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Education

2010	Assistant Professor (Research) of Pathology and Laboratory Medicine
2009	Instructor of Pathology and Laboratory Medicine, Brown University, RI
2007-2009	Postdoctorial Research Associate, Pathology and Laboratory Medicine, Brown University, RI
2001-2007	Research Associate, Liver Research Center, Rhode Island Hospital
PhD	PhD Biology (Cell biology and Microbiology)
1997-2001	Friedrich Wilhelms University Bonn, Germany
2001	Magna cum laude; Friedrich Wilhelms University, Bonn;

- Thesis: Hepatitis C virus NS2 protein inhibits gene expression from different cellular and viral promoters in hepatic and non hepatic cell lines

MS	MS Biology (Microbiology and Immunology)
1995-1997	Friedrich Wilhelms University Bonn, Germany

- Thesis: Hepatitis C virus Core protein does not inhibit apoptosis in hepatoma cells

July 1996 – January 1997	Internship at the Medical Institute of Microbiology, Immunology and Parasitology under Prof Dr. B Matz and Dr. R. Kaiser

- Designed and optimized primers and PCR protocols for the detection of specific conservative residues in the HIV genome

BS:	Biology (Chemistry, Physics, Microbiology and Genetics)
1992-1995	Friedrich Wilhelms University Bonn, Germany

Professional Experience

2014-2015
Mechanism of initiation of lysosomal membrane permeabilization in cellular response to carbon nanotubes
Interaction between 2D materials and cytoskeleton

2012-2013
Mechanism of cellular uptake of large multilayer graphene microsheets into eukaryotic cells through spontaneous membrane penetration

2011-2012
Assessment of the role of geometry in uptake, intracellular sequestration, and cytotoxicity of engineered carbon nanomaterials in hepatocytes

Determination of ER stress signaling pathways responsible for the cytotoxicity of hepatocytes exposed to high aspect ratio nanomaterials (HARNs)

2009-2010
Research Projects:
Determination of oxidative stress caused by MWCNTs in liver cells, activation of signal transduction pathways by nanoparticles

Collaboration projects with:
- NIST (National Institute of Standards and Technology): Determination of DNA damage in liver cells caused by carbon nanotubes; Collaborator: Dr. Bryant Nelson
- School of Engineering Brown University: Determination of oxidative stress caused by carbon nanotubes; Collaborator: Prof. Robert Hurt
- School of Engineering Brown University: Imaging and Molecular Simulation of Tip Entry Pathways in the Cellular Uptake of Carbon Nanotubes; Collaborators: Prof. Robert Hurt and Prof. Huajian Gao
- School of Engineering Brown University: Mechanism of initiation of lysosomal membrane permeabilization in cellular response to carbon nanotubes
Mechanism of initiation of lysosomal membrane permeabilization in cellular response to carbon nanotubes; Collaborators: Prof. Robert Hurt and Prof. Huajian Gao
Interaction between 2D materials and cytoskeleton; Collaborators: Prof. Robert Hurt and Prof. Huajian Gao

2007-2009
Research associate in the Department of Pathology and Laboratory Medicine at Brown University. Research projects:

- Toxicity of Quantum Dots and Multiwalled Carbon Nanotubes in hepatoma cell lines. Transfection and incubation of Quantum dots in

hepatoma cell line; determination of viability by using different cytotoxicity and apoptosis cell assays. Determination of gene upregulation by Realtime PCR and Westernblot.

2001-2007

- Research associate, Liver Research Center, Rhode Island Hospital and Brown Medical School. Providence, RI. Executed research projects independently under the mentorship of a principal investigator. Also guided and taught undergraduate students involved in the research. Responsible for two projects studying the pathogenesis of Hepatitis C.

