IL-RA Antibodies in Myocarditis after SARS-CoV-2 Vaccination

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Presentation content & objective

Objective: Discuss study data and future research agenda

Content: Part 1 (Christoph Kessel)

1. Brief background (IL-1/IL-1RA) and anti-IL-1Ra antibodies in MIS-C

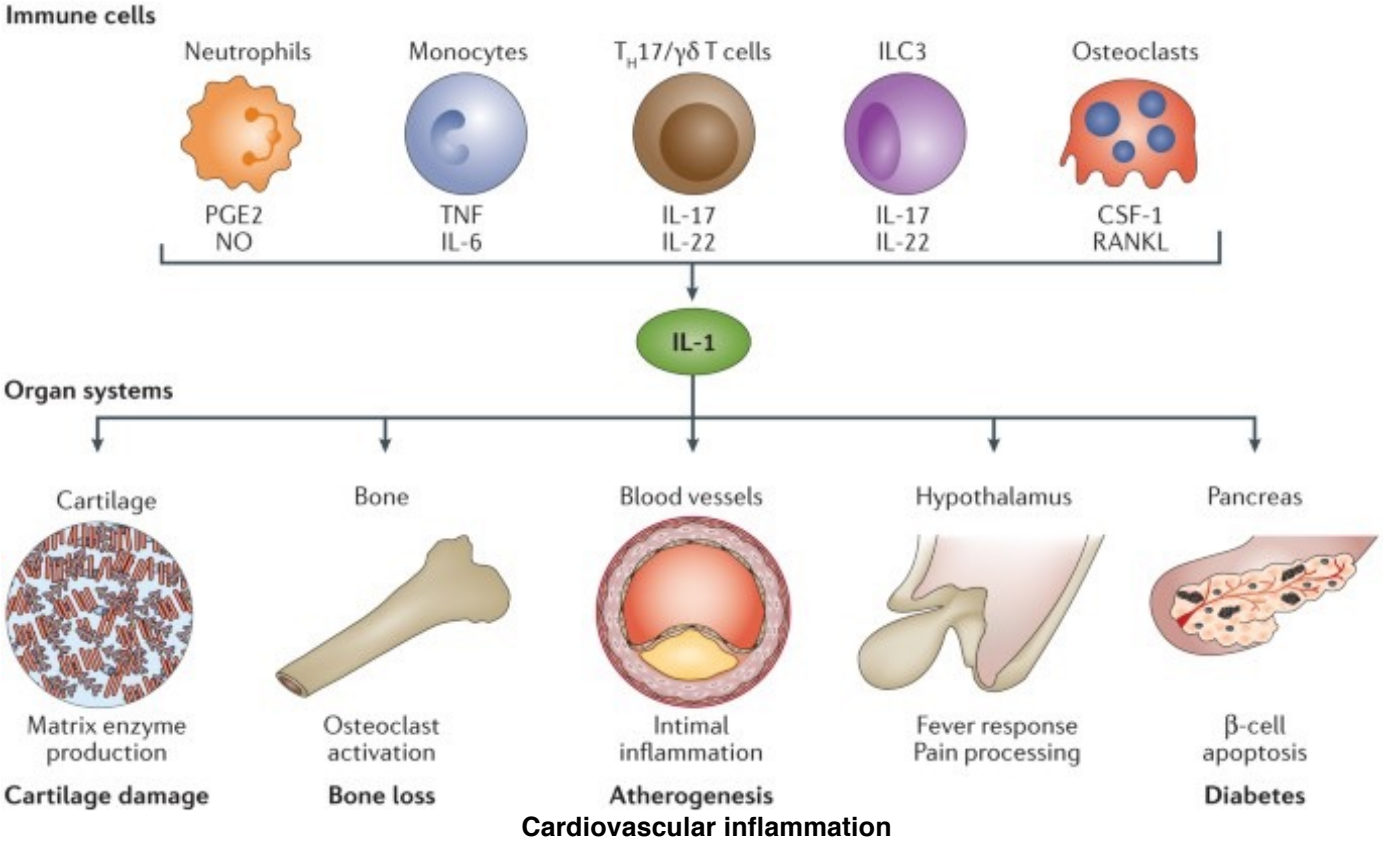
2. Anti-IL1RA antibodies in myocarditis after SARS-CoV-2 vaccination

Part 2 (Lorenz Thurner)

