

# MARKUS H. HEIM

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PRESENT POSITION	Chief, Division of Gastroenterology and Hepatology, University Hospital Basel and Research Group Leader, Department of Biomedicine, University Basel	
DATE OF BIRTH	30 April 1961	
CITIZENSHIP	Swiss, Italian	
CIVIL STATUS	married to Sonja Carrozzo, three children	
EDUCATION / TRAINING	University of Basel, Medical School <i>Medical Doctor</i>	1981-1987 1988
	Swiss Postgraduate Course in Experimental Medicine and Biology	1988
	University of Basel, Biozentrum, Postdoctoral Fellow (U.A.Meyer)	1988-1991
	University Hospital Basel, Internship/Residency, Internal Medicine	1991-1993
	Rockefeller University, New York, Postdoctoral Fellow (J.E. Darnell)	1993-1995
	University Hospital Basel, Residency, Internal Medicine <i>Swiss Board Certification Internal Medicine</i>	1995-1996 1997
	University Hospital Freiburg, Fellow, Gastroenterology & Hepatology	1996-1997
	University Hospital Basel, Fellow, Gastroenterology & Hepatology <i>Swiss Board Certification Gastroenterology</i> <i>Swiss Board Certification Hepatology</i>	1997-1999 1999 2012
ACADEMIC APPOINTMENTS	University of Basel <i>Assistant Professor of Medicine (Venia docendi, Habilitation)</i> <i>Associate Professor of Medicine (Titularprofessor)</i> <i>Professor of Hepatology</i>	1998 2003 2009
CLINICAL APPOINTMENTS	University Hospital Basel <i>Attending physician and Head of Hepatology</i> <i>Chief, Division of Gastroenterology and Hepatology</i>	2003 2012
HONORS	Alumni Prize of the Medical Faculty of the University of Basel	2001
	Hepatology Prize, Swiss Society for Gastroenterology and Hepatology	2002

	Honorary Prize of the Swiss Society for Gastroenterology and Hepatology	2003
	Otto Naegeli Prize	2012
	Dora Seitz Prize	2016
RESEARCH BOARDS	Agence national de recherches sur le sida et les hépatites virales (ANRS) <i>Membre du Comité Scientifique Sectoriel 4</i>	2007-2010
	Swiss National Science Foundation <i>Research Council Member Division III</i>	since 2009
STIPENDS	Postgraduate Course Scholarship Swiss National Science Foundation	1988-2001
	Advanced Postdoctoral Fellowship Swiss National Science Foundation	1993-1995
	SCORE A Fellowship Swiss National Science Foundation	1999-2002
MEMBERSHIPS	Swiss Association for the Study of the Liver (SASL) <i>Council Member</i> <i>President</i>	since 2001 <i>since 2001</i> 2003-2011
	Swiss Society for Gastroenterology	since 1997
	European Association for the Study of the Liver (EASL)	since 1998
	Swiss Society for Internal Medicine (SGIM)	since 1998
	American Association for the Study of Liver Diseases (AASLD)	since 1999
	American Gastroenterology Association (AGA) <i>Fellow</i>	since 2001 <i>since 2009</i>
	American Society for Microbiology (ASM)	since 2001
	American Society for Biochemistry and Molecular Biology (ASBMB)	since 2003
	International Society for Interferon and Cytokine Research (ISICR)	since 2005
	Ludwig-Heilmeyer-Gesellschaft	since 2008
EDITORIAL BOARDS	Journal of Hepatology <i>Editorial Board Member</i>	since 2005
CONGRESS ORGANIZATION	Vulpera Research Retreat <i>Co-Organizer</i>	since 2003
	Annual congress of the Swiss Society for Gastroenterology <i>Member of the Scientific Committee</i>	2003 and 2004
CLINICAL TRIAL EXPERIENCE	Principal Investigator and Co-Investigator in > 40 Phase II and Phase III clinical trials	since 1997
TEACHING EXPERIENCE	Since 1997 supervision of 18 PhD and MD-PhD students Lectures for Medical Students (Bachelor and Master courses in Gastroenterology and Hepatology)	

Bedside Group teaching for Medical Students  
Lectures at the Biozentrum (Course: Molecular medicine) since 1997

