Dr. Martin Vabulas

Group Leader

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Curriculum Vitae

2012 ERC Starting grant (Consolidator track)

Since 2011 Group leader, Buchmann Institute for Molecular Life Sciences

2002-2010 Project leader, Max Planck Institute of Biochemistry,

Martinsried, Germany

2000–2002 Postdoctoral studies, Technical University Munich

1999 Dr. med. (Immunology), Institute of Medical Microbiology, Immunology and Hygiene, Technical University Munich

1997 MD, Vilnius University, LithuaniaProf. Martin R. Vabulas

Field of interest - Protein Aggregation

The focus of research in my lab is on protein stability in cancer. Non-silent mutations often destabilize proteins which as a consequence misfold, aggregate or are degraded. However, mutant oncogenes obviously pass cellular quality checkpoints.

How do oncogenes manage to survive and remain functional? We believe that molecular chaperones stabilize them and thus critically contribute to tumor progression.

I. We focus on the HSP70 molecular chaperone superfamily. Our experimental model is based on transgenes where the diphtheria toxin receptor is under control of individual HSP70 chaperone promoters. This allows us to manipulate and investigate tumor progression depending on the need for a defined molecular chaperone from the HSP70 superfamily.

II. In our previous work we demonstrated that protein biogenesis is usually an efficient process and discovered that a close collaboration of protein synthesis and degradation machineries takes place to sustain it (Vabulas and Hartl, 2005). We are investigating the molecular details of this collaboration with the aim of identifying new targets for increased oncogene clearance in tumor cells.

III. We are investigating proteome stability, especially how cellular architecture is sustained under different physical and chemical insults relevant for tumor progression, such as acidosis or oxidative damage. Using de novo designed amyloid proteins we uncovered how aggregation results in the loss of a distinct set of polypeptides (Olzscha et al, 2011). Coaggregation of a substantial number of proteins with diverse functions inevitably leads to multifocal deficits and the collapse of the cellular protein network. In search of novel therapeutic strategies to prevent (for neurodegeneration prevention) or enhance (for tumor therapy) this cellular break-down, we want to understand the quantitative details of the bystander protein coaggregation. To this end, we use cell biological, biophysical and proteomic techniques; to identify and access relevant biological material for these investigations we are creating molecular chaperone-BAC-modified transgenic mice strains.

Selected publications

Ahmad-Nejad P, Hacker H, Rutz M, Bauer S, Vabulas RM, Wagner H (2002) Bacterial CpG-DNA and lipopolysaccharides activate Toll-like receptors at distinct cellular compartments. Eur J Immunol 32:1958-1968

Fonseca R, Vabulas RM, Hartl FU, Bonhoeffer T, Nagerl UV (2006) A balance of protein synthesis and proteasome-dependent degradation determines the maintenance of LTP. Neuron 52:239-245

Hacker H, Vabulas RM, Takeuchi O, Hoshino K, Akira S, Wagner H (2000) Immune cell activation by bacterial CpG-DNA through myeloid differentiation marker 88 and tumor necrosis factor receptorassociated factor (TRAF)6. J Exp Med 192:595-600

Maurer T, Heit A, Hochrein H, Ampenberger F, O'Keeffe M, Bauer S, Lipford GB, Vabulas RM, Wagner H (2002) CpG-DNA aided cross-presentation of soluble antigens by dendritic cells. Eur J Immunol 32:2356-2364

Olzscha H, Schermann SM, Woerner AC, Pinkert S, Hecht MH, Tartaglia GG, Vendruscolo M, HayerHartl M, Hartl FU, Vabulas RM (2011) Amyloid-like aggregates sequester numerous metastable proteins with essential cellular functions. Cell 144:67-78

Resenberger UK, Harmeier A, Woerner AC, Goodman JL, Muller V, Krishnan R, Vabulas RM, Kretzschmar HA, Lindquist S, Hartl FU, Multhaup G, Winklhofer KF, Tatzelt J (2011) The cellular prion protein mediates neurotoxic signalling of [beta]-sheet-rich conformers independent of prion replication. EMBO J 30:2057-2070

Sharma K, Vabulas RM, Macek B, Pinkert S, Cox J, Mann M, Hartl FU (2012) Quantitative proteomics reveals that Hsp90 inhibition preferentially targets kinases and the DNA damage response. Mol Cell Proteomics 11:M111.014654

Sparwasser T, Koch ES, Vabulas RM, Heeg K, Lipford GB, Ellwart JW, Wagner H (1998) Bacterial DNA and immunostimulatory CpG oligonucleotides trigger maturation and activation of murine dendritic cells. Eur J Immunol 28:2045-2054

Sparwasser T, Vabulas RM, Villmow B, Lipford GB, Wagner H (2000) Bacterial CpG-DNA activates dendritic cells in vivo: T helper cell-independent cytotoxic T cell responses to soluble proteins. Eur J Immunol 30:3591-3597

Vabulas RM (2007) Proteasome function and protein biosynthesis. Curr Opin Clin Nutr Metab Care 10:24-31

Vabulas RM, Ahmad-Nejad P, da Costa C, Miethke T, Kirschning CJ, Hacker H, Wagner H (2001) Endocytosed HSP60s use toll-like receptor 2 (TLR2) and TLR4 to activate the Toll/interleukin-1 receptor signaling pathway in innate immune cells. J Biol Chem 276:31332-31339

Vabulas RM, Ahmad-Nejad P, Ghose S, Kirschning CJ, Issels RD, Wagner H (2002) HSP70 as endogenous stimulus of the toll/interleukin-1 receptor signal pathway. J Biol Chem 277:15107-15112

Vabulas RM, Braedel S, Hilf N, Singh-Jasuja H, Herter S, Ahmad-Nejad P, Kirschning CJ, da Costa C, Rammensee HG, Wagner H, Schild H (2002) The endoplasmic reticulum-resident heat shock protein Gp96 activates dendritic cells via the toll-like receptor 2/4 pathway. J Biol Chem 277:20847- 20853

Vabulas RM, Hartl FU (2005) Protein synthesis upon acute nutrient restriction relies on proteasome function. Science 310:1960-1963

Vabulas RM, Hartl FU (2011) Aberrant protein interactions in amyloid disease. Cell Cycle 10:1512- 1513

Vabulas RM, Pircher H, Lipford GB, Hacker H, Wagner H (2000) CpG-DNA activates in vivo T cell epitope presenting dendritic cells to trigger protective antiviral cytotoxic T cell responses. J Immunol 164:2372-2378

Vabulas RM, Raychaudhuri S, Hayer-Hartl M, Hartl FU (2010) Protein folding in the cytoplasm and the heat shock response. Cold Spring Harbor Perspectives in Biology 2:a004390

Vabulas RM, Wagner H, Schild H (2002) Heat shock proteins as ligands of toll-like receptors Toll-Like Receptor Family Members and Their Ligands. Springer-Verlag Berlin, Berlin, pp 169-184 (Current Topics in Microbiology and Immunology vol 270)

Weighardt H, Kaiser-Moore S, Vabulas RM, Kirschning CJ, Wagner H, Holzmann B (2002) Myeloid differentiation factor 88 deficiency improves resistance against sepsis caused by polymicrobial infection. J Immunol 169:2823-2827