3. Unpublished data on IL-1Ra hyperphosphorylation

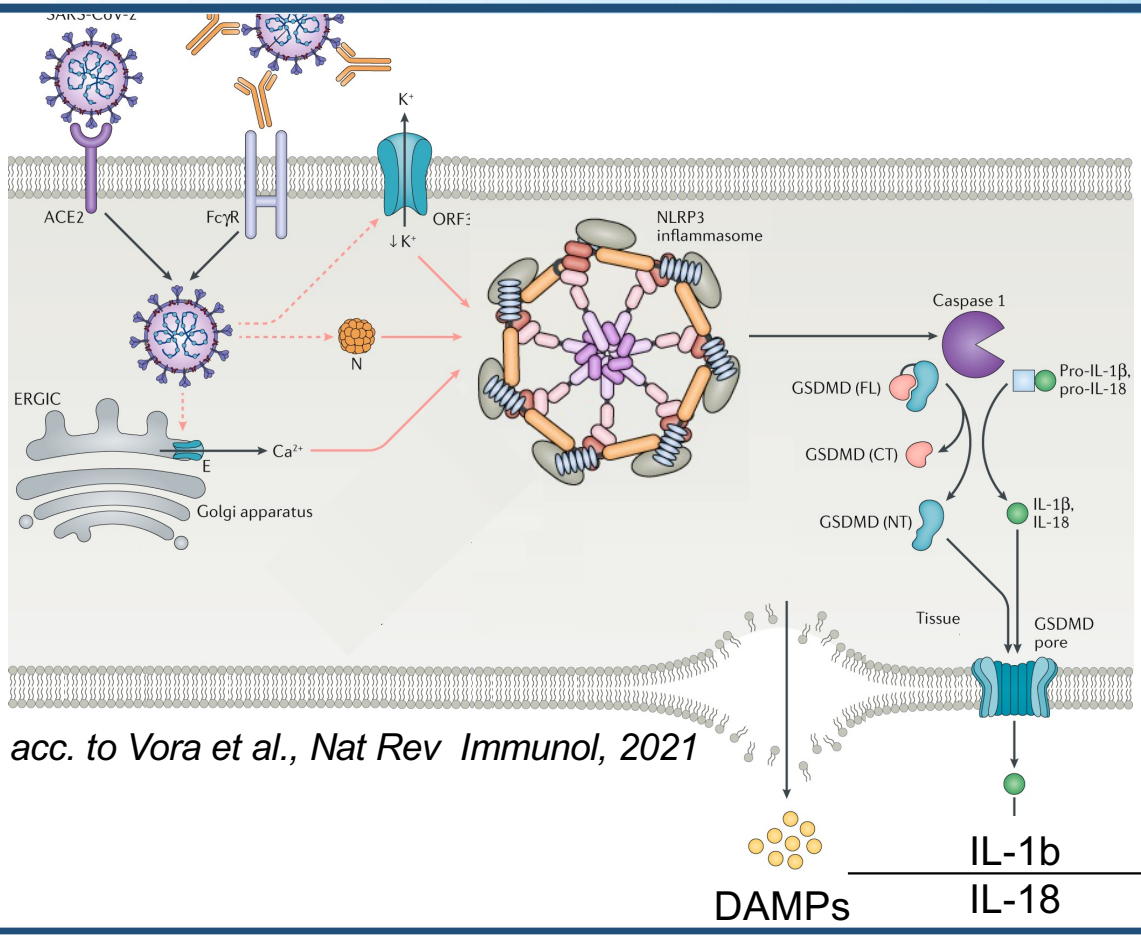
4. Discussion of open questions

IL-1: a powerful pro-inflammatory cytokine

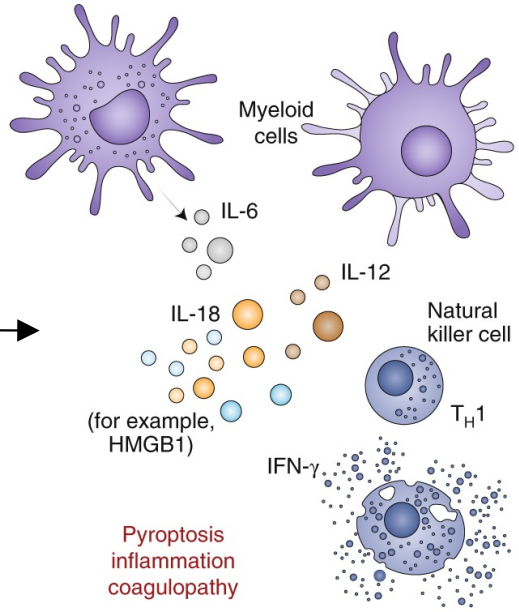


Schett et al., Nat Rev Rheumatol, 2015

IL-1 (family) cytokine release in SARS-CoV-2 infection

