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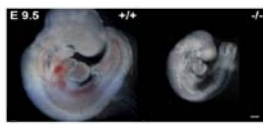


The magic touch – how keratins regulate cell adhesion

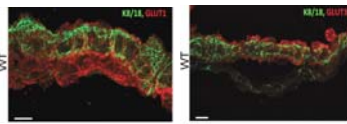
Prof. Dr. Thomas Magin
Translational Centre for Regenerative Medicine (TRM),
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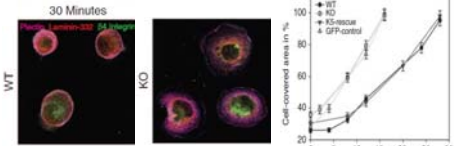
The keratin cycle.
R. Windoffer et al. JCB (2011) 194(5):669-678



Ktyll^{-/-} embryos.
P. Vijayaraj et al. Eur J Cell Biol (2010) 89:299-306



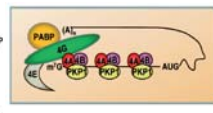
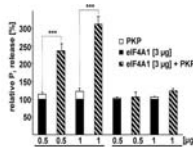
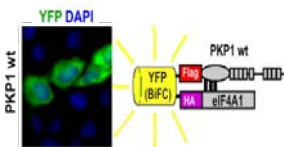
Keratins regulate AMPK activity through localization of GLUT1 and -3.
P. Vijayaraj et al. JCB (2009) 187(2):175-184



Keratin-free cells adhere much faster.
K. Seltmann et al. J Invest Dermatol (2012) in press

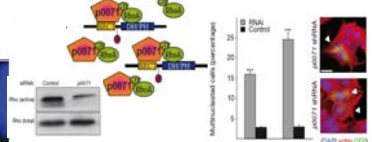
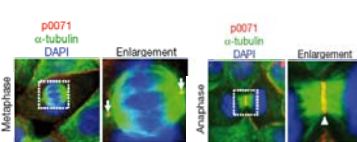
How cell contact proteins promote proliferation: there is more than β -catenin

Prof. Dr. Mechthild Hatzfeld
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Plakophilin 1 stimulates translation by promoting eIF4A1 activity.
A. Wolf et al. JCB (2010) 188(4):463-471

PKP1 in the translational initiation complex.
A. Wolf & M. Hatzfeld. Cell Cycle (2010) 9(15): 2973-2978



The armadillo protein p0071 regulates Rho signalling during cytokinesis
A. Wolf et al. Nature Cell Biol (2006) 8(12):1432-40

Monday, 17.09.2012, 9:00h
Department of Pathology, Lecture Hall
Auenbruggerplatz 25, ground floor



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Date of birth 1955
Place of birth Ludwigshafen/Rhein (Germany)

Scientific career

1965-1974 High School; High School Degree (Abitur).
1974-1982 University of Heidelberg, Studies of Biology, Chemistry and Physics with leave of absence for
1975-1976 Civil Service at Mannheim City Hospital, Dept. of Medicine.
1979 Pre-Diploma in Biology, Chemistry, Physics.
1980-1981 Senior advisory student at the Dept. of Molecular Genetics, with Prof. Eckart Fuchs.
1983-1987 First class PhD degree in Cell Biology (University of Heidelberg). PhD thesis work with Prof. Werner W. Franke at the Div. of Cell and Tumour Biology at the German Cancer Research Centre, Heidelberg.
1987-1990 Postdoctoral fellow with Prof. W. W. Franke, Heidelberg
1988 Award of GFM (Society for the Advancement of Molecular Biology; Gesellschaft zur Förderung der Molekularbiologischen Forschung, Heidelberg) for PhD thesis.
1990-1991 Research fellow with Dr. David Melton, Institute of Cell and Molecular Biology, University of Edinburgh (on leave of absence from German Cancer Centre, Heidelberg).
1991-1993 Recipient of research fellowship from DFG (German Research Association) in the lab of Dr. David W. Melton.
1993 Recipient of Foreign Research Fellowship of Wellcome Trust in conjunction with a Wellcome Research Grant shared between Dr. D. W. Melton and Dr. T. M. Magin (Establishing mouse models of human inherited skin disorders by gene targeting).
1995 Since March 1995, Group leader at the Dept of Genetics, Division of Molecular Genetics, University of Bonn.

