Prof. Michael Kann, MD

Chair
UMR 5234 CNRS - University of Bordeaux
Fundamental Microbiology and Pathogenicity
Zone Nord, Bat 3A
146 rue Léo Saignat
F-33076 Bordeaux CEDEX
France

Tel. (secretariat): +33 5 57 57 17 63
Tel. (direct): +33 5 57 57 17 60

Department of Virological Diagnostics
and Biological Surveillance
University Hospitals of Bordeaux
– Hôpital Pellegrin –
Place Amélie Raba-Léon
F-33 076 Bordeaux CEDEX
France
michael.kann@u-bordeaux.fr

Nationality: German

Personal data sheet

Current situation:

- Chair of the Department "Fundamental Microbiology and Pathogenicity" (Microbiologie fondamentale et pathogénicité, MFP, UMR 5234) of the CNRS and the University of Bordeaux. http://www.mfp.cnrs.fr/mfp/index_en.php. In France, this position is an elected one allowing two 5-year mandates. I was recently re-elected for the second period.

  The Department has c. 80 staff members and trainees working in Parasitology, Bacteriology, Mycology and in particular Virology. The academic staff of the Diagnostic Virology Service of the University Hospitals of Bordeaux (CHU de Bordeaux) and also the WHO reference center for HIV resistance is part of the Department. MDs in Infectious Diseases are associated. In contrast to the nationwide funding reduction, I could increase the subventions. I could was further able to attract in 2015 and for 2016 two new research teams, which are excellent in cryo electron microscopy (Rémi Fronzes) and in Trypanosome metabolism (Frédérick Bringaud).

- Full Professor of Medicine in the Diagnostic Virology Service of the University Hospitals of Bordeaux with a specialization in "Biologie Médicale", which comprises Microbiology but also related domains as Immunology and Laboratory Medicine. The Service in which I am working is the largest in South-Western France, performing c. 250.000 serological and c. 80.000 PCR analyses per year.

- Responsible for a research team "Intracellular dynamics of subviral structures", which focuses on hepatitis B virus (HBV), parvoviruses and adenoviruses.

- Teaching of Virology for students in Medicine and Life Sciences (c. 80 h/year). Training of MDs in virology of hepatitis viruses. Responsible for Virology-Parasitology-Immunology training for Master students in Life Sciences.

- Invited Professor at the University of Tsukuba, Japan.

- Director of Aquitaine Microbiologie. This start-up is focused on test development in Microbiology for industry in particular in human and veterinary medicine.
  http://www.mfp.cnrs.fr/mfp/team_am.php

since 2012	Full professor in Medicine at the University of Bordeaux, France.
since 2011	Invited professor at the University of Tsukuba, Japan.
	Accreditation as specialist for “Medical Biologist” in France, which comprises Microbiology and Immunology but also Hematology and Biochemistry.
	Chair of the Department “Fundamental Microbiology and Pathogenicity”.
since 2010	Director of “Aquitaine Microbiologie”.
since 2009	Physician at the Virological Diagnostic Department at the University Hospitals of Bordeaux, France.
2006 - 2012	Full professor in Life Science at the University Victor Ségalen Bordeaux, France.
2006 - 2010	Member of the Faculty Board in Life Sciences, University of Bordeaux, France.
2005 - 2006	Associated Professor at the University Victor Ségalen Bordeaux, France.
2005	Habilitation in Life Sciences at the University of Bordeaux Ségalen.
2003 - 2005	Deputy Director of the Institute of Medical Virology at Giessen University.
2003	Löffler-Frosch research award for “The fundamental Research on the Life cycle of the Hepatitis B Virus” by the Society of Virology (Germany-Austria-Switzerland).
2002 – 2004	Head of the study group "Cell biology of viral infections" at the Society of Virology (Germany-Austria-Switzerland).
since 2000	Member of the International Committee for the Taxonomy of Viruses (ICTV).
2000 - 2005	Assistant Professor for Clinical Virology at the Justus Liebig University Giessen.
	Expert for Hepatitis B nominated by the Germany Ministery of Health.
1998 – 2000	Lecturer at Justus Liebig University Giessen, Germany.
1997 – 2005	Principle investigator of a research group at Justus Liebig University Giessen, Germany.
	Deputy Director of the virological diagnostic department at the University Hospital, Giessen, Germany.
1997	Habilitation in Medicine at the Justus Liebig University Giessen, Germany.
1995 - 1996	Scholarship of the Deutsche Forschungsgemeinschaft to acquire qualification as a university lecturer.
1995	Postdoc at the Department of Cell Biology, Yale University, New Haven, CT, U.S.A.
1992 – 1995	Postdoc at the Institute of Virology, Justus Liebig University Giessen, Germany (National Reference Centre for Hepatitis B).
	Vocational training in Virology and in Internal Medicine.
1990	Defense of thesis “Characterization of hepatitis B virus polymerase by prokaryotic expression”, University of Göttingen, Germany.
1988 – 1992	Physician at the Institute of Hygiene, Göttingen University, Germany.
	Vocational training to get the degree as specialist for Microbiology.
1988	End of medical studies and certificate to practice.
1982 - 1988	Studies of human medicine at Georg August University, Göttingen, Germany, including training at Green College, Oxford University, UK.