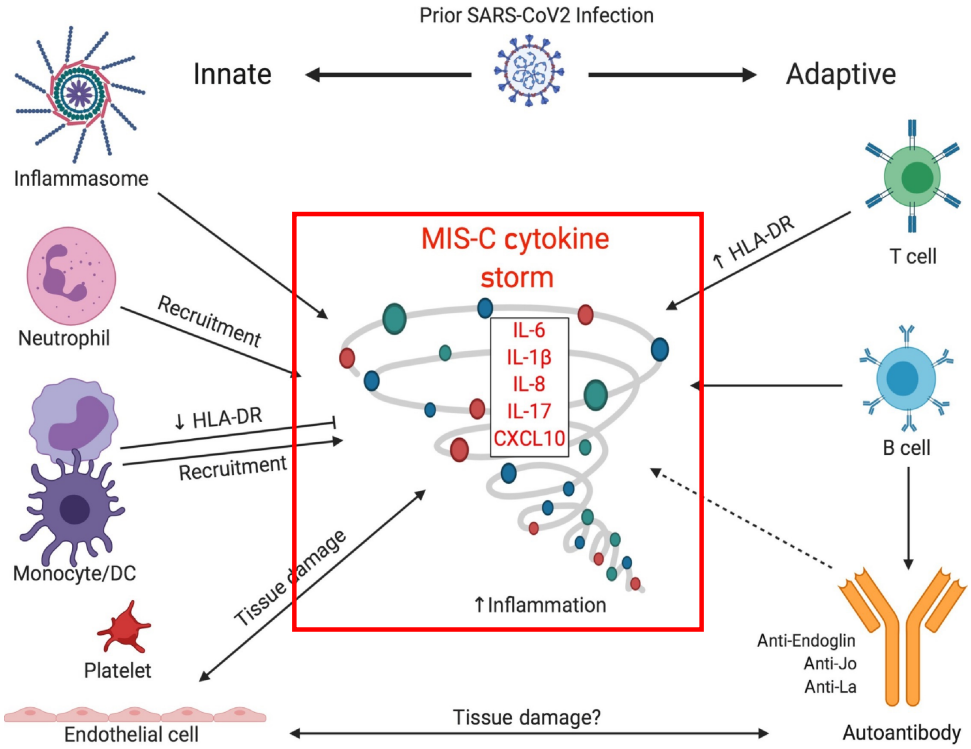


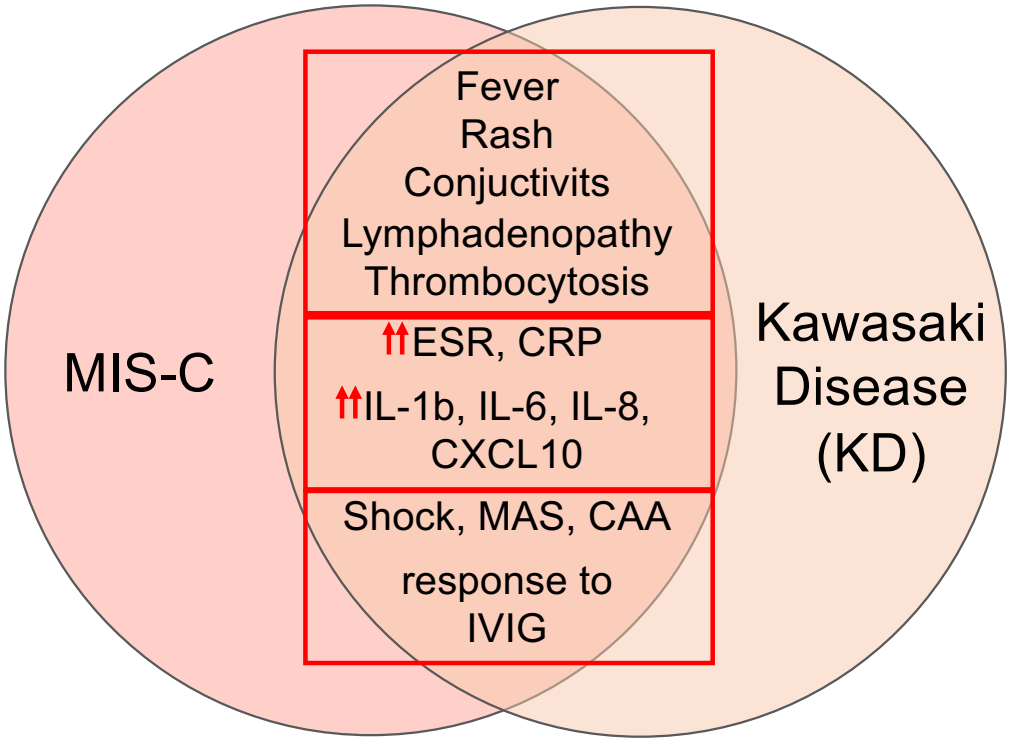
acc. to Vora et al., Nat Rev Immunol, 2021



acc. to Brodin, Nat Med, 2021

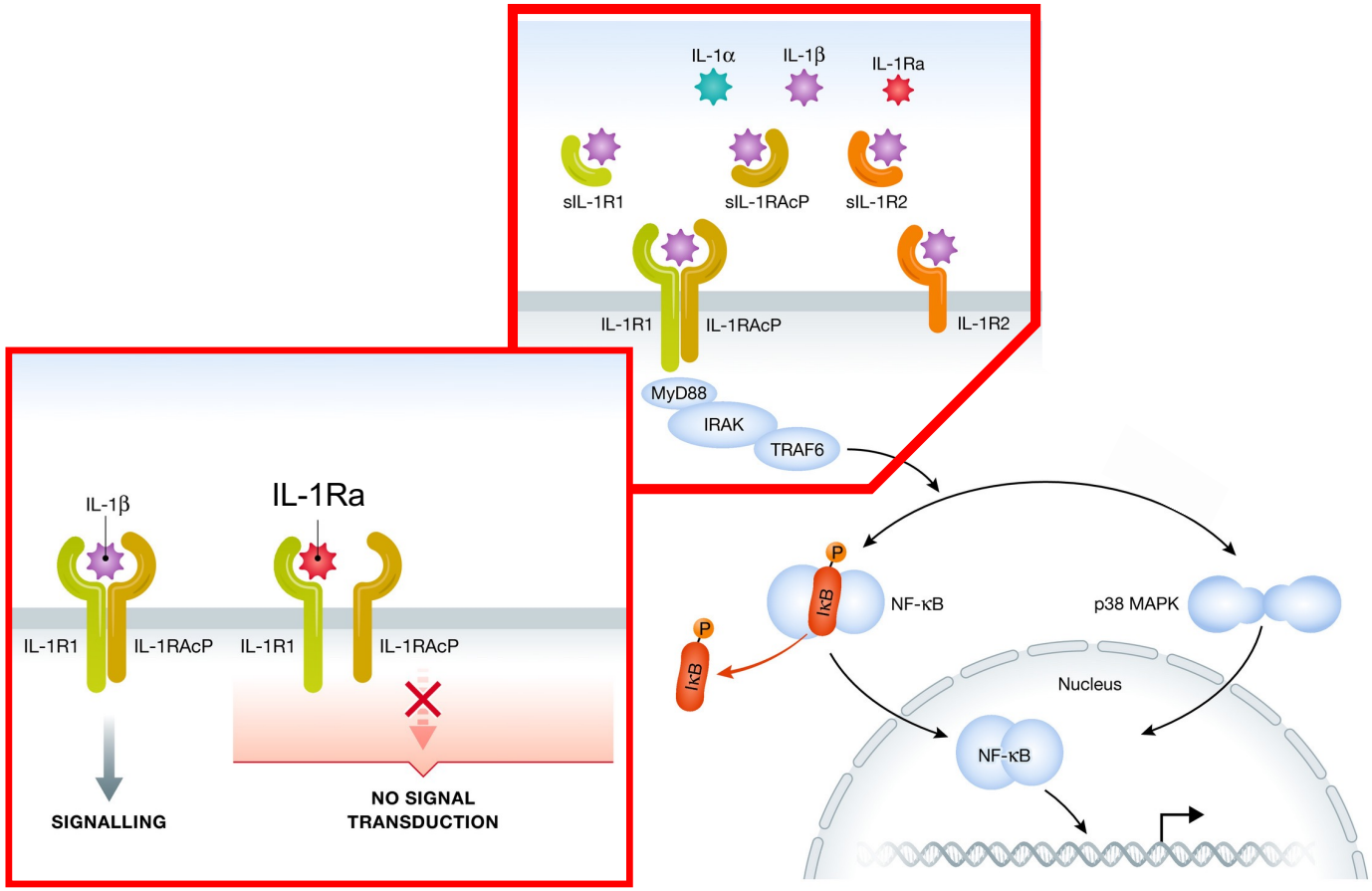
IL-1 in multisystem inflammatory syndrome in children (MIS-C)