- 1998 Founding Member of "Bonner Forum Biomedizin", an interdisciplinary group of researchers from the faculties of medicine, biology and biochemistry.
Habilitation in Molecular Genetics ("Privatdozent"), University of Bonn.
- 2001 Nominated C3-professor at the Institute of Physiological Chemistry, Univ. Bonn Med. School.
- 2003 Organizer of 28th Annual Meeting of German Society for Cell Biology in Bonn (March)
- 2005 Organizer of 4th European Intermediate Filament Workshop, Bonn
- 2006 Offered W3 professorship in biochemistry (University Halle), declined
- 2008 Offered W3 professorship in developmental and cell biology (University of Leipzig)
- 2010 W3 professor, University of Leipzig
- 2010 Member of scientific advisory board of DGZ (Deutsche Gesellschaft für Zellbiologie)
- 2011 Member editorial board of *Molecular Biology of the Cell*

Research interest Function of intermediate filament proteins during differentiation, regeneration and pathogenesis of epithelia

Short version

Thomas Magin studied biology at the University of Heidelberg and received his PhD in cell biology in 1987, following thesis work on keratins in the group of Prof. W.W. Franke at the German Cancer Research Center, Heidelberg. He was a DFG and Wellcome research fellow at the University of Edinburgh from 1990-1995. From 1995-2000, he was independent group leader at the Institute of Genetics, University of Bonn. From 2001-2010, he was professor of biochemistry at the University of Bonn, Medical Faculty. Since April 2010, he is professor of cell and developmental biology at the Translational Center for Regenerative Medicine and the Institute of Biology, University of Leipzig. His major research interest is on understanding the function of intermediate filament proteins during differentiation, regeneration and pathogenesis of epithelia.

Selected publications

Magin TM, Jorcano JL, Franke WW. Translational products of mRNAs coding for non-epidermal cytokeratins. *EMBO J* 2, 1387-1392 (1983).

Venetianer A, Schiller DL, Magin T, Franke WW. Cessation of cytokeratin expression in a rat hepatoma cell line lacking differentiated functions. *Nature* 305, 730-733 (1983).

Magin TM, Hatzfeld M, Franke WW. Analysis of cytokeratin domains by cloning and expression of intact and deleted polypeptides in *Escherichia coli*. *EMBO J* 6, 2607-2615 (1987).

R M Porter, S Leitgeb, DW Melton, O Swensson, RAJ Eady and TM Magin. Disruption of the mouse cytokeratin 10 gene leads to severe skin fragility and alterations in cytokeratin expression in the epidermis. *J. Cell Biol.* 132, 925-936 (1996).

TM Magin, R Schröder, S Leitgeb, F Wanninger, K Zatloukal, C Grund and DW Melton. Lessons from keratin 18 knockout mice: Formation of novel keratin filaments, secondary loss of keratin 7 and accumulation of liver-specific K8-positive aggregates. *J. Cell Biol.* 140, 1441-1451 (1998).

M Hesse, T Franz, Y Tamai, M Taketo and TM Magin. Targeted deletion of keratins 18 and 19 leads to trophoblast fragility and early embryonic lethality. *EMBO J.* 19, 5060-5070 (2000).

J Reichelt and TM Magin. Beyond structure: Hyperproliferation, induction of c-myc and 14-3-3 sigma, but no cell fragility in adult keratin 10 null mice. *J Cell Sci.* 115, 2639-2650 (2002).

TM Magin. A keeper and a striker maintain epidermal homeostasis. *Nat. Genet.* 35, 202-204 (2003).

R Bornheim, M Müller, UH Herrmann, H Bussow, and TM Magin. A dominant vimentin mutant upregulates Hsp70 and the activity of the ubiquitin-proteasome system and causes a posterior cataract in mice. *J Cell Science*, 121, 3737-3746 (2008).