CURRENT FUNDING Swiss National Science Foundation grant 310030\_166202 / 1  
Title: Interferon Regulated Immune Responses in Viral Hepatitis 2016-2019

European Research Council: MERiC synergy grant  
Title: Mechanisms of Evasive Resistance in Cancer 2014-2020

Systems X  
Title: Mechanisms of Evasive Resistance in Cancer 2014-2017

BIOSKETCH

**Markus H. Heim, M.D., Professor of Medicine, Chief, Division of Gastroenterology and Hepatology, University Hospital Basel and Group Leader of the Hepatology Laboratory at the Department of Biomedicine of the University Basel, Switzerland**

Heim earned his medical degree at the University of Basel, Switzerland. He then trained for 3 years in basic biomedical science at the Biozentrum in Basel with U.A.Meyer investigating genetic polymorphisms of drug metabolism. Following two years in Internal Medicine at Basel University Hospital, Heim joined the laboratory of James E. Darnell at Rockefeller University, New York, as a postdoctoral fellow, where he worked on basic aspects of Jak-STAT signal transduction. He then completed his internal medicine training and obtained a full training in gastroenterology and hepatology at the University Hospitals in Freiburg, Germany, and Basel, Switzerland. Since 1999 he is Group Leader of the Hepatology Laboratory. He was appointed head of the Hepatology service at the Basel University Hospital in 2003, and chief of the division of Gastroenterology and Hepatology in 2012. In 2011, Heim spent a sabbatical in Frank Chisari's Lab at the Scripps Research Institute in La Jolla, CA. In 2012, Heim was awarded the Otto-Naegeli Prize.

His research focuses on innate immunity in liver disease and hepatocellular carcinoma.

RESEARCHER ID (ISI WEB OF KNOWLEGDE): [A-7526-2008](#)

PUBLICATIONS IN PUBMED (NCBI): [PUBMED](#)

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## ORIGINAL PUBLICATIONS BASIC RESEARCH