Research

Summary

Aim of my research team is the identification of cellular and viral factors linked to efficiency of infection. This research is performed on three viruses: HBV, parvoviruses including adeno-associated virus (AAV) vectors and adenoviruses. Given that the experimental systems have virus-dependent limits not all steps can be addressed with all viruses. This is exemplified by HBV for which no culture system exists, which allow virus propagation. On the other hand, HBV allows the assembly of clinical data, which are difficult to obtain for AAV.

- Hepatitis B: the aim of our studies is the understanding of the impact of fundamental processes of hepatitis B virus trafficking and variability on disease development. This includes the development of model systems allowing the verification of future treatment options.
- Parvoviruses: we analyze the biology of different parvoviruses for their capacity of DNA delivery into the nucleus. These investigations are driven by the successful use of parvoviruses in gene therapy.

The activities on HBV and parvoviruses are currently executed by one senior scientist, one postdoc, two PhD students and one technician. Research on adenoviruses is supervised by my co principle investigator.

Research projects

HBV (capsids) and parvoviruses (PV) have in common that they replicate in the nucleus. In analogy to other viruses, it was thought that their genome is liberated from the surrounding capsid in the cytoplasm or at the cytoplasmic face of the nuclear pore complex (NPC). Our electron microscopy-based finding in collaboration with Nelly Panté, Vancouver, Canada, showed that the functional diameter of the NPC is 40 nm instead of 26 nm, which was furthermore thought to be restricted by an additional central transport complex (Panté and Kann, Mol Biol Cell, 2002; 353 – 900 x cited, dependent upon source). This observation changed the perspective in that both capsids – HBV 36 nm; PV 18 to 25 nm - could pass the NPC followed by genome release inside the nucleus.

Hepatitis B. Analyzing the nuclear transport of HBV capsids we observed however that the capsids passed the NPC intact mediated by the cellular transport receptors importin α and β (Kann et al., J Cell Biol, 1999). Unlike classical karyophilic cargos, the capsids became however arrested on the nuclear side of the NPC by interaction with a specific NPC protein called Nup153 (Schmitz et al., PLoS Pathog, 2010). This strategy was a unique new finding and raised our interest in cell biology of the nuclear pore. Exclusively at the NPC (Rabe et al., J Vir, 2006) the capsids dissociate to capsid (core) protein dimers, followed by re-association to genome-devoid capsids (Rabe et al., PLoS Pathog, 2009). The dissociation was strictly correlated to genome maturation (Rabe et al., PNAS, 2003; recommended by the faculty of 1000), which transforms the viral RNA pregenome into a partially double stranded DNA, and which linked to structural changes of the capsid. These changes also occur upon capsid protein phosphorylation (Kann et al., J Cell Biol, 1999; Rabe et al., PNAS 2003) and in capsids devoid of nucleic acids (Chen et al., PLoS Pathog, 2016). Despite of this detailed knowledge there are, however, significant lacks, which are important for developing experimental systems, also needed for verification of therapeutical concepts.

The recently discovered receptor for HBV – hNTCP – allow after expression in non-permissive cultured cells infection although no virus propagation was achieved in culture. Expressing hNTCP in transgenic mice however failed to generate HBV susceptible animals although another virus, which uses the same receptor and import pathway, multiplies. Our recent findings showed that the intracytoplasmic

transport of the capsid is facilitated via the dynein light chain Dyn LL1 (Osseman et al., PLoS Pathog, in review), which is conserved in man and mice without exhibiting any polymorphism. We thus hypothesize that the block occurs after arrival of the capsid at the NPC and after entering the nuclear phase of the pore. The HBV replication cycle demands a repair of the genome to a chromatinized covalently closed form needing several enzymatic activities, which are poorly known. Having identified some candidates which are different in man and mice we focus on the understanding of genome repair also assuming that these protein(s) are involved in genome liberation. This project is strongly enhanced by an agreement with the company Neovirtech, which gives me the exclusive right to use their patented system allowing the real time follow-up of single HBV genomes.