Cataract formation in association with a vimentin assembly-disrupting mutation. M Müller, SS Bhattacharya, T Moore, Q Prescott, T Wedig, H Herrmann and TM Magin. *Human Molec. Genetics* 18, 1052-1057 (2009).

W Roth, U Reuter, C Wohlenberg, L Bruckner-Tuderman and TM Magin. Cytokines as genetic modifiers in $K5^{-/-}$ mice and in human epidermolysis bullosa simplex. *Human Mutation* 30, 832-841 (2009).

P Vijayaraj, C Kroeger, U Reuter, R Windoffer, RL Leube and TM Magin. Keratins regulate protein biosynthesis through localization of GLUT1 and GLUT3 upstream of AMPK and Raptor. *J Cell Biol*, 187, 175-184 (2009).

S Löffek, S Wöll, J Höfeld, RE Leube, C Has, L Bruckner-Tuderman and TM Magin. Targeting of mutant keratins by CHIP offers a novel therapy approach for the dominant skin disorder epidermolysis bullosa simplex. *Human Mutation* 31, 466-476 (2010).

R Windoffer, M. Beil, TM Magin and RL Leube. Cytoskeleton in Motion: The Case of Keratin Intermediate Filaments. *J Cell Biol.* 194, 669-678 (2011).

W Roth, M Hatzfeld and TM Magin. Targeting the palm: a leap forward towards treatment of keratin disorders. *J Invest Dermatol.* 132, 1541-1542 (2012).

K Seltmann, W Roth, C Kröger, F Loschke & Thomas M Magin. Keratins mediate localization of hemidesmosomes and represses cell motility. *J Invest Dermatol* Aug 16 doi: 10.1038/jid.2012.256. [Epub ahead of print] (2012).

Prof. Dr. Mechthild Hatzfeld

Curriculum Vitae

Place/Date of birth	Aachen, 20.08.57
<u>Studies</u> 1976-1983	Biochemistry at the University of Tübingen
<u>Thesis</u> 1983-1987	Institute for Cell and Tumor Biology at the German Cancer Research Center DKFZ Heidelberg (Prof. Dr. WW Franke). Titel: Cytokeratin subunits and cytotkeratin interactions.
<u>Postdoc</u> 1987 1987-1996	Institute for Cell and Tumor Biology at the German Cancer Research Center DKFZ Heidelberg (Prof. Dr. WW Franke) Dept. of Biochemistry, Max-Planck Institute for Biophysical Chemistry Göttingen (Prof. K. Weber).
<u>Habilitation:</u> 1995	Technische Universität Braunschweig (Prof. BM Jockusch) in biochemistry and cell biology Title: Keratin filaments, structure, function and interaction with the plasma membrane.
<u>Scientific career</u> 1997-2001 2001-2002 2002-	NBL2-“Nachwuchsgruppenleiterin” – University of Halle, Medical Faculty “Nachwuchsgruppenleiterin” (Fakultäts-finanziert) University of Halle, Medical Faculty C3-Professor of Pathobiochemistry University of Halle, Medical Faculty
<u>Awards</u> 1996	Heisenberg-Stipendium, DFG
<u>Current Research topics:</u>	Characterization of the p120 family of armadillo proteins in intercellular adhesion, cytoskeletal organization and cell signaling