1. Blum M, Grant DM, McBride W, Heim M, Meyer UA. Human arylamine N-acetyltransferase genes: isolation, chromosomal localization, and functional expression. *DNA Cell Biol* 1990;9:193-203.
2. Blum M, Heim M, Meyer UA. Nucleotide sequence of rabbit NAT2 encoding polymorphic liver arylamine N-acetyltransferase (NAT). *Nucleic Acids Res* 1990;18:5295.
3. Blum M, Heim M, Meyer UA. Nucleotide sequence of rabbit NAT1 encoding monomorphic arylamine N-acetyltransferase. *Nucleic Acids Res* 1990;18:5287.
4. Heim M, Meyer UA. Genotyping of poor metabolisers of debrisoquine by allele-specific PCR amplification. *Lancet* 1990;336:529-532.
5. Kagimoto M, Heim M, Kagimoto K, Zeugin T, Meyer UA. Multiple mutations of the human cytochrome P450IID6 gene (CYP2D6) in poor metabolizers of debrisoquine. Study of the functional significance of individual mutations by expression of chimeric genes. *J Biol Chem* 1990;265:17209-17214.
6. Blum M, Demierre A, Grant DM, Heim M, Meyer UA. Molecular mechanism of slow acetylation of drugs and carcinogens in humans. *Proc Natl Acad Sci U S A* 1991;88:5237-5241.
7. Broly F, Gaedigk A, Heim M, Eichelbaum M, Morike K, Meyer UA. Debrisoquine/sparteine hydroxylation genotype and phenotype: analysis of common mutations and alleles of CYP2D6 in a European population. *DNA Cell Biol* 1991;10:545-558.
8. Heim MH, Blum M, Beer M, Meyer UA. Acetylation of serotonin in the rabbit pineal gland: an N-acetyltransferase with properties distinct from NAT1 and NAT2 is responsible. *J Neurochem* 1991;57:1095-1099.
9. Johansson I, Yue QY, Dahl ML, Heim M, Sawe J, Bertilsson L, Meyer UA, Sjoqvist F, Ingelman-Sundberg M. Genetic analysis of the interethnic difference between Chinese and Caucasians in the polymorphic metabolism of debrisoquine and codeine. *Eur J Clin Pharmacol* 1991;40:553-556.
10. Heim MH, Meyer UA. Evolution of a highly polymorphic human cytochrome P450 gene cluster: CYP2D6. *Genomics* 1992;14:49-58.
11. Heim MH, Kerr IM, Stark GR, Darnell JE, Jr. Contribution of STAT SH2 groups to specific interferon signaling by the Jak-STAT pathway. *Science* 1995;267:1347-1349.
12. Ghilardi N, Ziegler S, Wiestner A, Stoffel R, Heim MH, Skoda RC. Defective STAT signaling by the leptin receptor in diabetic mice. *Proc Natl Acad Sci U S A* 1996;93:6231-6235.
13. Heim MH, Gamboni G, Beglinger C, Gyr K. Specific activation of AP-1 but not Stat3 in regenerating liver in mice. *Eur J Clin Invest* 1997;27:948-955.
14. Lugli SM, Feng N, Heim MH, Adam M, Schnyder B, Etter H, Yamage M, Eugster HP, Lutz RA, Zurawski G, Moser R. Tumor necrosis factor alpha enhances the expression of the interleukin (IL)-4 receptor alpha-chain on endothelial cells increasing IL-4 or IL-13-induced Stat6 activation. *J Biol Chem* 1997;272:5487-5494.
15. Pless M, Norga K, Carroll M, Heim MH, D'Andrea AD, Mathey-Prevot B. Receptors that induce erythroid differentiation of Ba/F3 cells: structural requirements and effect on STAT5 binding. *Blood* 1997;89:3175-3185.
16. Fasler-Kan E, Pansky A, Wiederkehr M, Battagay M, Heim MH. Interferon-alpha activates signal transducers and activators of transcription 5 and 6 in Daudi cells. *Eur J Biochem* 1998;254:514-519.
17. Feng N, Lugli SM, Schnyder B, Gauchat JF, Graber P, Schlagenhauf E, Schnarr B, Wiederkehr-Adam M, Duschl A, Heim MH, Lutz RA, Moser R. The interleukin-4/interleukin-13 receptor of human synovial fibroblasts: overexpression of the non-signaling interleukin-13 receptor alpha2. *Lab Invest* 1998;78:591-602.
18. Heuss LT, Heim MH, Schultz U, Wissmann D, Offensperger WB, Staeheli P, Blum HE. Biological efficacy and signal transduction through STAT proteins of recombinant duck interferon in duck hepatitis B virus infection. *J Gen Virol* 1998;79 (Pt 8):2007-2012.
19. Pansky A, Hildebrand P, Heim MH, Eberhard M, Kissel T, Beglinger C. Growth effects of alpha-interferon but not of bombesin or angiotensin II are mediated by activation of STAT proteins. *Eur J Clin Invest* 1998;28:398-406.
20. Steiger JU, Nickerson PW, Hermle M, Thiel G, Heim MH. Interferon-gamma receptor signaling is not required in the effector phase of the alloimmune response. *Transplantation* 1998;65:1649-1652.
21. Heim MH, Moradpour D, Blum HE. Expression of hepatitis C virus proteins inhibits signal transduction through the Jak-STAT pathway. *J Virol* 1999;73:8469-8475.
22. Donda A, Mori L, Shamshiev A, Carena I, Mottet C, Heim MH, Beglinger C, Grunert F, Rochlitz C, Terracciano L, Jantschke P, De Libero G. Locally inducible CD66a (CEACAM1) as an amplifier of the human intestinal T cell response. *Eur J Immunol* 2000;30:2593-2603.
23. Pansky A, Hildebrand P, Fasler-Kan E, Baselgia L, Ketterer S, Beglinger C, Heim MH. Defective Jak-STAT signal transduction pathway in melanoma cells resistant to growth inhibition by interferon-alpha. *Int J Cancer* 2000;85:720-725.
24. Schnyder B, Schnyder-Candrian S, Panski A, Bommel H, Heim M, Duschl A, Moser R. Phytochemical inhibition of interleukin-4-activated Stat6 and expression of VCAM-1. *Biochem Biophys Res Commun* 2002;292:841-847.
25. Blindenbacher A, Duong FH, Hunziker L, Stutvoet ST, Wang X, Terracciano L, Moradpour D, Blum HE, Alonzi T, Tripodi M, La Monica N, Heim MH. Expression of hepatitis c virus proteins inhibits interferon alpha signaling in the liver of transgenic mice. *Gastroenterology* 2003;124:1465-1475.
26. Blindenbacher A, Wang X, Langer I, Savino R, Terracciano L, Heim MH. Interleukin 6 is important for survival after partial hepatectomy in mice. *Hepatology* 2003;38:674-682.