In patients, the HBV viral load is largely controlled by the immune system, namely CD8+ T cells but establishment of infection is likely also controlled by the intrinsic immune response of the cell. In a collaborative project with Percy Knolle, Munich, Germany, we investigate the phenomenon that the TNFalpha sensitizing activity of some adenoviral proteins is counterbalanced by HBV (upon transduction). This finding is in agreement with the proposed longer life span of HBV infected hepatocytes. Further remarkable is that it also occurs in TNF2 negative mice, showing that the $CD8^+$ response is not required indicating a new pathway of innate immune response.

Yet another factor influencing the viral load is the variability of HBV genomes. This assumption is supported by early findings of others showing that the viral load is genotype-dependent. For better understanding the underlying molecular background we performed full genome sequencing of >400 samples from untreated, chronically infected patients. This work was based on a pilot study in which we sequenced the core protein ORF in 50 patients and which revealed a cluster of four amino acids statistically correlated with a 2 logs higher viral load (Wittkop et al., Antivir Ther, 2009). Consistently, transfection also resulted in a higher virus concentration in cell culture supernatants. In collaboration with Maura Dandri, Hamburg, we are currently investigating the replication capacity in liver-humanized mice.

The full genome Sanger sequencing showed a remarkable variability but also exhibited that the majority of sera contained just one sequence. Of note, deep sequencing of 28 sera showed only polymorphisms, which were also represented in the panel of Sanger sequences. We thus conclude that the spectrum of polymorphisms obtained by Sanger sequencing represents a very large percentage – if not all - of theoretically existing HBV sequences. This allowed us to determine the impact of intracellular mutations on virus release, which are known to be strictly controlled in HBV. Having clinical data of most patients we conclude that e.g. APOBECG modifications do not have a significant impact, arguing against a recent hypothesis published in Science. However, the statistical analyses in particular with regard to the correlation of the viral load with specific genome sequences is ongoing in collaboration with the local centre of biostatistics and epidemiology in Bordeaux (Linda Wittkop, ISPED).

Parvoviruses. In analogy to the HBV research, we investigated the nuclear interactions of different PV. We investigated intact PV capsids for analyzing the infection process but also the transport of partially preassembled capsid proteins. The latter step is required for assembling progeny virus, which occurs intranuclear. While the import of preassembled capsid proteins occurred “normally” through the NPCs although by an unknown transport receptor pathway (collaboration with Jose-Maria Almendral, Madrid, Spain; Riolobos et al., J Vir 2010; Gil-Renando et al., PLoS Pathog 2015), we observed that different PV did not only bind to the NPC but made holes in the nuclear envelope (Porval et al., PLoS Pathog 2013). This finding was exciting, as such an effect of viruses on the nucleus was never observed. Collaborating with Mario Schelhaas, Muenster, Germany, we observed that these hole were large enough to allow diffusion of even larger structures as e.g. papillomavirus capsids (50 – 60 nm) after PV infection (Aydin et al., PLoS Pathog, 2014). Using different approaches, we could unravel a part of the underlying mechanisms, which is similar in different cell types. We could show that interaction with the NPC changes PV structure, which than makes holes in the nuclear envelope, leading to Ca^{++} efflux from the space between inner and outer leaflet of the nuclear membrane. According to the current models of

how nuclear envelope breakdown (NEBD) is initiated upon mitosis, we found that several enzymes involved in mitosis were also required for PV-mediated NEBD. Of note, this NEBD was independent upon soluble cytosolic proteins allowing to investigate mitotic processes in the absence of shuttling proteins. There are however significant differences between mitotic and parvoviral NEBD namely that the latter was temporary and local. Microinjection experiments revealed that although being a stable phenomenon PV NEBD varied between cells in terms of time after injection.

Collaborative transduction experiments with Giovanni Di Pasquale, NIH, U.S.A., using a GFP-expressing adeno-associated virus (AAV) vector also showed a huge variability between individual cells despite of the fact that all cells were permissive. Combining transduction with microinjection showed a correlation between the entry on NEBD and the permissiveness of the cells (unpublished). We thus conclude that NEBD and infection correlates. This is in agreement with earlier finding of us, showing that PV H-1 mutants deficient in infection also failed to cause NEBD in permeabilized cells (Popa-Wagner, J Vir, 2012). Given the importance of efficient infection/transduction in gene therapy, we currently investigate the restricting factors in collaboration with Martin Mueller and Oliver Mueller, Heidelberg, Germany, aiming to increase transduction efficiency in epithelial cells.