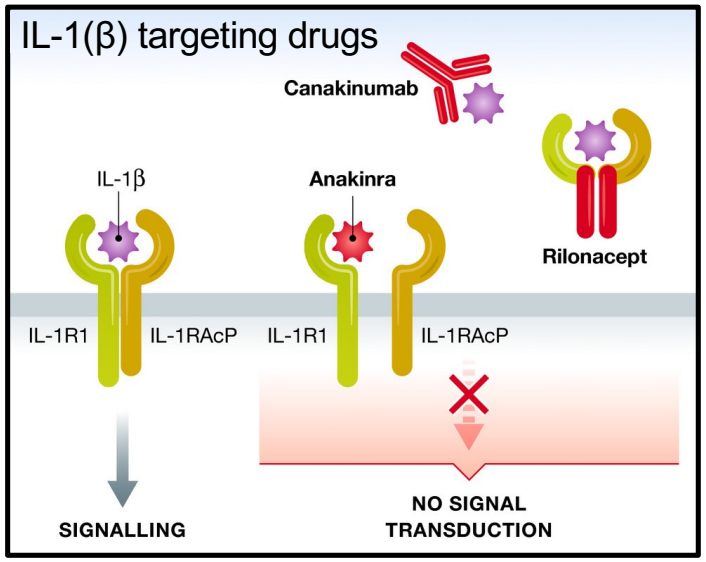




Brodsky et al., Trends Microbiol, 2020

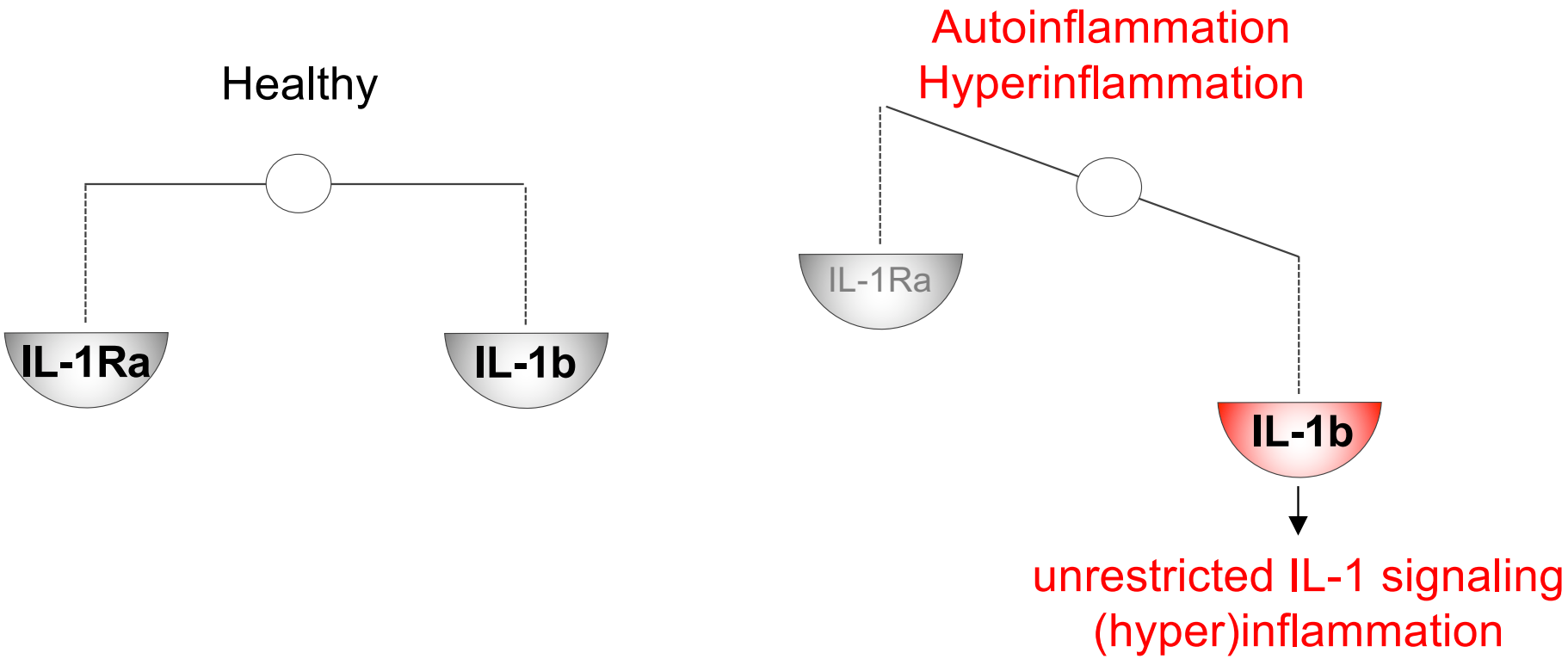
Endogenous control of IL-1 family cytokine signaling