27. Wiederkehr-Adam M, Ernst P, Muller K, Bieck E, Gombert FO, Ottl J, Graff P, Grossmuller F, Heim MH. Characterization of phosphopeptide motifs specific for the Src homology 2 domains of signal transducer and activator of transcription 1 (STAT1) and STAT3. *J Biol Chem* 2003;278:16117-16128.
28. Blanchard C, Durual S, Estienne M, Bouzakri K, Heim MH, Blin N, Cuber JC. IL-4 and IL-13 up-regulate intestinal trefoil factor expression: requirement for STAT6 and de novo protein synthesis. *J Immunol* 2004;172:3775-3783.
29. Duong FH, Filipowicz M, Tripodi M, La Monica N, Heim MH. Hepatitis C virus inhibits interferon signaling through up-regulation of protein phosphatase 2A. *Gastroenterology* 2004;126:263-277.
30. Croquelois A, Blindenbacher A, Terracciano L, Wang X, Langer I, Radtke F, Heim MH. Inducible inactivation of Notch1 causes nodular regenerative hyperplasia in mice. *Hepatology* 2005;41:487-496.
31. Duong FH, Christen V, Berke JM, Penna SH, Moradpour D, Heim MH. Upregulation of protein phosphatase 2A by hepatitis C virus modulates NS3 helicase activity through inhibition of protein arginine methyltransferase 1. *J Virol* 2005;79:15342-15350.
32. Schnyder B, Schnyder-Candrian S, Pansky A, Schmitz ML, Heim M, Ryffel B, Moser R. IL-17 reduces TNF-induced Rantes and VCAM-1 expression. *Cytokine* 2005;31:191-202.
33. Duong FH, Christen V, Filipowicz M, Heim MH. S-Adenosylmethionine and betaine correct hepatitis C virus induced inhibition of interferon signaling in vitro. *Hepatology* 2006;43:796-806.
34. Christen V, Duong F, Bernsmeier C, Sun D, Nassal M, Heim MH. Inhibition of alpha interferon signaling by hepatitis B virus. *J Virol* 2007;81:159-165.
35. Christen V, Treves S, Duong FH, Heim MH. Activation of endoplasmic reticulum stress response by hepatitis viruses up-regulates protein phosphatase 2A. *Hepatology* 2007;46:558-565.
36. Bernsmeier C, Duong FH, Christen V, Pugnale P, Negro F, Terracciano L, Heim MH. Virus-induced over-expression of protein phosphatase 2A inhibits insulin signalling in chronic hepatitis C. *J Hepatol* 2008;49:429-440.
37. Ciuffreda D, Comte D, Cavassini M, Giostra E, Buhler L, Perruchoud M, Heim MH, Battegay M, Genne D, Mulhaupt B, Malinverni R, Oneta C, Bernasconi E, Monnat M, Cerny A, Chuard C, Borovicka J, Mentha G, Pascual M, Gonvers JJ, Pantaleo G, Dutoit V. Polyfunctional HCV-specific T-cell responses are associated with effective control of HCV replication. *Eur J Immunol* 2008;38:2665-2677.
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39. Bochud PY, Cai T, Overbeck K, Bochud M, Dufour JF, Mullhaupt B, Borovicka J, Heim M, Moradpour D, Cerny A, Malinverni R, Francioli P, Negro F, Swiss Hepatitis CCSG. Genotype 3 is associated with accelerated fibrosis progression in chronic hepatitis C. *J Hepatol* 2009;51:655-666.