Variability of nuclear import. The well-known phenomenon that the efficiency of nuclear localization of karyophilic structures is variable between individual cells let us investigate potential mechanisms existing aside of established modifications of the target proteins. These analyses were largely driven by our observations using HBV and PV considering that nuclear import receptors mediating transport are homogenously expressed amongst different cells and organs. We thus focused systematically on proteins of the NPC and in particular on their posttranslational modifications. Using thousands of permeabilized cells, exposed to artificial substrates and identical cytosol, we observed fulminant differences for two different import pathways (via transportins and importins), which could be modulated by changing cell growth conditions. This in turn allowed the analysis if the different transport capacity was correlated with posttranslational Nup modifications. Statistical analysis revealed that only one modification of one Nup (Nup62 glycosylation) explained import modifications via the nuclear transport receptor transportin, while the importin-mediated pathway was dependent upon modification/quantity of seven Nups (manuscript submitted). Aside of showing a new regulation mechanism of how cells can respond to external triggers, we assume that this principle can also play an essential role in infection efficiency of viruses when individual cells serve as super spreader as it is established in epidemiology. Considering the correlation of nuclear import capacity – also of housekeeping proteins - with the cell environment of the cells we hypothesize that the Nup modifications could also be important in cancer development or metastasis.

Future aspects. The overall aim is the understanding the determinants for virus spread and, for HBV, the mechanisms linked to disease development. This requires translational approaches as limiting factors can be on the cellular level, on the level of the organism, which includes host genetics but also on the level of the pathogen. Linking the results from these very different domains requires biostatistics already because not all processes are homogenous. Mathematical will be helpful for predictions, which are e.g. required if a phenomenon cannot be experimentally addressed.

In the mid-term range, I plan to investigate the molecular reasons and the impact of cell variability in the context of genomic viral variability. This requires high throughput microscopy after siRNA application and single cell RNAseq for quantitatively measure cellular and viral processes. Correlation with clinical data will help to identify key elements determinating infection outcome. This research as far as HBV is concerned also needs support from immunological and if possible genetic departments.

Publications

Gallucci L and **Kann M**. Nuclear import of hepatitis B virus capsids and genome. Viruses, 2017 (Jan).

Chen C, Joseph Wang JCY, Pierson EE, Kiefer DZ, Delaleau M, Gallucci L, Cazenave C, **Kann M**, Jarrold MF, Zlotnick A. Importin β can bind Hepatitis B Virus core protein and empty core-like particles and induce structural changes. **PLoS Pathog. 2016** Aug 12, 2016: http://dx.doi.org/10.1371/journal.ppat.1005802

Alarcón V, Hernández S, Rubio L, Alvarez F, Flore Y, Varas-Godoy M, De Ferrari GV, **Kann M**, Villanueva RA, and Loyola A. The histone demethylase LSD1 and the viral protein HBx cooperate to establish an active hepatitis B viral chromatin state. **Scientific Reports**, 2016; 6: 25901

Blondot ML, Bruss V, **Kann M**. Intracellular Transport and Egress of Hepatitis B Virus. **J Hepatol,** 2016; 64(1 Suppl):S49-59; review

Osseman Q, **Kann M**. Intracytoplasmic transport of hepatitis B virus capsids. **Methods in Molecular Biology**, accepted

Gil-Ranedo J, Hernando E, Riolobos L, Domínguez C, **Kann M**, Almendral JM. The Mammalian Cell Cycle Regulates Parvovirus Nuclear Capsid Assembly. **PLoS Pathog.** 2015 Jun 11;11(6):e1004920. doi: 10.1371/journal.ppat.1004920. eCollection 2015 Jun.

*Boyer A, Couallier V, Clouzeau B, Lasheras A, M'zali F, **Kann M**, Rogues AM, Gruson D. Control of extended-spectrum β-lactamase-producing Enterobacteriaceae nosocomial acquisition in an intensive care unit: A time series regression analysis. **Am J Infect Control.** 2015 Sep 10. pii: S0196-6553(15)00797-X. doi: 10.1016/j.ajic.2015.07.026.

Cassany A, Ragues J, Guan T, Bégu D, Wodrich H, **Kann M**, Nemerow GR, Gerace L. Nuclear import of adenovirus DNA involves direct interaction of hexon with an N-terminal domain of the nucleoporin nup214. **J Virol**. 2015 Feb 1;89(3):1719-30. doi: 10.1128/JVI.02639-14. Epub 2014 Nov 19.

