CV PAVEL KOVARIK

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EDUCATION

1990–1995 Ph.D. thesis, Institute of Biochemistry, University of Vienna, Prof Helmut Ruis
1989–1990 MSc thesis in Biochemistry, University of Vienna, Austria
1984–1989 Studies of Biochemistry, University of Vienna, Austria
1982–1983 Studies of Molecular Biology, University of Brno, Czech Republic
1977–1981 Secondary school, Gymnasium Krenova, Brno, Czech Republic

CURRENT POSITION

2012 - now Professor of Immunobiology, Max Perutz Labs, University of Vienna
2022 - now Director of the ViennaBioCenter PhD program
2022 - now Director of Doctoral studies in Molecular Biology, University of Vienna

PREVIOUS POSITIONS

2003–2011 Associate Professor, Max F. Perutz Laboratories, University of Vienna
2000–2003 Assistant Professor, Institute of Microbiology and Genetics, University of Vienna
1995 Postdoc, Institute of Molecular Pathology, Vienna
1994 Consultant “Environmental Impact of Biotechnology”, United Nations, Vienna

RESEARCH INTERESTS

The research interests of the lab are mechanisms ensuring that the immune response is efficient and successfully prevents infections, but not exaggerated and harmful to the host. This sensitive balance is orchestrated by precise timing and selectivity of activating and inactivating events which we investigate at the level of mRNA decay, transcription and cytokine signaling. The lab employs a range of biochemical and cell-based approaches, genome- and proteome-wide analyses including computational methods, in combination with animal models of infection and inflammation to address the research question.

Key scientific achievements: **(i)** The mRNA-destabilizing protein TTP is indispensable in inflammation control. Our most recent study established that the cytoplasmic degradation of TTP targets is licensed in the nucleus by TTP binding to pre-mRNA, not mRNA. The nuclear licensing step ensures that, following splicing and nuclear export, the TTP target mRNAs are efficiently degraded while their translation is avoided (*Bestehorn et al., Mol Cell 2025*). This represents a major conceptual advance in understanding the efficient control of immune responses and mRNA decay in general. **(ii)** We demonstrated that type I IFN signaling balances IL-1 levels such that they are protective against infection yet not destructive for the

host tissue (*Castiglia et al., Cell Host & Microbe 2016*). Furthermore, we addressed the long-standing question of the non-redundancy of IL-1α and IL-1β in host defense and discovered that IL-1β drives the pathogen clearance (i.e. resistance to infection) while IL-1α is associated with tolerance to infection (*Eislmayr et al., Science Advances 2022*). **(iii)** We established that the Mediator kinase phosphorylates the transcription factor STAT1 and that this fine-tuning event in inflammatory transcription occurs only if STAT1 is promoter-bound (*Bancerek et al., Immunity 2013*). Later we showed that the Mediator kinases CDK8 and CDK19 have mechanistically distinct functions in regulation of IFN-induced transcription (*Steinparzer et al., Mol Cell 2019*).

Keywords: Inflammation, innate immunity, mRNA decay, RNA binding proteins, transcription, Mediator kinase, cytokine signaling

TOP 10 PUBLICATIONS

1. Bestehorn, A., von Wiren, J., Zeiler, C., Fesselet, J., Didusch, S., Forte, M., Doppelmayer, K., Borroni, M., Le Heron, A., Scinicariello, S., Chen, W., Baccarini, M., Pfanzagl, V., Versteeg, G. A., Hartl, M., and **Kovarik, P.** (2025) Cytoplasmic mRNA decay controlling inflammatory gene expression is determined by pre-mRNA fate decision. ***Mol Cell*** doi: 10.1016/j.molcel.2025.01.001; doi: 10.1016/j.molcel.2025.01.001

2. Eislmayr, K., Bestehorn, A., Morelli, L., Borroni, M., Walle, L. V., Lamkanfi, M., and **Kovarik, P.** (2022) Nonredundancy of IL-1alpha and IL-1beta is defined by distinct regulation of tissues orchestrating resistance versus tolerance to infection. ***Sci Adv*** **8**, eabj7293; doi: 10.1126/sciadv.abj7293

3. Steinparzer, I., Sedlyarov, V., Rubin, J. D., Eislmayr, K., Galbraith, M. D., Levandowski, C. B., Vcelkova, T., Sneezum, L., Wascher, F., Amman, F., Kleinova, R., Bender, H., Andrysik, Z., Espinosa, J. M., Superti-Furga, G., Dowell, R. D., **Taatjes, D. J.**, and **Kovarik, P.** (2019) Transcriptional Responses to IFN-gamma Require Mediator Kinase-Dependent Pause Release and Mechanistically Distinct CDK8 and CDK19 Functions. ***Mol Cell*** **76**, 485-499 e8; doi: 10.1016/j.molcel.2019.07.034