    - Project 1: Studying how NS2 influences intracellular pathways by inhibiting protein expression in hepatoma cell lines; detection and characterization of the activated ER stress specific pathway in hepatoma cell lines using the following methods: DNA/ RNA: Cloning, subcloning promoter sequences into reporter to show activation of stress specific genes after transfection of Hepatitis C NS2 protein, *in vitro* mutagenesis, *in vitro* transcription/ translation, PCR, Realtime PCR, including replicon and subgenomic replicon systems (Hepatitis C virus); Northern blots to determine if NS2 down-regulates the transcription of most cellular genes while up-regulating ER stress specific genes that lead to inhibition of transcription/translation in the cell. The following methods for cell culture were used: Standard cell culture systems and various methods of transfection: electroporation, lipofection and also the lentiviral system. For protein biochemistry: Immunoprecipitation, Western blot, Immunocytochemistry, ELISA assays, reporter assays, and also viability, apoptosis and proliferation assays.

    - Project 2: Influence of Hepatitis C Core protein in the proliferation rate of hepatoma cell lines. Determination of genes up-regulated by Hepatitis C Core protein through analysis of micro array data after transfection of HUH7 cells. Identifying and cloning of the WISP2 promoter of this gene into reporter plasmid. Through reporter assays and real time PCR the up-regulation of these genes was verified. To determine the function of WISP2 in hepatoma cell lines the WISP2 gene was cloned into an expression vector. Viability and proliferation assays verified that WISP2 activates cell proliferation in hepatoma cell lines. Protein expression of WISP2 was verified by Western blot. To determine how HCV Core protein activates WISP2 promoter assays were established. The activation of Wnt1/WISP2 pathway induced by Core protein was also demonstrated and the activated transcription factor was defined.

1995 – 2001
Graduate student at Friedrich Wilhelms University
Executed research projects under mentorship of principal investigator. Established DNA and RNA based molecular biology methods in the immunology lab internal medicine; University Hospital, Bonn
Directly responsible for two research projects:

- Project 1: Studying if Hepatitis C Core protein induces apoptosis in hepatoma cell lines. The following methods were used: cloning of Hepatitis C virus gene sequences into expression vectors; different transfection methods (lipofection and electroporation) for various hepatoma cell lines to determine highest transfection efficiency. Studied the effects of viral proteins, especially HCV Core protein involved in apoptosis by using different methods, DAPI, LDH etc.

- Project 2: Studying the function of the Hepatitis C NS2 protein and its effects on hepatoma cell lines: cloned different promoters (cellular and viral) into reporter constructs and studied the regulation of these promoters by Hepatitis C NS2 protein in different cell lines. Studied viability and apoptosis of NS2 in different hepatoma cell lines.

Funding

Travel award for oral presentation at the international symposium on HCV and related viruses 2004
Travel award for poster presentation at the international symposium on HCV and related viruses 2005

Miscellaneous

Reviewer of the journal Carbon, Nanotoxicology and Chemical Research in Toxicology

Publications

Wang Z, **von dem Bussche A**, Kabadi PK, Kane AB, Hurt RH. Biological and Environmental Transformations of Copper-Based Nanomaterials. ACS Nano. 2013, 7 (10), pp 8715–8727

Lia Y*, Yuana H*, **von dem Bussche A***, Creighton M, Hurt R, Kane A, and Huajian Gao. Graphene microsheets enter cells through spontaneous membrane penetration at edge asperities and corner sites. Proc Natl Acad Sci U S A. 2013;110 (30):12295-300 * these 3 authors contributed equally to the work

Shi X, **von dem Bussche A**, Hurt R, Kane A, Gao H. Cell entry of one-dimensional nanomaterials occurs by tip recognition and rotation. Nat Nanotechnol. 6: 714-719 (2011).

von dem Bussche A, Machida R, Li K, Loevinsohn G, Khander A, Wang J, Wakita T, Wands J, Li J, Hepatitis C virus NS2 protein triggers endoplasmic reticulum stress and suppresses its own viral replication, Journal of Hepatology 2010, Volume 53, Issue 5, Pages 797-804