*Boyer A, Clouzeau B, M'zali F, **Kann M**, Gruson-Vescovali D. Comment utiliser les aminosides en réanimation. **Réanimation** . May 2015, Volume 24, Issue 3, pp 328-336 DOI 10.1007/s13546-15-1067-1

*Clouzeau B, Boyer A, M'zali F, **Kann M**, Gruson-Vescovali D. Nouvelles stratégies thérapeutiques contre les entérobactéries productrices de β-lactamases à spectre étendu. **Réanimation.** May 2015, Volume 24, Issue 3, pp 270-277 DOI 10.1007/s13546-15-1059-1

Deroubaix A, Osseman Q, Cassany A, Bégu D, Ragues J, Kassab S, Lainé S, **Kann M**. Expression of viral polymerase and phosphorylation of core protein determine core and capsid localization of the human hepatitis B virus. **J Gen Virol.** 2015 Jan;96(Pt 1):183-95. doi: 10.1099/vir.0.064816-0. Epub 2014 Oct 1.

Zeisel MB, Lucifora J, Mason WS, Sureau C, Beck J, Levrero M, **Kann M**, Knolle PA, Benkirane M, Durantel D, Michel ML, Autran B, Cosset FL, Strick-Marchand H, Trépo C, Kao JH, Carrat F, Lacombe K, Schinazi RF, Barré-Sinoussi F, Delfraissy JF, Zoulim F. Towards an HBV cure: state-of-the-art and unresolved questions-report of the ANRS workshop on HBV cure. **Gut.** 2015 Feb 10. pii: gutjnl-2014-308943. doi: 10.1136/gutjnl-2014-308943. [Epub ahead of print] Review.

Snoussi K, **Kann M.** 2015. Chapter 8. General Considerations and Examples.Viral Nanotechnology. Khudyakov Y, Pumpens P (eds). pp129-134. CRC Press, Taylor & Francis Group, Boca Raton, Florida, U.S.A

*Leroy S, M'Zali F, **Kann M**, Weber DJ, Smith DD. Impact of vaginal-rectal ultrasound examinations with covered and low-level disinfected transducers on infectious transmissions in france. **Infect Control Hosp Epidemiol.** 2014 Dec;35(12):1497-504. doi: 10.1086/678604. Epub 2014 Nov 5.

Aydin I, Weber S, Snijder B, Samperio Ventayol P, Kühbacher A, Becker M, Day PM, Schiller JT, **Kann M**, Pelkmans L, Helenius A, Schelhaas M. Large Scale RNAi Reveals the Requirement of Nuclear Envelope Breakdown for Nuclear Import of Human Papillomaviruses. **PLoS Pathog.** 2014 May 29;10(5):e1004162.

*M'Zali F, Bounizra C, Leroy S, Mekki Y, Quentin-Noury C, **Kann M**. Persistence of microbial contamination on transvaginal ultrasound probes despite low-level disinfection procedure. **PLoS One.** 2014 Apr 2;9(4):e93368.

Snoussi K, **Kann M**. Interaction of parvoviruses with the nuclear envelope. **Adv Biol Regul.** 2014 Jan;54:39-49.

Porwal M, Cohen S, Snoussi K, Popa-Wagner R, Anderson F, Dugot-Senant N, Wodrich H, Dinsart C, Kleinschmidt JA, Panté N and **Kann M**. Parvoviruses Cause Nuclear Envelope Breakdown by Activating Key Enzymes of Mitosis. **PloS Pathog** 2013 Oct;9(10):e1003671

Trimoulet P, Pinson P, Papuchon J, Foucher J, Vergniol J, Chermak F, Wittkop L, Castaing N, Merrouche W, Reigadas S, Molimard M, **Kann M**, Fleury H, de Lédinghen V. Dynamic and rapid changes in viral quasispecies by UDPS in chronic hepatitis C patients receiving telaprevir-based therapy. **Antivir Ther.** 2013;18(5):723-7

Abdul F, Ndeboko B, Buronfosse T, Zoulim F, **Kann M**, Nielsen PE, Cova L. Potent inhibition of late stages of hepadnavirus replication by a modified cell penetrating peptide. **PLoS One.** 2012;7(11):e48721.

Popa-Wagner R, Porwal M, **Kann M**, Reuss M, Weimer M, Florin L, Kleinschmidt JA. Impact of VP1-specific protein sequence motifs on adeno-associated virus type 2 intracellular trafficking and nuclear entry. **J Virol**. 2012 Sep;86(17):9163-74.