Publications

- Roth W, Hatzfeld M, Magin TM. Targeting the palm: a leap forward toward treatment of keratin disorders. *J Invest Dermatol.* 2012 Jun;132(6):1541-2.
- Hatzfeld M. A nuclear function for plakophilin-1 in the DNA damage response? *J Invest Dermatol.* 2010 Nov;130(11):2538-40.
- Wolf A, Hatzfeld M. A role of plakophilins in the regulation of translation. *Cell Cycle.* 2010 Aug 1;9(15):2973-8.
- Wolf A, Krause-Gruszczynska M, Birkenmeier O, Ostareck-Lederer A, Hüttelmaier S, Hatzfeld M. Plakophilin 1 stimulates translation by promoting eIF4A1 activity. *J Cell Biol.* 2010 Feb 22;188(4):463-71.
- Mirecka EA, Hey T, Fiedler U, Rudolph R, Hatzfeld M. Affilin molecules selected against the human papillomavirus E7 protein inhibit the proliferation of target cells. *J Mol Biol.* 2009 Jul 24;390(4):710-21.
- Keil R, Kiessling C, Hatzfeld M. Targeting of p0071 to the midbody depends on KIF3. *J Cell Sci.* 2009 Apr 15;122(Pt 8):1174-83.
- Keil R, Wolf A, Hüttelmaier S, Hatzfeld M. Beyond regulation of cell adhesion: local control of RhoA at the cleavage furrow by the p0071 catenin. *Cell Cycle.* 2007 Jan 15;6(2):122-7.
- Wolf A, Keil R, Götzl O, Mun A, Schwarze K, Lederer M, Hüttelmaier S, Hatzfeld M. The armadillo protein p0071 regulates Rho signalling during cytokinesis. *Nat Cell Biol.* 2006 Dec;8(12):1432-40.
- Stöhr N, Lederer M, Reinke C, Meyer S, Hatzfeld M, Singer RH, Hüttelmaier S. ZBP1 regulates mRNA stability during cellular stress. *J Cell Biol.* 2006 Nov 20;175(4):527-34.
- Hatzfeld M. Plakophilins: Multifunctional proteins or just regulators of desmosomal adhesion? *Biochim Biophys Acta.* 2007 Jan;1773(1):69-77. Review.
- Hatzfeld M. The p120 family of cell adhesion molecules. *Eur J Cell Biol.* 2005 Mar;84(2-3):205-14. Review.
- Magin TM, Reichelt J, Hatzfeld M. Emerging functions: diseases and animal models reshape our view of the cytoskeleton. *Exp Cell Res.* 2004 Nov 15;301(1):91-102. Review.
- Straub BK, Boda J, Kuhn C, Schnoelzer M, Korf U, Kempf T, Spring H, Hatzfeld M, Franke WW. A novel cell-cell junction system: the cortex adhaerens mosaic of lens fiber cells. *J Cell Sci.* 2003 Dec 15;116(Pt 24):4985-95.
- Bonné S, Gilbert B, Hatzfeld M, Chen X, Green KJ, van Roy F. Defining desmosomal plakophilin-3 interactions. *J Cell Biol.* 2003 Apr 28;161(2):403-16.
- Hatzfeld M, Green KJ, Sauter H. Targeting of p0071 to desmosomes and adherens junctions is mediated by different protein domains. *J Cell Sci.* 2003 Apr 1;116(Pt 7):1219-33.
- Calkins CC, Hoepner BL, Law CM, Novak MR, Setzer SV, Hatzfeld M, Kowalczyk AP. The Armadillo family protein p0071 is a VE-cadherin- and desmoplakin-binding protein. *J Biol Chem.* 2003 Jan 17;278(3):1774-83.
- Gruber J, Harborth J, Schnabel J, Weber K, Hatzfeld M. The mitotic-spindle-associated protein astrin is essential for progression through mitosis. *J Cell Sci.* 2002 Nov 1;115(Pt 21):4053-9.
- Chen X, Bonne S, Hatzfeld M, van Roy F, Green KJ. Protein binding and functional characterization of plakophilin 2. Evidence for its diverse roles in desmosomes and beta -catenin signaling. *J Biol Chem.* 2002 Mar 22;277(12):10512-22.
- Jaulin-Bastard F, Arsanto JP, Le Bivic A, Navarro C, Vély F, Saito H, Marchetto S, Hatzfeld M, Santoni MJ, Birnbaum D, Borg JP. Interaction between Erbin and a Catenin-related protein in epithelial cells. *J Biol Chem.* 2002 Jan 25;277(4):2869-75.
- Weiske J, Schöneberg T, Schröder W, Hatzfeld M, Tauber R, Huber O. The fate of desmosomal proteins in apoptotic cells. *J Biol Chem.* 2001 Nov 2;276(44):41175-81.

