UNIVERSITÀ DEGLI STUDI FIRENZE
NEUROFARBA
DIPARTIMENTO DI NEUROSCIENZE, PSICOLOGIA, AREA DEL FARMACO E SALUTE DEL BAMBINO

PeptLab UNIFI

**Attività formativa del Dottorato in Area del Farmaco e Trattamenti Innovativi**

## Avviso di seminario

**Aula 43, Via U. Schiff 6**

**Venerdì 5 luglio 2019 ore 11.00**

# Professor Jürgen Bernhagen

*Chair of Vascular Biology, Institute for Stroke and Dementia Research*
*Ludwig-Maximilians-University, Munich, Germany*

terrà una conferenza dal titolo:

## The emerging role of atypical chemokines in inflammation and cardiovascular diseases: from the characterization of the ligand/receptor interfaces to potential therapeutic strategies”

Sono invitati a partecipare i dottorandi e i membri del Collegio dei docenti del dottorato

Prof. Paolo Rovero
Unità di Ricerca Interdipartimentale PeptLab

**Prof. Dr. Jürgen Bernhagen**

**Title**: „The emerging role of atypical chemokines in inflammation and cardiovascular diseases: from the characterization of the ligand/receptor interfaces to potential therapeutic strategies"

**Abstract:**

Chemokines orchestrate leukocyte recruitment in atherosclerosis and their blockade is a promising anti-atherosclerotic strategy. Macrophage migration inhibitory factor (MIF) is a pivotal mediator of atherosclerotic lesion formation. It has been characterized as an inflammatory cytokine and chemokine-like mediator that promotes atherogenic leukocyte recruitment and lesional inflammation through interactions with the chemokine receptors CXCR2 and CXCR4, but MIF also exhibits phase-specific CD74-mediated cardioprotective activity. Of note, MIF is the founding member of the MIF protein family and we are currently comprehensively characterizing their role in atherosclerosis, stroke, and cardiac ischemia. MIF also is a prototypical member of the emerging family of atypical chemokines (ACKs), which also encompasses alarmin-like mediators such as HMGB1 as well as several antimicrobial peptides. Although ACKs do not structurally belong to any of the classical chemokine categories, they bind to classical chemokine receptors by molecular mimicry or "molecular hijacking". In the lecture, I will focus on our current mechanistic and molecular understanding of how MIF proteins and other ACKs mimic classical chemokine structures to engage into high-affinity binding to chemokine receptors and will discuss how this could be exploited for novel therapeutic approaches in cardiovascular and inflammatory diseases.

Jürgen Bernhagen is Professor and Chair of Vascular Biology at Ludwig-Maximilians-University (LMU) Munich and a Principal Investigator and Member of the Board of Directors at the Institute for Stroke and Dementia Research (ISD). Formerly, he was the Director of the Institute of Biochemistry and Molecular Cell Biology at RWTH Aachen University and a Group Leader and Department Head at Stuttgart-based Fraunhofer Institute. Bernhagen's research centers on mechanisms driving inflammation and cardiovascular disease with a focus on cytokines, chemokines, their receptors, and signaling platforms. He contributed to the characterization of the cytokine MIF as a central player in inflammation. He also identified the MIF/chemokine receptor axis as a driver of atherosclerosis and elucidated inflammatory mechanisms of the COP9 signalosome. His lab is currently studying the larger MIF family of proteins and receptors, atypical chemokines, and the COP9 signalosome in the context inflammation and cardiovascular diseases. Bernhagen is a member of the Collaborative Research Cluster on Atherosclerosis, the SyNergy Excellence Cluster, and the Munich Heart Alliance. He has received the Paul-Martini Award for Clinical Pharmacology and serves on the Editorial Boards of the FASEB Journal, Quarterly Journal of Medicine, and Frontiers in Cardiovascular Medicine. Bernhagen received his PhD from the University of Tübingen and was a postdoctoral investigator with Richard Bucala and Antony Cerami at the Picower Institute for Medical Research in Manhasset, NY.