40. Sarasin-Filipowicz M, Krol J, Markiewicz I, Heim MH, Filipowicz W. Decreased levels of microRNA miR-122 in individuals with hepatitis C responding poorly to interferon therapy. *Nat Med* 2009;15:31-33.
41. Sarasin-Filipowicz M, Wang X, Yan M, Duong FH, Poli V, Hilton DJ, Zhang DE, Heim MH. Alpha interferon induces long-lasting refractoriness of JAK-STAT signaling in the mouse liver through induction of USP18/UBP43. *Mol Cell Biol* 2009;29:4841-4851.
42. Tchorz JS, Kinter J, Muller M, Tornillo L, Heim MH, Bettler B. Notch2 signaling promotes biliary epithelial cell fate specification and tubulogenesis during bile duct development in mice. *Hepatology* 2009;50:871-879.
43. Bellecave P, Sarasin-Filipowicz M, Donze O, Kennel A, Gouttenoire J, Meylan E, Terracciano L, Tschopp J, Sarrazin C, Berg T, Moradpour D, Heim MH. Cleavage of mitochondrial antiviral signaling protein in the liver of patients with chronic hepatitis C correlates with a reduced activation of the endogenous interferon system. *Hepatology* 2010;51:1127-1136.
44. Duong FH, Christen V, Lin S, Heim MH. Hepatitis C virus-induced up-regulation of protein phosphatase 2A inhibits histone modification and DNA damage repair. *Hepatology* 2010;51:741-751.
45. Rauch A, Kutalik Z, Descombes P, Cai T, Di Iulio J, Mueller T, Bochud M, Battegay M, Bernasconi E, Borovicka J, Colombo S, Cerny A, Dufour JF, Furrer H, Gunthard HF, Heim M, Hirschel B, Malinverni R, Moradpour D, Mullhaupt B, Witteck A, Beckmann JS, Berg T, Bergmann S, Negro F, Telenti A, Bochud PY, Swiss Hepatitis CCS, Swiss HIVCS. Genetic variation in IL28B is associated with chronic hepatitis C and treatment failure: a genome-wide association study. *Gastroenterology* 2010;138:1338-1345, 1345 e1331-1337.
46. Ripoli M, D'Aprile A, Quarato G, Sarasin-Filipowicz M, Gouttenoire J, Scrima R, Cela O, Boffoli D, Heim MH, Moradpour D, Capitano N, Piccoli C. Hepatitis C virus-linked mitochondrial dysfunction promotes hypoxia-inducible factor 1 alpha-mediated glycolytic adaptation. *J Virol* 2010;84:647-660.
47. Dill MT, Duong FH, Vogt JE, Bibert S, Bochud PY, Terracciano L, Papassotiropoulos A, Roth V, Heim MH. Interferon-induced gene expression is a stronger predictor of treatment response than IL28B genotype in patients with hepatitis C. *Gastroenterology* 2011;140:1021-1031.
48. Makowska Z, Duong FH, Trincucci G, Tough DF, Heim MH. Interferon-beta and interferon-lambda signaling is not affected by interferon-induced refractoriness to interferon-alpha in vivo. *Hepatology* 2011;53:1154-1163.
49. Mueller KM, Kornfeld JW, Friedbichler K, Blaas L, Egger G, Esterbauer H, Hasselblatt P, Schleder M, Haindl S, Wagner KU, Engblom D, Haemmerle G, Kratky D, Sexl V, Kenner L, Kozlov AV, Terracciano L, Zechner R, Schuetz G, Casanova E, Pospisilik JA, Heim MH, Moriggl R. Impairment of hepatic growth hormone and glucocorticoid receptor signaling causes steatosis and hepatocellular carcinoma in mice. *Hepatology* 2011;54:1398-1409.