Schröder R, van der Ven PF, Warlo I, Schumann H, Fürst DO, Blümcke I, Schmidt MC, Hatzfeld M. p0071, a member of the armadillo multigene family, is a constituent of sarcomeric I-bands in human skeletal muscle. *J Muscle Res Cell Motil.* 2000;21(6):577-86.

Bornslaeger EA, Godsel LM, Corcoran CM, Park JK, Hatzfeld M, Kowalczyk AP, Green KJ. Plakophilin 1 interferes with plakoglobin binding to desmoplakin, yet together with plakoglobin promotes clustering of desmosomal plaque complexes at cell-cell borders. *J Cell Sci.* 2001 Feb;114(Pt 4):727-38.

Hatzfeld M, Haffner C, Schulze K, Vinzens U. The function of plakophilin 1 in desmosome assembly and actin filament organization. *J Cell Biol.* 2000 Apr 3;149(1):209-22.

Schumann H, Holtz J, Zerkowski HR, Hatzfeld M. Expression of secreted frizzled related proteins 3 and 4 in human ventricular myocardium correlates with apoptosis related gene expression. *Cardiovasc Res.* 2000 Feb;45(3):720-8.

North AJ, Bardsley WG, Hyam J, Bornslaeger EA, Cordingley HC, Trinnaman B, Hatzfeld M, Green KJ, Magee AI, Garrod DR. Molecular map of the desmosomal plaque. *J Cell Sci.* 1999 Dec;112 (Pt 23):4325-36.

Kowalczyk AP, Hatzfeld M, Bornslaeger EA, Kopp DS, Borgwardt JE, Corcoran CM, Settler A, Green KJ. The head domain of plakophilin-1 binds to desmoplakin and enhances its recruitment to desmosomes. Implications for cutaneous disease. *J Biol Chem.* 1999 Jun 25;274(26):18145-8.

Hatzfeld M. The armadillo family of structural proteins. *Int Rev Cytol.* 1999;186:179-224. Review.

Calautti E, Cabodi S, Stein PL, Hatzfeld M, Kedersha N, Paolo Dotto G. Tyrosine phosphorylation and src family kinases control keratinocyte cell-cell adhesion. *J Cell Biol.* 1998 Jun 15;141(6):1449-65.

Schnabel J, Weber K, Hatzfeld M. Protein-protein interactions between keratin polypeptides expressed in the yeast two-hybrid system. *Biochim Biophys Acta.* 1998 Jun 22;1403(2):158-68.

Hatzfeld M, Nachtsheim C. Cloning and characterization of a new armadillo family member, p0071, associated with the junctional plaque: evidence for a subfamily of closely related proteins. *J Cell Sci.* 1996 Nov;109 (Pt 11):2767-78.

Hatzfeld M, Kristjansson GI, Plessmann U, Weber K. Band 6 protein, a major constituent of desmosomes from stratified epithelia, is a novel member of the armadillo multigene family. *J Cell Sci.* 1994 Aug;107 (Pt 8):2259-70.

Hatzfeld M, Burba M. Function of type I and type II keratin head domains: their role in dimer, tetramer and filament formation. *J Cell Sci.* 1994 Jul;107 (Pt 7):1959-72.

Kouklis PD, Hatzfeld M, Brunkener M, Weber K, Georgatos SD. In vitro assembly properties of vimentin mutagenized at the beta-site tail motif. *J Cell Sci.* 1993 Nov;106 (Pt 3):919-28.

Hatzfeld M, Dodemont H, Plessmann U, Weber K. Truncation of recombinant vimentin by ompT. Identification of a short motif in the head domain necessary for assembly of type III intermediate filament proteins. *FEBS Lett.* 1992 May 18;302(3):239-42.

Hatzfeld M, Weber K. A synthetic peptide representing the consensus sequence motif at the carboxy-terminal end of the rod domain inhibits intermediate filament assembly and disassembles preformed filaments. *J Cell Biol.* 1992 Jan;116(1):157-66.