**Selected publications**


1. Stoppe C*, Averdunk L, Goetzenich A, Soppert J, Marlier A, Kraemer S, Vieten J, Coburn M, Kowark A, Kim BS, Marx G, Rex S, Ochi A, Leng L, Moeckel G, Linkermann A, El Bounkari O, Zarbock A, **Bernhagen J***, Djudjaj S, Bucala R, Boor P*. The protective role of macrophage migration inhibitory factor in acute kidney injury after cardiac surgery. ***Sci Transl Med.*** 2018;10eaan
2. Schmitz C, Noels H, El Bounkari O, Straussfeld E, Megens RTA, Sternkopf M, Alampour-Rajabi S, Krammer C, Tilstam PV, Gerdes N, Bürger C, Kapurniotu A, Bucala R, Jankowski J, Weber C, **Bernhagen J***. *Mif*-deficiency favors an atheroprotective autoantibody phenotype in atherosclerosis. ***FASEB J.*** 2018;32:4428-4443.
3. Asare Y, Ommer M, Azombo FA, Alampour-Rajabi S, Sternkopf M, Sanati M, Gijbels MJ, Schmitz C, Sinitski D, Tilstam PV, Lue H, Gessner A, Lange D, Schmid JA, Weber C, Dichgans M, Jankowski J, Pardi R, de Winther MP, Noels H, **Bernhagen J*.** Inhibition of atherogenesis by the COP9 signalosome subunit 5 *in vivo*. ***Proc Natl Acad Sci U S A.*** 2017;114:E2766-E2775.
4. Stoppe C, Rex S, Goetzenich A, Kraemer S, Emontzpohl C, Soppert J, Averdunk L, Sun Y, Rossaint R, Lue H, Huang C, Song Y, Pantouris G, Lolis E, Leng L, Schulte W, Bucala R, Weber C, **Bernhagen J*.** Interaction of MIF family proteins in myocardial I/R damage and their influence on clinical outcome of cardiac surgery patients. ***Antioxid Redox Signal*** 2015;23, 865-879.
5. Luedike P, Hendgen-Cotta UB, Sobierajski J, Totzeck M, Reeh M, Dewor M, Lue H, Krisp C, Wolters D, Kelm M, **Bernhagen J***, Rassaf T*. Cardioprotection through S-nitros(yl)ation of MIF. ***Circulation***. 2012;125:1880-1889.
6. Heinrichs D, Knauel M, Offermanns C, Berres ML, Nellen A, Leng L, Schmitz P, Bucala R, Trautwein C, Weber C, **Bernhagen J***, Wasmuth HE*. MIF exerts antifibrotic effects in experimental liver fibrosis via CD74. ***Proc Natl Acad Sci USA***. 2011;108:17444-17449.
7. Weber C*, Kraemer S, Drechsler M, Lue H, Koenen RR, Kapurniotu A, Zernecke A, **Bernhagen J*.** Structural determinants of MIF functions in CXCR2-mediated inflammatory and atherogenic leukocyte recruitment. ***Proc Natl Acad Sci USA.*** 2008;105:16278-16283.
8. **Bernhagen J***, Krohn R, Lue H, Gregory JL, Zernecke A, Koenen RR, Dewor M, Georgiev I, Schober A, Leng L, Kooistra T, Fingerle-Rowson G, Ghezzi P, Kleemann R, McColl SR, Bucala R, Hickey MJ, Weber C*. MIF is a noncognate ligand of CXC chemokine receptors in inflammatory and atherogenic cell recruitment. ***Nat Med*** 2007;13:587-596.
9. Kleemann R, Hausser A, Geiger G, Mischke R, Burger-Kentischer A, Flieger O, Johannes FJ, Roger T, Calandra T, Kapurniotu A, Grell M, Finkelmeier D, Brunner H, **Bernhagen J*.** Intracellular action of the cytokine MIF to modulate AP-1 activity & cell cycle through Jab1. ***Nature*** 2000;408:211-216.
10. **Bernhagen J,** Calandra T, Mitchell RA, Martin SB, Tracey KJ, Voelter W, Manogue KR, Cerami A, Bucala R. MIF is a pituitary-derived cytokine that potentiates lethal endotoxaemia. ***Nature*** 1993;365:756-759.


**corresponding author*