Haryanto A, Schmitz A, Rabe B, Gassert E, Vlachou A, **Kann M**. Analysis of the nuclear localization signal of the hepatitis B virus capsid. **IRJBB** 2012, Aug; 2(8):174-185

Sureau C, Norder H, Taylor J, Magnius L, Loeb D, **Kann M**, Mizokami M, Gerlich W, Mason W. Hepadnaviridae. In : AMQ King, MJ Adams, EB Carstens, EJ Lefkowitz, editors, Viral Taxonomy. Oxford: Elsevir, 2011, pp445-456

Sureau C, Norder H, Taylor J, Magnius L, Loeb D, **Kann M**, Mizokami M, Gerlich W, Mason W. Deltavirus. In : AMQ King, MJ Adams, EB Carstens, EJ Lefkowitz, editors, Viral Taxonomy. Oxford: Elsevir, 2011, pp763-766

Schmitz A, Schwarz A, Foss M, Zhou L, Rabe B, Hoellenriegel J, Stoeber M, Panté N, **Kann M**. Nucleoporin 153 arrests the nuclear import of hepatitis B virus capsids in the nuclear basket. **PLoS Pathog.** 2010 Jan 29;6(1):e1000741

Wittkop L, Schwarz A, Cassany A, Grün-Bernhard S, Delaleau M, Rabe B, Cazenave C, Gerlich W, Glebe D, **Kann M**. Inhibition of protein kinase C phosphorylation of hepatitis B virus capsids inhibits virion formation and causes intracellular capsid accumulation **Cell Microbiol.** 2010 Jul;12(7):962-75

Riolobos L, Valle N, Hernando E, Maroto B, **Kann M**, Almendral JM. Viral oncolysis that targets Raf-1 signaling control of nuclear transport. **J Virol.** 2010 Feb;84(4):2090-9.

Rabe B, Delaleau M, Bischof A, Foss M, Sominskaya I, Pumpens P, Cazenave C, Castroviejo M, **Kann M**. Nuclear entry of hepatitis B virus capsids involves disintegration to protein dimers followed by nuclear reassociation to capsids. **PLoS Pathog.** 2009 Aug;5(8):e1000563. Epub 2009 Aug 28.

Kantelhardt VC, Schwarz A, Wend U, Schüttler CG, Willems WR, Trimoulet P, Fleury H, Gerlich WH, **Kann M**. 2009. Re-evaluation of anti-HBc non-reactive serum samples from patients with persistent hepatitis B infection by immune precipitation with labelled HBV core antigen. **J Clin Virol.** 2009 Oct;46(2):124-8.

Lang M, **Kann M,** Zahner H, Taubert A, Hermosilla C. Inhibition of host cell apoptosis by Eimeria bovis sporozoites. **Vet Parasitol.** 2009 Mar 9;160(1-2):25-33.

L Wittkop, A Cassany, M Delaleau, P Trimoulet, J Foucher, R Thiébaut, H Fleury and **M Kann**. Impact of genotypic mutations of the hepatitis B virus capsid on viral load and liver enzymes in hepatitis B virus-infected patients. **Antivir Ther** 2009; 14 Suppl 1:A70

Kann M. 2008. Chapter 2. Structural and Molecular Biology. 2nd edition. In: Hepatitis B Virus Guide. S. Locarnini and C.L.Lai (eds). pp 9-22. London, Atlanta: International Medical Press Ltd.

Jilbert A, Mason, W, **Kann M**. 2008. Chapter 4. Hepatitis B Virus Replication. 2nd edition. In: Hepatitis B virus Human Virus Guide. S. Locarnini and C.L.Lai (eds). pp 43-54. London, Atlanta: International Medical Press Ltd.

Kann M. 2008. Chapter 3. Entry and intracellular transport of viruses. In: Medical Virology. 2nd edition. Basis, diagnostic and therapy of viral Diseases. Doerr HW and Gerlich WH (eds). Georg-Thieme Verlag, Stuttgart

Kann M, Schmitz A and Rabe B. Intracellular transport of hepatitis B viruses. 2007. **World J Gastroenterol** (13)1:39-47 (review)

Haryanto A, Wijayanti N, **Kann M**. Effect of the HBV Capsid Assembly Inhibitor Bayer 41-4109 on the Intracellular Localization of EGFP-Core Fusion Proteins. **I J Biotech** 2007, Dec, 12(2):998-1004

Haryanto A, Wijayanti N, **Kann M**. Effect of Staurosporine on the Intracellular Localization of Hepatitis B Virus Core Protein. **I J Biotech** 2007, Jun; 12(1):958-966

Rabe B, Glebe D, **Kann M**. 2006. Lipid-mediated entry of hepatitis B virus capsids in non-susceptible cells allows highly efficient replication and the analysis of the early infection events. **J Virol** 80(11):5465-5473

Damianov A, **Kann M**, Lane WS, and Bindereif A. 2006. The human RBM28 protein is a specific nucleolar component of the spliceosomal snRNPs. **Biol Chem** 387,1455-1460

Rösler C, Köck J, **Kann M**, Malim MH, Blum HE, Baumert TF, von Weizsäcker F. 2005. APOBEC-mediated Interference with Hepadnavirus Production. **Hepatology**, Aug;42(2):301-9.