Hatzfeld M, Weber K. Modulation of keratin intermediate filament assembly by single amino acid exchanges in the consensus sequence at the C-terminal end of the rod domain. *J Cell Sci.* 1991 Jun;99 (Pt 2):351-62.

Hatzfeld M, Weber K. Tailless keratins assemble into regular intermediate filaments in vitro. *J Cell Sci.* 1990 Oct;97 (Pt 2):317-24.

Hatzfeld M, Weber K. The coiled coil of in vitro assembled keratin filaments is a heterodimer of type I and II keratins: use of site-specific mutagenesis and recombinant protein expression. *J Cell Biol.* 1990 Apr;110(4):1199-210.

- Geisler N, Hatzfeld M, Weber K. Phosphorylation in vitro of vimentin by protein kinases A and C is restricted to the head domain. Identification of the phosphoserine sites and their influence on filament formation. *Eur J Biochem.* 1989 Aug 1;183(2):441-7.
- Hatzfeld M, Maier G, Franke WW. Cytokeratin domains involved in heterotypic complex formation determined by in-vitro binding assays. *J Mol Biol.* 1987 Sep 20;197(2):237-55.
- Magin TM, Hatzfeld M, Franke WW. Analysis of cytokeratin domains by cloning and expression of intact and deleted polypeptides in *Escherichia coli*. *EMBO J.* 1987 Sep;6(9):2607-15.
- Quinlan RA, Hatzfeld M, Franke WW, Lustig A, Schulthess T, Engel J. Characterization of dimer subunits of intermediate filament proteins. *J Mol Biol.* 1986 Nov 20;192(2):337-49.
- Bader BL, Magin TM, Hatzfeld M, Franke WW. Amino acid sequence and gene organization of cytokeratin no. 19, an exceptional tail-less intermediate filament protein. *EMBO J.* 1986 Aug;5(8):1865-75.
- Knapp AC, Franke WW, Heid H, Hatzfeld M, Jorcano JL, Moll R. Cytokeratin No. 9, an epidermal type I keratin characteristic of a special program of keratinocyte differentiation displaying body site specificity. *J Cell Biol.* 1986 Aug;103(2):657-67.
- Achtstaetter T, Hatzfeld M, Quinlan RA, Parmelee DC, Franke WW. Separation of cytokeratin polypeptides by gel electrophoretic and chromatographic techniques and their identification by immunoblotting. *Methods Enzymol.* 1986;134:355-71.
- Romano V, Hatzfeld M, Magin TM, Zimbelmann R, Franke WW, Maier G, Ponstingl H. Cytokeratin expression in simple epithelia. I. Identification of mRNA coding for human cytokeratin no. 18 by a cDNA clone. *Differentiation.* 1986;30(3):244-53.
- Hatzfeld M, Franke WW. Pair formation and promiscuity of cytokeratins: formation in vitro of heterotypic complexes and intermediate-sized filaments by homologous and heterologous recombinations of purified polypeptides. *J Cell Biol.* 1985 Nov;101(5 Pt 1):1826-41.
- Quinlan RA, Schiller DL, Hatzfeld M, Achtstätter T, Moll R, Jorcano JL, Magin TM, Franke WW. Patterns of expression and organization of cytokeratin intermediate filaments. *Ann N Y Acad Sci.* 1985;455:282-306. Review.
- Quinlan RA, Cohlberg JA, Schiller DL, Hatzfeld M, Franke WW. Heterotypic tetramer (A2D2) complexes of non-epidermal keratins isolated from cytoskeletons of rat hepatocytes and hepatoma cells. *J Mol Biol.* 1984 Sep 15;178(2):365-88.
- Franke WW, Schiller DL, Hatzfeld M, Winter S. Protein complexes of intermediate-sized filaments: melting of cytokeratin complexes in urea reveals different polypeptide separation characteristics. *Proc Natl Acad Sci U S A.* 1983 Dec;80(23):7113-7.