Guo L[1], **von Dem Bussche A[2]**, Buechner M[2], Yan A[3], Kane[2]A, Hurt[1] R
Adsorption of Essential Micronutrients by Carbon Nanotubes and its Implications for Nanotoxicity Testing, Small 2008 Volume 4 Issue 6, Pages 721 – 727

Yan A, **von dem Bussche A**, Kane A, Hurt R
Tocopheryl polyethylene glycol succinate as a safe, antioxidant surfactant for processing carbon nanotubes and fullerenes, Carbon 45 (2007) 2463–2470

Merle P, de la Monte S, Herrmann M, Tanaka S, Kim M, **von dem Bussche A**, Kew M, Trepo C and Wands J
Functional consequences of frizzled-7 receptor overexpression in human hepatocellular carcinoma, Gastroenterology. 2004 Oct;127(4):1110-22

de la Monte SM, Chiche J, **von dem Bussche A**, Sanyal S, Lahousse SA, Janssens SP, Bloch KD. Nitric oxide synthase-3 overexpression causes apoptosis and impairs neuronal mitochondrial function: relevance to Alzheimer's-type neurodegeneration.
Lab Invest. 2003 Feb;83(2):287-98

Dumoulin FL, **von dem Bussche A**, Li J, Khamzina L, Wands JR, Sauerbruch T, Spengler U. Hepatitis C virus NS2 protein inhibits gene expression from different cellular and viral promoters in hepatic and nonhepatic cell lines.
Virology. 2003 Jan 20; 305(2):260-6.

Duesberg U, **von dem Bussche A**, Kirschning C, Miyake K, Sauerbruch T, Spengler U. Related Cell activation by synthetic lipopeptides of the hepatitis C virus (HCV)--core protein is mediated by toll like receptors (TLRs) 2 and 4.
Immunol Lett. 2002 Nov 1;84(2):89-95.

Dumoulin FL, Nischalke HD, Leifeld L, **von dem Bussche A**, Rockstroh JK, Sauerbruch T, Spengler U. Semi-quantification of human C-C chemokine mRNAs with reverse transcription/real-time PCR using multi-specific standards.

J Immunol Methods. 2000 Jul 31;241(1-2):109-19.

Dumoulin FL, **von dem Bussche A**, Sohne J, Sauerbruch T, Spengler U. Hepatitis C virus core protein does not inhibit apoptosis in human hepatoma cells.
Eur J Clin Invest. 1999 Nov;29(11):940-6

Abstracts

Annette von dem Bussche, Charles Vaslet, Paulette Ferland, Paula Weston, Norma Messier, Robert Hurt and Agnes Kane. MWCNTs induce oxidative stress response in immortalized murine hepatocytes. SOT Annual Meeting, San Francisco, USA, March 2012

Annette von dem Bussche, Aihui Yan, Robert Hurt, Agnes Kane
The effect of covalent and non-covalent functionalization on carbon nanotube interactions with AML12 hepatocytes: cellular uptake, localization, and cytotoxicity
Nanotoxicology, 2nd international conference, Switzerland, Zurich, September 2008

Aihui Yan, **Annette von dem Bussche,** Agnes B Kane, and Robert Hurt
TPGS as a safe antioxidant surfactant for dispersing Carbon Nanotubes and Fullerenes
8th World Biomaterial Congress, international conference, Netherland, Amsterdam May 2008

Annette von dem Bussche, Takayoshi Fukutomi, Jack R Wands and Jisu Li
Upregulation of Wnt1 and WISP2 signaling pathway by Hepatitis C virus Core protein, Submitted

Annette von dem Bussche, Franz Ludwig Dumoulin, Jack R. Wands, Ji Su Li
Characterization of cellular ER stress induced by the Hepatitis C virus NS2 protein in context of HCV polyprotein expression and replication
AASLD Hepatology Suppl. 1, Vol 42 No 4, October 2005

