

[Seminar] Structural and functional plasticity of cytokine receptor signaling complexes

Date-Time:

Tuesday, November 17, 2026 - 10:00 to 10:40

Location: Seminar room C700, Lab 3



Description

Title: Structural and functional plasticity of cytokine receptor signaling complexes

Speaker: Prof. Jacob Piehler

Professor, University of Münster

Managing Director, the Center for Cellular Nanoanalytics (CellNanOs)

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Summary

Signal transduction by class I/II cytokine receptors requires the assembly of complexes comprising two or more receptor subunits. Downstream signaling is mediated by non-covalently associated Janus kinases (JAKs), which phosphorylate STAT proteins, a family of latent transcription factors. Given their central roles in hematopoiesis and immunity, dysregulated JAK/STAT signaling contributes to autoimmune and inflammatory disorders as well as leukemias and other cancers. Our group aims to uncover the mechanistic principles governing the assembly, activation, and dysregulation of cytokine receptor signaling complexes in the cellular context. To this end, we have developed live-cell single-molecule imaging approaches to quantify receptor assembly and conformational dynamics by single-molecule FRET (smFRET). While we found no evidence for receptor pre-assembly in the absence of agonists, diverse oncogenic receptor and JAK mutations induce constitutive dimerization. smFRET further revealed striking conformational plasticity of receptor dimers, with distinct oncogenic mutations biasing different conformational states. Together with molecular dynamics simulations, our data suggest that active signaling complexes are governed by partially cooperative, weak protein-protein and protein-lipid interactions encoded within the transmembrane and cytosolic receptor domains. These principles may explain the structural and functional plasticity of cytokine receptor signaling complexes and provide a mechanistic basis for selectively targeting oncogenic variants.

Short Bio

1993, Diploma in Chemistry, Tübingen/Germany.

1997, PhD in Physical Chemistry, Tübingen/Germany

1997-2000, Postdoc in Protein Science at the Weizmann Institute of Science/Israel

2001-2008, Independent Research Group Leader/Heisenberg Professor for Membrane Protein Biophysics, Frankfurt a. M./Germany

2008-Present, full professor for Biophysics, Osnabrück/Germany

2018-Present, Managing Director of the Center for Cellular Nanoanalytics (CellNanOs)

Short abstract

Class I/II cytokine receptors signal through multi-subunit complexes that activate JAKs and STAT transcription factors. Dysregulated JAK/STAT signaling causes inflammatory disease and cancer. We use live-cell single-molecule imaging and smFRET to define how these complexes assemble and become dysregulated. We find little evidence for ligand-independent pre-assembly, whereas oncogenic receptor or JAK mutations drive constitutive dimerization and bias distinct dimer conformations. Combined with molecular dynamics simulations, our results reveal weak, partially cooperative protein–protein and protein–lipid interactions that may enable selective targeting of oncogenic variants.