Haryanto A and **Kann M**. Nuclear Import Analysis of Two Different Fluorescent Marker Proteins into Hepatocyte Cell Lines (HuH-7 Cell). **I J Biotech** 2005, Dec, 10(2):807-813

Kann M and Gerlich WH. 2005. Structure and Molecular Virology. In: Viral Hepatitis. Zuckerman AJ and Thomas HC (eds). pp 149-180 Edinburgh, London, Madrid, Melbourne, New York, Tokyo: Churchill Livingston.

Gerlich WH and **Kann M**. 2005. Hepatitis B. In: Topley & Wilson´s Microbiology and Microbial Infections. 9th edition. Collier L, Balows A, Sussman M (eds). pp 1226-1269 Edward Arnold (Publishers) Ltd., London, U.K.

Kann M. 2004. Nucleoprotein Transport of HBV Capsid Particles. **Methods Mol Med**. 2004:213-226

Kann M. 2004. Interfering with capsid formation: a practicable antiviral strategy against hepatitis B virus? Hepatology, Mar;39(3):838-40

Lischka P, Sorg G, Kann M, Winkler M and Stamminger T. 2003. A non-conventional nuclear localization signal within the UL84-protein of human cytomegalovirus mediates nuclear import via the importin α/β-pathway. J Virol 77(6): 3734-48

Köck J, Kann M, Pütz G, Blum HE, von Weizsäcker F. 2003. Regulation of duck hepatitis B virus capsid trafficking and targeted genome release by core protein phosphorylation. J Biol Chem; 278(30):28123-9

Rabe B, Vlachou A, Panté N, Helenius A, Kann M. 2003. Nuclear Import of Hepatitis B Virus Capsids and Genome. Proc Natl Acad Sci U.S.A. 100 (17): 9849-9854
(recommended by the Faculty of 1000: evaluations for Rabe B et al Proc Natl Acad Sci U S A 2003 Aug 19 100 (17) :9849-54 http://www.f1000biology.com/article/12909718/evaluation)

Isken O, Grassmann CW, Sarisky RT, Kann M, Zhang S, Grosse F, Kao PN, Behrens SE. 2003. Members of the NF90/NFAR protein group are involved in the life cycle of a positive-strand RNA virus. EMBO J Nov 3; 22 (21): 5655-5665

Panté N and Kann M. 2002. The Nuclear Pore Complex is Able to Transport Macromolecules with Diameters of ~39 nm. Mol Biol Cell. 13(2):425-34.

Wolff T, Unterstab G, Heins G, Richt JA, and Kann M. 2002. Characterization of an unusual importin a binding motif in the Borna disease virus p10 protein which directs nuclear import J. Biol. Chem. 277(14):12151-12157

Elmshauser C, Bechtel J, Motta I, Schipke C, Kettenmann H, Schmalbruch H, Kann M, Beck E, Chen U. 2002. Characterization of a mouse tet-on glia precursor cell line in vitro and in vivo using the electrophysiological measurement. J Physiol Paris. 2002 May-Aug;96(3-4):329-38.

Mason, W.S., Burrell CJ, Casey J, Gerlich WH, Howard CR, Kann M, Lanford R, Newbold J, Schaefer S, Taylor JM, and Will H. 2002. Hepadnaviridae. In VIIIth ICTV Report. C. Büchen-Osmond, editor. Columbia University, New York, USA.

Kann M. 2002. Chapter 2. Structural and Molecular Biology. In: Hepatitis B Virus Guide. S. Locarnini and C.L.Lai (eds). pp 9-22. London, Atlanta: International Medical Press Ltd.

Jilbert A, Burrell CJ, Triyatni M, Kann M. 2002. Chapter 4. Hepatitis B Virus Replication. In: Hepatitis B virus Human Virus Guide. S. Locarnini and C.L.Lai (eds). pp 43-54. London, Atlanta: International Medical Press Ltd.

