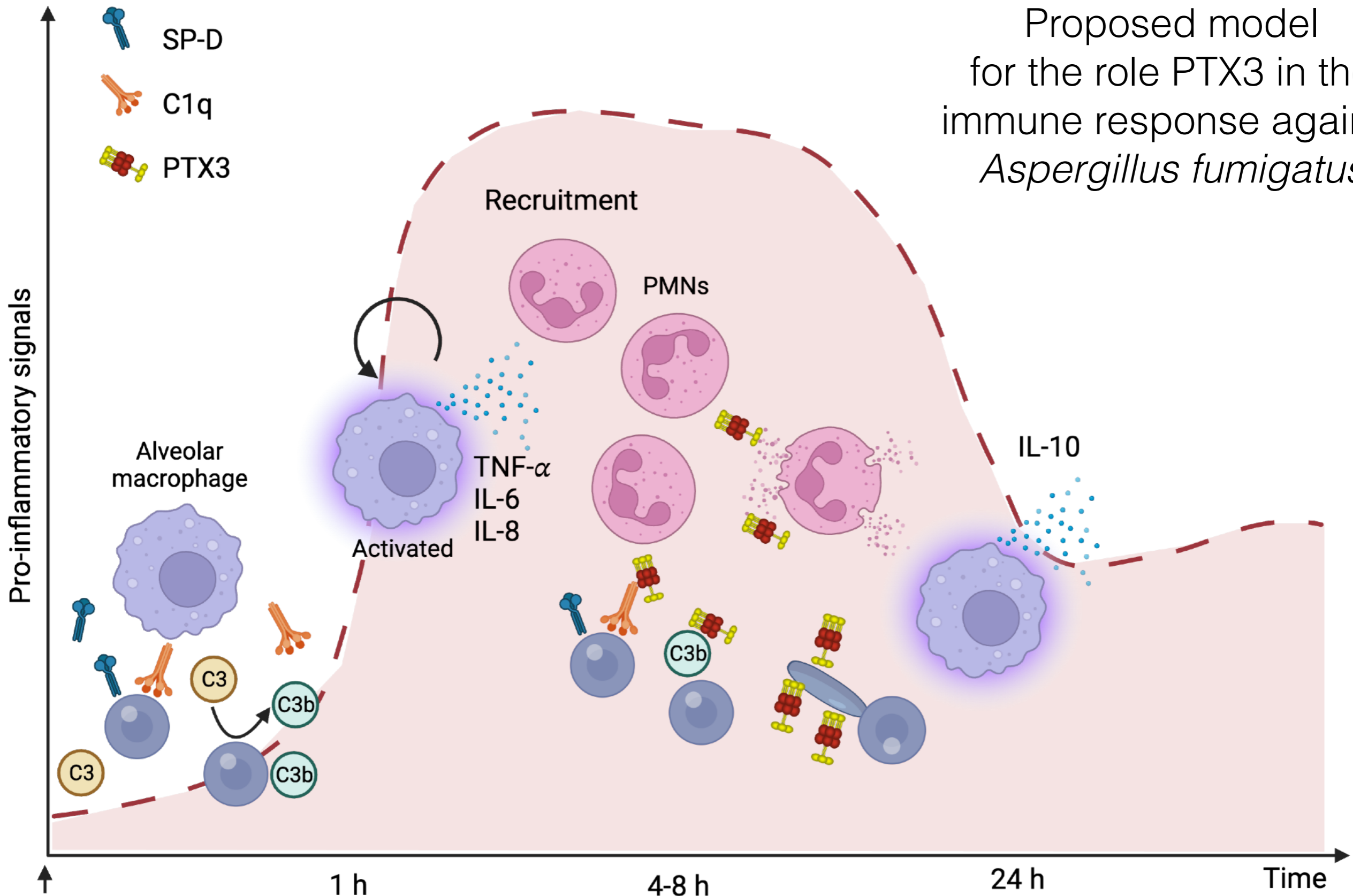


= IL-6 and IL-1β





Proposed model
for the role PTX3 in the
immune response against
Aspergillus fumigatus



Thank you for your attention

Immunobiology of *Aspergillus*

Vishukumar Aimanianda

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Sangeeta Roy
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Marie Desnos-Ollivier
Théo Ghelfenstein-Ferreira
Emilie Fruquière
Dea Garcia-Hermoso
Fanny Lanternier
Olivier Lortholary
Aude Sturny-Leclerc



Antonio Inforzato



Uday Kishore



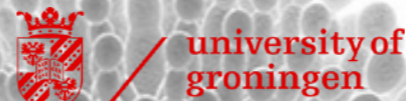
Camille Chauvin
Jagadeesh Bayry

CHU de Rennes

Jean-Pierre Gangneux
Hélène Guégan



Agostinho Carvalho



Vinodkumar
Magadigopalaiah



PBI Imagopole

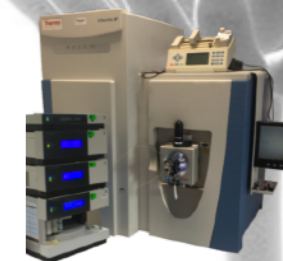
Audrey Salles
Julien Hernandez
Jean-Yves Tinevez

Molecular Biophysic

Patrick England



Samia Hamane
Alexandre Alanio
Stéphane Bretagne
Anne Bergeron
Stéphane Cassonnet
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