

## Regular Wednesday IMG seminar



**Tomáš Paulenda**

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### **“The immunoregulatory properties of the metabolite itaconate”**

In this talk I will present my latest findings of the function of immunoregulatory metabolite itaconate. Itaconate accumulates in innate immune cells upon Toll-like receptor stimulation. In response to macrophage activation by lipopolysaccharide, itaconate inhibits inflammasome activation and boosts type I interferon signalling; however, the molecular mechanism of this immunoregulation remained unclear. Here, we show that the enhancement of type I interferon secretion by itaconate depends on the inhibition of peroxiredoxin 5 and on mitochondrial reactive oxygen species. We find that itaconate non-covalently inhibits peroxiredoxin 5, leading to the modulation of mitochondrial peroxide in activating macrophages. Through genetic manipulation, we confirm that peroxiredoxin 5 modulates type I interferon secretion in macrophages. The non-electrophilic itaconate mimetic 2-methylsuccinate inhibits peroxiredoxin 5 and phenocopies immunoregulatory action of itaconate on type I interferon and inflammasome activation, providing further support for a non-covalent inhibition of peroxiredoxin 5 by itaconate. Our work shows Peroxiredoxin 5 as a novel Type I interferon regulator with big potential to future research of redox regulation of immune responses.

**The seminar will be held  
on Wednesday 26<sup>th</sup> November 2025 at 15:00  
in the Milan Hašek Auditorium at IMG**

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)

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