Annette von dem Bussche, Takayoshi Fukutomi, Jack R. Wands and Jisu Li
Contribution of Wnt1/WISP2 signaling in hepatocyte proliferation induced by Hepatitis C virus Core protein
AASLD Hepatology Suppl. 1, Vol 42 No 4, October 2005

Annette von dem Bussche, Takayoshi Fukutomi, Jack R. Wands and Jisu Li
Contribution of Wnt1/WISP2 signaling in hepatocyte proliferation induced by Hepatitis C virus Core protein
12 th International Symposium on Hepatitis C Virus and related viruses; 2005

Annette von dem Bussche, Franz Ludwig Dumoulin, Jack R. Wands, Ji Su Li
Characterization of cellular ER stress induced by the Hepatitis C virus NS2 protein in context of HCV polyprotein expression and replication

12 th International Symposium on Hepatitis C Virus and related viruses; 2005

Annette von dem Bussche, Franz Ludwig Dumoulin, Jack R. Wands, and Jisu Li
The Hepatitis C virus NS2 protein activates ER stress signaling pathways: Implication on viral pathogenesis. Hepatology, Vol 40, No 4, Suppl.1- October 2004

Annette von dem Bussche, Franz Ludwig Dumoulin, Jack R. Wands, Ji Su Li
Broad transcriptional repression by Hepatitis C Virus NS2 protein is mediated by activation of ER stress signaling; 11 th International Symposium on Hepatitis C Virus and related virus; Germany, Heidelberg; October 2004

Annette von dem Bussche, Takayoshi Fukutomi, Jack R. Wands and Jisu Li
Upregulation of Wnt-1 and WISP2 signaling pathway by hepatitis C virus core protein; 11 th International Symposium on Hepatitis C Virus and related viruses; 2004

Annette von dem Bussche, Jack Wands and Jisu Li.
Characterization of the functional domain in Hepatitis C virus NS2 protein that mediates repression of cellular and viral gene transcription activity. Hepatology, Vol 38, No 4 Suppl.1, October 2003

Annette von dem Bussche, Franz L. Dumoulin, Philippe Merle, Jacks Wands and Jisu Li. Regulation of viral and cellular gene transcription and Hepatitis B replication by hepatitis C virus NS2 protein. Hepatology, Vol. 36, No.4, October 2002

F.L. Dumoulin, **Annette von dem Bussche**, Ji Su Li, Leila Khamzina, Jack R Wands, Tilman Sauerbruch, Ulrich Spengler
Hepatitis C Virus NS2 protein inhibits transcription of cellular and viral promoters, Digestive Disease Week, 2002

F.L. Dumoulin, **Annette von dem Bussche**, Ulrich Spengler, Tilman Sauerbruch, Jack R Wands
Analysis of the impact of Hepatitis C Virus NS2 protein and steady state m-RNA levels in human hepatoma cells using c-DNA array screens, Hepatology; Vol 34 No4, Oct 2001

Proposals submitted

R21: Geometric determinants of toxicity pathways activated by engineered carbon nanomaterials (resubmitted at 11/09/2012).

The goal of this grant is to assess the causal relationship between geometry of HARNs, lysosomal membrane permeabilization and downstream toxicity signaling pathways.

Current grant support

R01 ES 016178-03S1 Kane (PI, Hurt (Co-PI) 09/17/09-05/31/12
von dem Bussche (Investigator)
NIH/NIEHS

Chemical, structural, and superstructural determinants of nanocarbon toxicity

The goal of this grant issued under the American Recovery and Reinvestment Act is to use novel imaging techniques to study interactions of carbon nanotubes with target cells.

Completed grant support

RD-83386201 Hurt (PI), Kane (Co-PI) 08/01/08-03/31/11
von dem Bussche (Investigator)
EPA

Bioavailability, environmental transformation, and detoxification of core/shell nanomaterials

The goal of this grant is to develop and validate chemical screening assays for bioavailability assessment and toxicant release throughout product lifecycle of quantum dots and silver nanoparticles.