50. Trajkovski M, Hausser J, Soutschek J, Bhat B, Akin A, Zavolan M, Heim MH, Stoffel M. MicroRNAs 103 and 107 regulate insulin sensitivity. *Nature* 2011;474:649-653.
51. Bochud PY, Bibert S, Kutalik Z, Patin E, Guergnon J, Nalpas B, Goossens N, Kuske L, Mullhaupt B, Gerlach T, Heim MH, Moradpour D, Cerny A, Malinverni R, Regenass S, Dollenmaier G, Hirsch H, Martinetti G, Gorgiewski M, Bourliere M, Poynard T, Theodorou I, Abel L, Pol S, Dufour JF, Negro F, Swiss Hepatitis CCSG, Group AHEGS. IL28B alleles associated with poor hepatitis C virus (HCV) clearance protect against inflammation and fibrosis in patients infected with non-1 HCV genotypes. *Hepatology* 2012;55:384-394.
52. Dill MT, Makowska Z, Duong FH, Merkofer F, Filipowicz M, Baumert TF, Tornillo L, Terracciano L, Heim MH. Interferon-gamma-stimulated genes, but not USP18, are expressed in livers of patients with acute hepatitis C. *Gastroenterology* 2012;143:777-786 e771-776.
53. Dill MT, Rothweiler S, Djonov V, Hlushchuk R, Tornillo L, Terracciano L, Meili-Butz S, Radtke F, Heim MH, Semela D. Disruption of Notch1 induces vascular remodeling, intussusceptive angiogenesis, and angiosarcomas in livers of mice. *Gastroenterology* 2012;142:967-977 e962.
54. Friedbichler K, Themanns M, Mueller KM, Schleder M, Kornfeld JW, Terracciano LM, Kozlov AV, Haindl S, Kenner L, Kolbe T, Mueller M, Snibson KJ, Heim MH, Moriggl R. Growth-hormone-induced signal transducer and activator of transcription 5 signaling causes gigantism, inflammation, and premature death but protects mice from aggressive liver cancer. *Hepatology* 2012;55:941-952.
55. Garaigorta U, Heim MH, Boyd B, Wieland S, Chisari FV. Hepatitis C virus (HCV) induces formation of stress granules whose proteins regulate HCV RNA replication and virus assembly and egress. *J Virol* 2012;86:11043-11056.
56. Hagiwara A, Cornu M, Cybulski N, Polak P, Betz C, Trapani F, Terracciano L, Heim MH, Ruegg MA, Hall MN. Hepatic mTORC2 activates glycolysis and lipogenesis through Akt, glucokinase, and SREBP1c. *Cell Metab* 2012;15:725-738.
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58. Dill MT, Tornillo L, Fritzius T, Terracciano L, Semela D, Bettler B, Heim MH, Tchorz JS. Constitutive Notch2 signaling induces hepatic tumors in mice. *Hepatology* 2013;57:1607-1619.
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60. Lupberger J, Duong FH, Fofana I, Zona L, Xiao F, Thumann C, Durand SC, Pessaux P, Zeisel MB, Heim MH, Baumert TF. Epidermal growth factor receptor signaling impairs the antiviral activity of interferon-alpha. *Hepatology* 2013;58:1225-1235.
61. Makowska Z, Blumer T, Duong FH, La Monica N, Kandimalla ER, Heim MH. Sequential induction of type I and II interferons mediates a long-lasting gene induction in the liver in response to a novel toll-like receptor 9 agonist. *J Hepatol* 2013;58:743-749.
62. Shanker V, Trincucci G, Heim HM, Duong HT. Protein phosphatase 2A impairs IFNalpha-induced antiviral activity against the hepatitis C virus through the inhibition of STAT1 tyrosine phosphorylation. *J Viral Hepat* 2013;20:612-621.
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66. Bernsmeier C, Meyer-Gerspach AC, Blaser LS, Jeker L, Steinert RE, Heim MH, Beglinger C. Glucose-induced glucagon-like Peptide 1 secretion is deficient in patients with non-alcoholic fatty liver disease. *PLoS One* 2014;9:e87488.
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71. Haid S, Grethe C, Dill MT, Heim M, Kaderali L, Pietschmann T. Isolate-dependent use of claudins for cell entry by hepatitis C virus. *Hepatology* 2014;59:24-34.
72. Jansen L, de Niet A, Makowska Z, Dill MT, van Dort KA, Terpstra V, Bart Takkenberg R, Janssen HL, Heim MH, Kootstra NA, Reesink HW. An intrahepatic transcriptional signature of enhanced immune activity predicts response to peginterferon in chronic hepatitis B. *Liver Int* 2014.
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