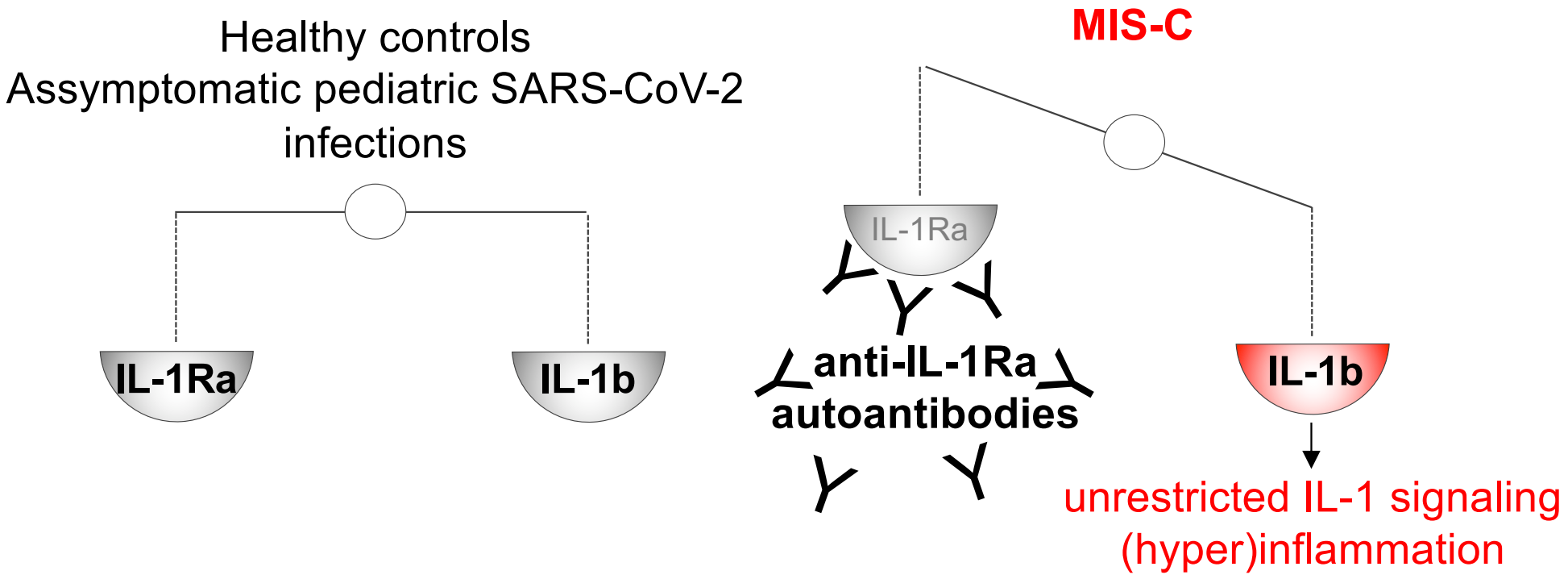


acc. to van Gorp & Lamkanfi, EMBO, 2019

IL-1b:IL-1Ra dysbalance in excessive (auto)inflammation



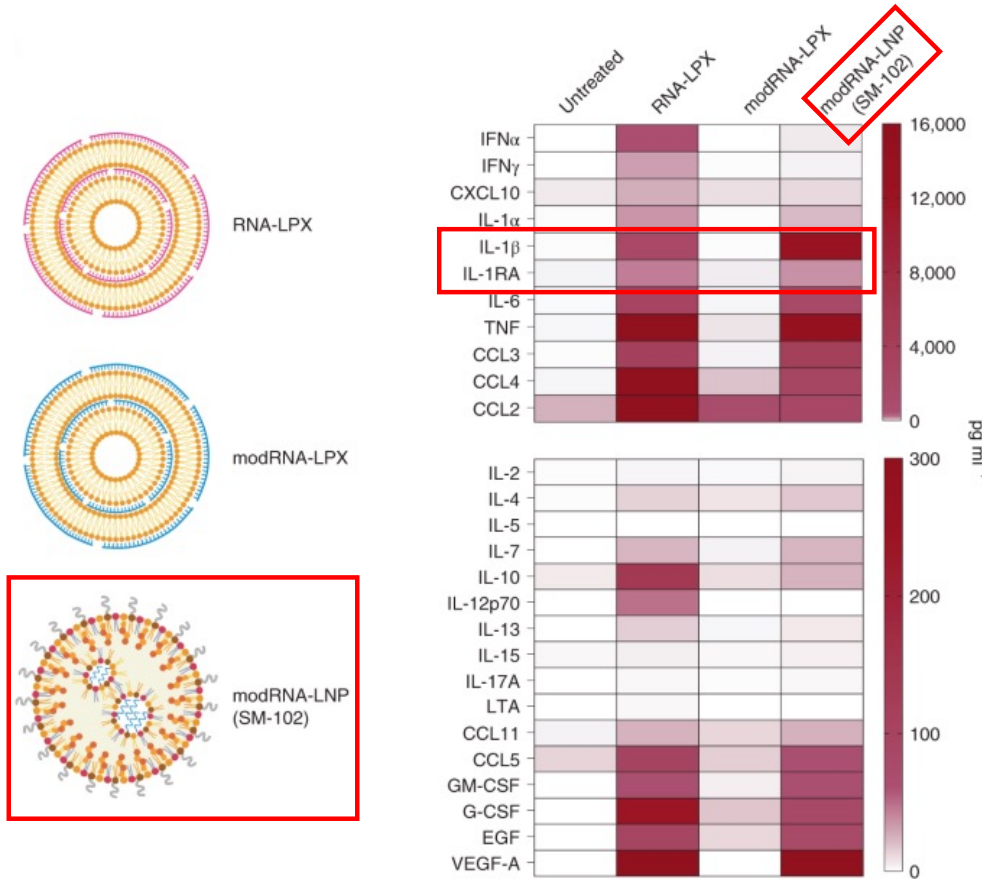
Autoantibody impaired immunity in MIS-C: **targeting IL-1Ra**



Pfeifer, Thurner*, Kessel* et al., Lancet Rheumatol, 2022*

Thurner and Kessel, textbook chapter in 'Autoimmunity in COVID-19', Elservier 2022