4. Sedlyarov, V., Eichner, R., Girardi, E., Essletzbichler, P., Goldmann, U., Nunes-Hasler, P., Srndic, I., Moskovskich, A., Heinz, L. X., Kartnig, F., Bigenzahn, J. W., Rebsamen, M., **Kovarik, P**., Demaurex, N., and Superti-Furga, G. (2018) The Bicarbonate Transporter SLC4A7 Plays a Key Role in Macrophage Phagosome Acidification. ***Cell Host & Microbe*** **23**, 766-774 e5; doi: 10.1016/j.chom.2018.04.013

5. Ivin, M., Dumigan, A., de Vasconcelos, F. N., Ebner, F., Borroni, M., Kavirayani, A., Przybyszewska, K. N., Ingram, R. J., Lienenklaus, S., Kalinke, U., Stoiber, D., **Bengoechea, J. A.**, and **Kovarik, P**. (2017) Natural killer cell-intrinsic type I IFN signaling controls Klebsiella pneumoniae growth during lung infection. ***PLoS Pathogens*** **13**, e1006696; doi: 10.1371/journal.ppat.1006696

6. Ebner, F., Sedlyarov, V., Tasciyan, S., Ivin, M., Kratochvill, F., Gratz, N., Kenner, L., Villunger, A., Sixt, M., and **Kovarik, P.** (2017) The RNA-binding protein tristetraprolin schedules apoptosis of pathogen-engaged neutrophils during bacterial infection. ***J Clin Invest*** **127**, 2051-2065; doi: 10.1172/JCI80631

7. Sedlyarov, V., Fallmann, J., Ebner, F., Huemer, J., Sneezum, L., Ivin, M., Kreiner, K., Tanzer, A., Vogl, C., **Hofacker, I.**, and **Kovarik, P.** (2016) Tristetraprolin binding site atlas in the macrophage transcriptome reveals a switch for inflammation resolution. ***Molecular Systems Biology*** **12**, 868; doi: 10.15252/msb.20156628

8. Castiglia, V., Piersigilli, A., Ebner, F., Janos, M., Goldmann, O., Dambock, U., Kroger, A., Weiss, S., Knapp, S., Jamieson, A. M., Kirschning, C., Kalinke, U., Strobl, B., Muller, M.,

Stoiber, D., Lienenklaus, S., and Kovarik, P. (2016) Type I Interferon Signaling Prevents IL-1beta-Driven Lethal Systemic Hyperinflammation during Invasive Bacterial Infection of Soft Tissue. ***Cell Host & Microbe*** **19**, 375-87; doi: 10.1016/j.chom.2016.02.003

9. Bancerek, J., Poss, Z. C., Steinparzer, I., Sedlyarov, V., Pfaffenwimmer, T., Mikulic, I., Dolken, L., Strobl, B., Muller, M., Taatjes, D. J., and **Kovarik, P.** (2013) CDK8 kinase phosphorylates transcription factor STAT1 to selectively regulate the interferon response. ***Immunity*** **38**, 250-62; doi: 10.1016/j.immuni.2012.10.017

10. Kratochvill, F., Machacek, C., Vogl, C., Ebner, F., Sedlyarov, V., Gruber, A. R., Hartweger, H., Vielnascher, R., Karaghiosoff, M., Rulicke, T., Muller, M., Hofacker, I., Lang, R., and **Kovarik, P.** (2011) Tristetraprolin-driven regulatory circuit controls quality and timing of mRNA decay in inflammation. ***Molecular Systems Biology*** **7**, 560; doi: 10.1038/msb.2011.93

ADDITIONAL CAREER-RELATED ACTIVITIES (10 selected)

2009-2020	Deputy head of the Department of Microbiology Immunobiology and Genetics, Max Perutz Labs, University of Vienna
2009-2015	Coordinator of network grant: University of Vienna Research Platform “mRNA decay in inflammation”
2009-2012	Coordinator of network grant “ERA-NET Pathogenomics”
2007-2009	Coordinator of network grant: University of Vienna Doctoral Program “Initiativkolleg”
2006-2009	Coordinator of network grant: ESF Eurocores “EURODYNA”

2001-present Supervision of 7 postdoctoral fellows, 23 PhD theses (5 ongoing) and 30 master’s theses (one ongoing)

Funding: ~2 million Euro grant money in the last 10 years

Publications: 65 peer reviewed papers, >8500 citations (Google Scholar)

Reviewer/board member for funding agencies: Medical Research Council (UK), Welcome Trust (UK), DFG (Germany), ANR (France), RGC Hong Kong, Luxemburg, Singapore, Czech Republic, Switzerland, Slovenia

Reviewer for scientific journals: Nat Immunol, Science Advances, Mol Cell, EMBO J, PNAS, JBC, MolSystBiol, MBio, RNA, MolCellBiol, PLoS Biology, PLoS Pathogens, J Immunol, EJB etc.