IL-1 and IL-1Ra are key regulators of the inflammatory response to RNA vaccines

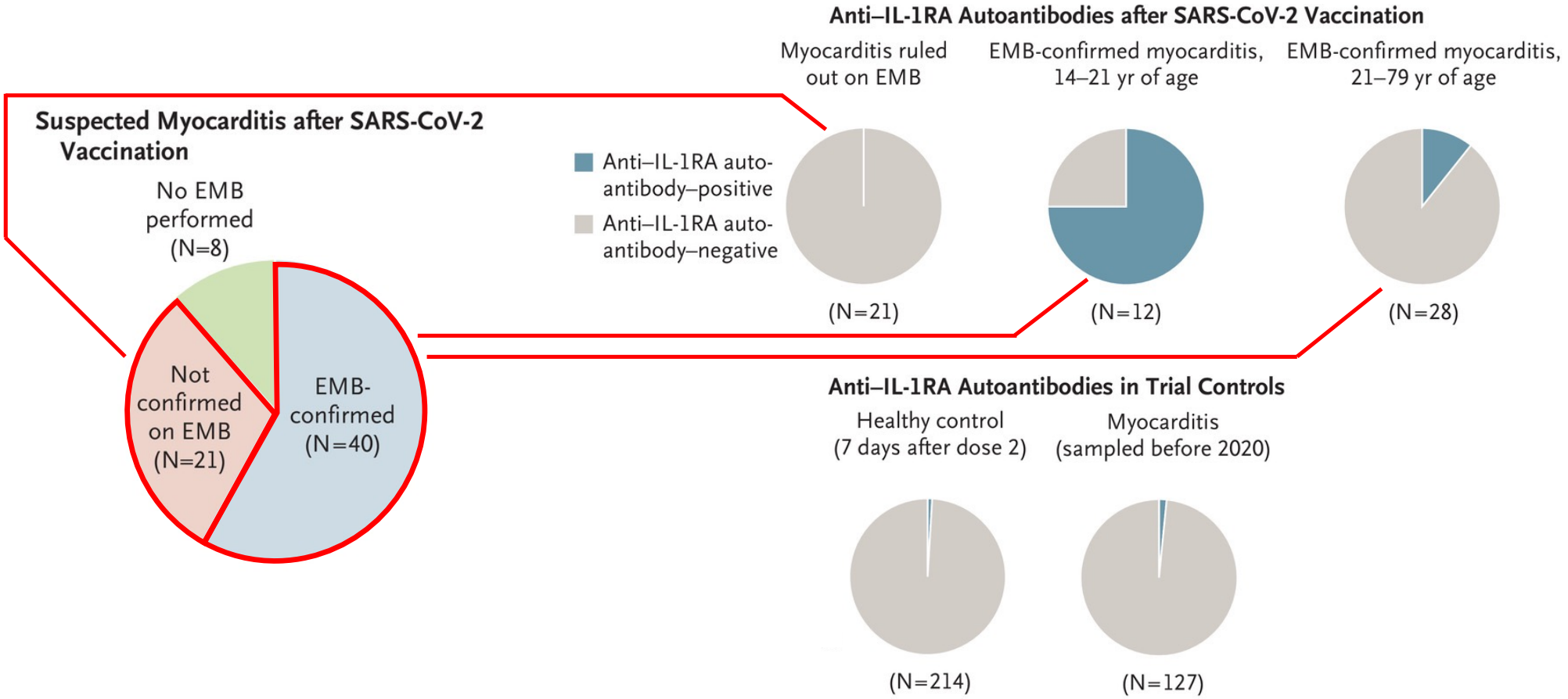


Tahtinen et al., Nat Immunol, 2022

Tahtinen & Mellmann, Nat Immunol, 2022

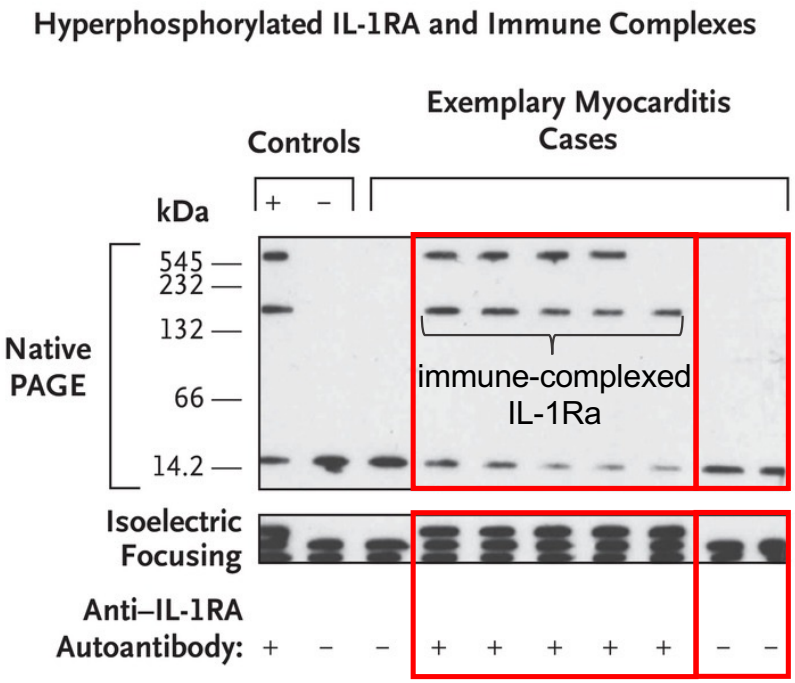
Kobiyama & Ishii, Nat Immunol, 2022

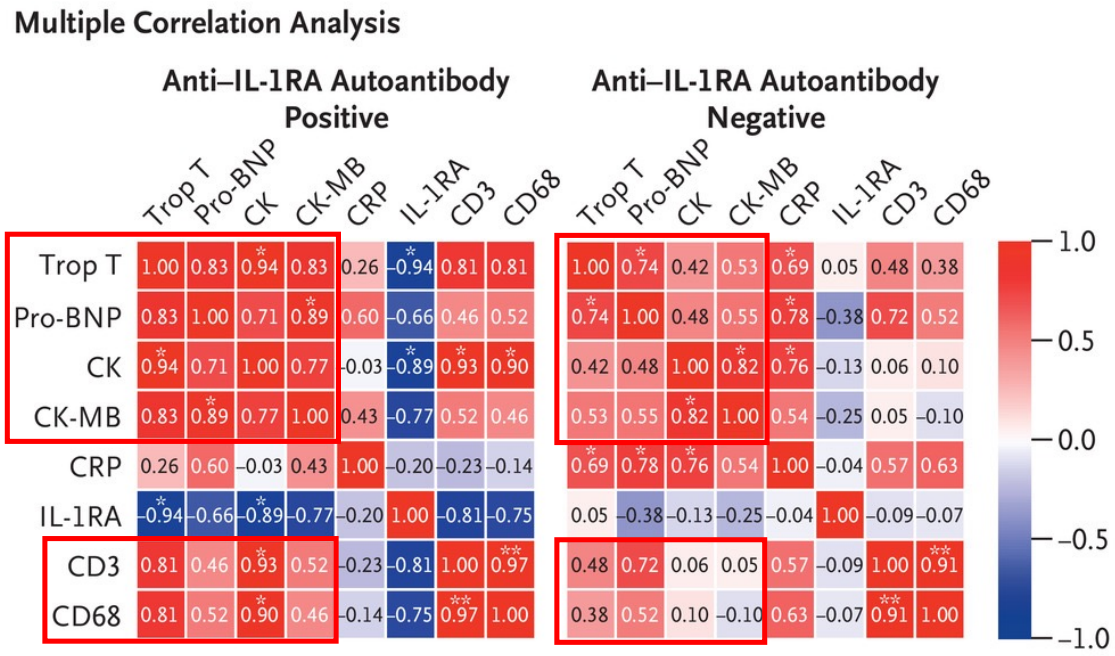
Study cohort and frequency of anti-IL-1RA antibodies



acc. to Thurner, Kessel*, …, Pfeifer**, Klingel**, NEJM, 2022*

Seropositve patients hyperphosphorylate the IL-1RA and reveal tight association of cardiac inflammation markers



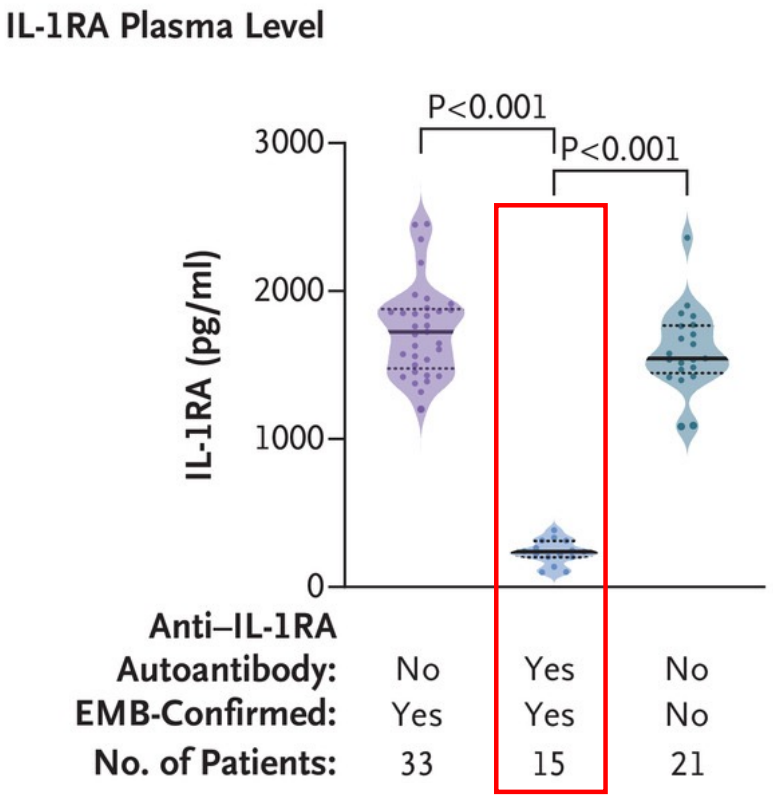


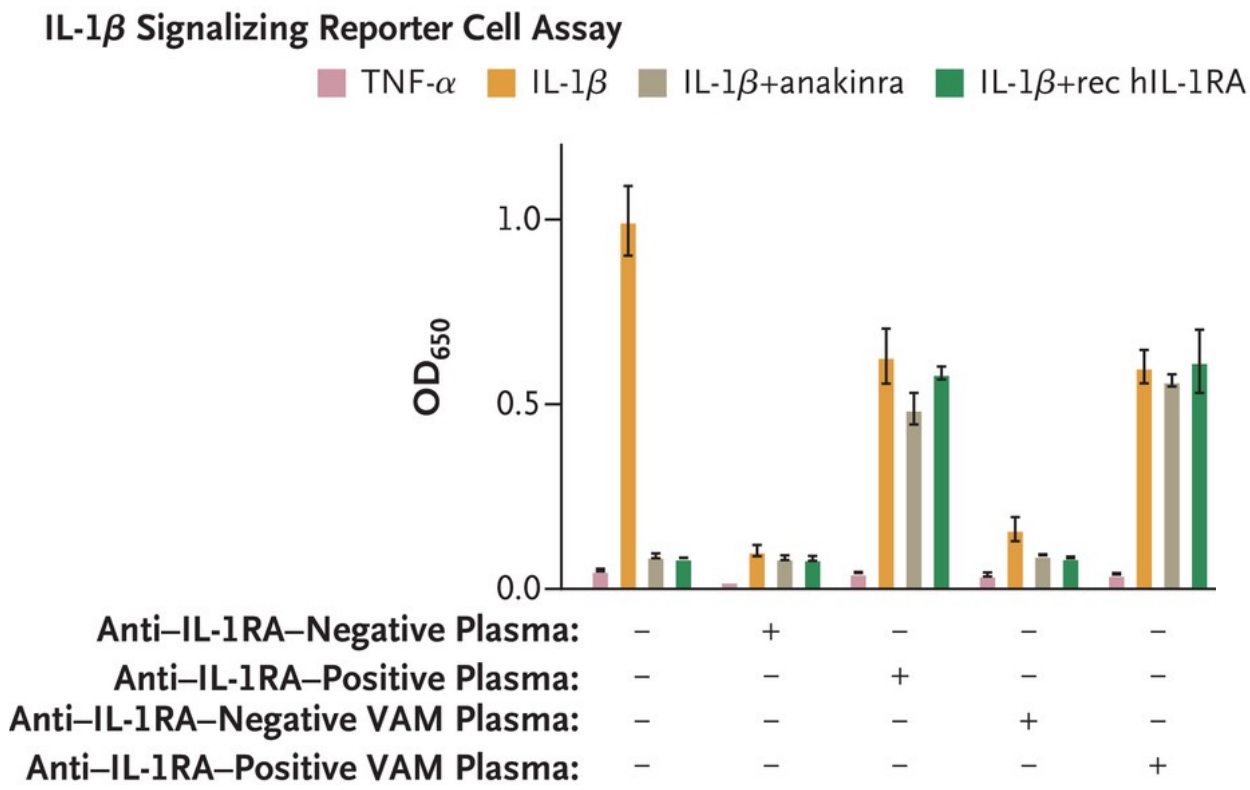
P P

… SCVK**S**^{97}GDETRLQLEAVNI**T**^{111}DLSEN …

acc. to Thurner, Kessel*, …, Pfeifer**, Klingel**, NEJM, 2022*

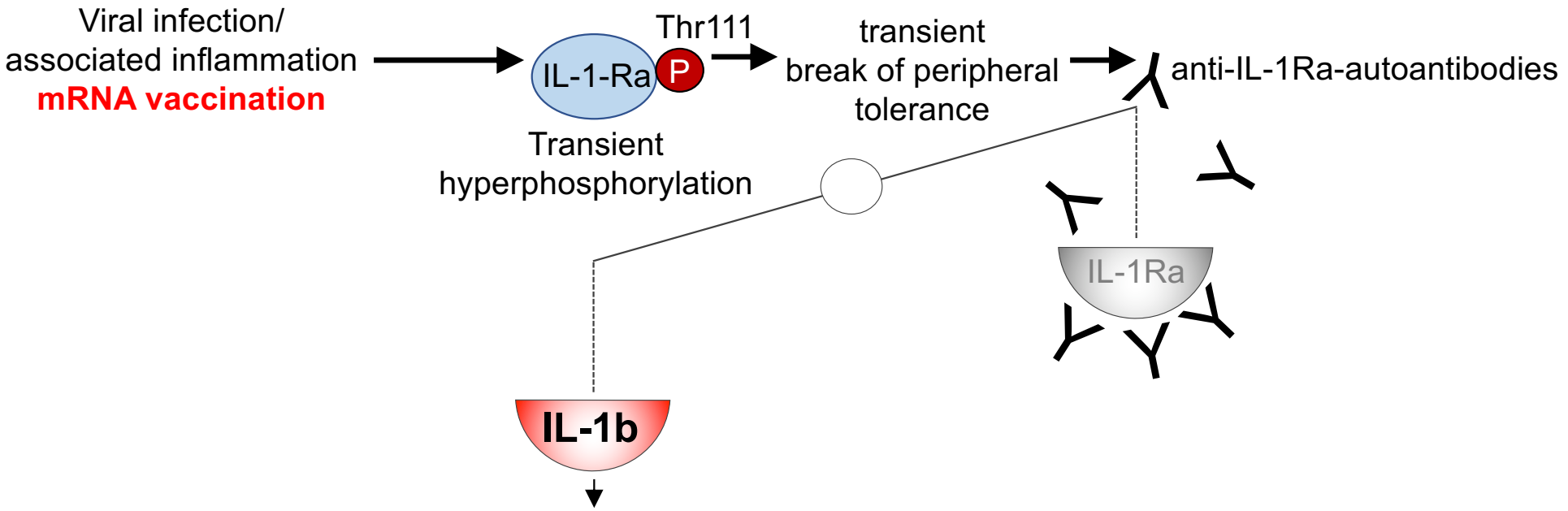
Depletion of circulating IL-1Ra and reduction of bioactivity





acc. to Thurner, Kessel*, …, Pfeifer**, Klingel**, NEJM, 2022*

Autoantibody impaired immunity in context of SARS-CoV-2 infection **and mRNA vaccination**



Thurner et al., Nat Com, BioRxiv 21, Nat Com in revision

Thurner, Kessel*, …, Pfeifer**, Klingel**, NEJM, 2022*

Pfeifer, Thurner*, Kessel* et al., Lancet Rheumatol, 2022*

Some insights, many more questions

- Specific disease contribution?
- Specific mechanism of hyperphosphorylation?
- Contribution of genetic determinants (i.e. HLA) in break of peripheral tolerance?
- Impact of IL-1 targeting treatment?
- Prediction of susceptibility?

In context of vaccine associated myocarditis:

- Role of spike protein or vaccine liposomes on IL-1Ra hyperphosphorylation?
- Stain for phosphorylated IL-1Ra in cardiac tissue
- Test break-of-tolerance impact on disease course in myocarditis model

Acknowledgements

(Inter)national collaborators

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