Muth H, Elmshauser C, Broad S, Watt F, Schipke C, Kettenman H, Trotter J, Kann M, Motta I, Schimpl A, Beck E and Chen U. 2001. Conditional immortalization and partial cellular characterization of a doxycycline-inducible oligodendrocyte precursor cell line in vitro. J Gene Med 3(6):585-98

Whittaker G, Kann M and Helenius A. 2000. Viral Entry into the Nucleus (Review). Annu Rev Cell Dev Biol 16:627-51

Kann M. 2000. Delivering the goods: how a viral genome transfers from the virus to the nucleus. (Minireview). The ELSO Gazette: e-magazine of the European Life Scientist Organization (http://www.the-elso-gazette/magazines/issue1/mreviews/mreviews1.asp), Issue 2 (6 November, 2000)

Burrell CJ, Chisari FV, Gerlich WH, Gowans EJ, Howard CR, Kann M and Marion PL. 2000. Hepadnaviridae, in Virus Taxonomy, M.H.V. van Regenmortel et al. (ed), Academic Press, San Diego. pp 325-334

Kann M, Sodeik B, Vlachou A, Gerlich, WH and Helenius A. 1999. Phosphorylation-dependent binding of hepatitis B virus core particles to the nucleus. J Cell Biol (1):145:45-55

Izzauralde E, Kann M, Panté N, Sodeik B and Hohn T. 1999. Viruses, microorganisms and scientists meet the Nuclear Pore. (Review). EMBO J 18(2):289-296

Kann M and Gerlich WH. 1998. Hepatitis B. In: Topley & Wilson´s Microbiology and Microbial Infections. 9th edition. Collier L, Balows A, Sussman M (eds). pp 745-774. Edward Arnold (Publishers) Ltd., London, U.K.

Kann M and Gerlich WH. 1998. Structure and Molecular Virology. In: Viral Hepatitis. Zuckerman AJ and Thomas HC (eds). pp 77-105. Edinburgh, London, Madrid, Melbourne, New York, Tokyo: Churchill Livingston.

Kann M, Bischof A and Gerlich WH. 1997. In vitro model for the nuclear transport of the hepadnavirus genome. J Virol 71(2):1310-1316

Stoll-Becker S, Repp R, Glebe D, Schaefer S, Kruder J, Kann M, Lampert F and Gerlich WH. 1997. Transcription of hepatitis B virus in peripheral blood mononuclear cells from persistently infected patients. J Virol 71(7):5399-5407

Kann M and Gerlich WH. 1997. Replication of hepatitis B virus. In: The molecular Medicine of Hepatitis. TJ Harrison and A Zuckerman (eds). pp63-77, John Wiley & Sons, Ltd.

Erhardt A, Schaefer S, Athanassiou N, Kann M and Gerlich WH. 1996. Quantitative Assay of PCR-Amplified Hepatitis B Virus DNA using a Peroxidase-labelled DNA Probe and Enhanced Chemoluminescence. J Clin Microbiol 34 (8):1885-1891

Kann M, Lu X, Gerlich WH. 1995. Recent studies on replication of hepatitis B virus. J Hepatol 22:9-13

Kann M and Gerlich WH. 1994. Effect of core protein phosphorylation by protein kinase C on encapsidation of RNA within core particles of hepatitis B virus. J Virol 68(12):7993-8000

Kann M, Köchel HG, Uy A and Thomssen R. 1993. Diagnostic significance of antibodies to hepatitis B virus polymerase in acutely and chronically HBV-infected individuals. J Med Virol 40 (4):285-290

Borg-von Zepelin M, Eiffert H, Kann M and Rüchel R. 1993. Changes in the spectrum of fungal isolates: results from clinical specimen gathered in 1987/88 compared with those in 1991/92 in The University Hospital Göttingen, Germany. Mycoses 36 (7-8):247-253

Kann M, Thomssen R, Köchel HG and Gerlich WH. 1993. Characterization of the endogenous protein kinase activity of the hepatitis B virus. Arch Virol 8:53-62

Köchel HG; Kann M, Thomssen R. 1991. Identification of a binding site in the hepatitis B virus RNA pregenome for the viral Pol gene product. Virology 182(1):94-101

Bashir Y, Kann M and Stradling JR. 1990. The effect of acetazolamine on hypercapnic and eucapnic/poikilocapnic hypoxic ventilatory responses in normal subjects. Pulm Pharmacol Ther 3(3):151-154

*paper derived from R&D of the start-up

Funding since 2006*

- 6 contracts of the ANRS (funding quota 12 %) 411700 €
- 3 fundings of the local government (funding quota 25 %) 465000 €
- 2 supports from the Fondation pour la Recherche Médicale (FRM) This includes the prestigious "équipe label FRM" from which the FRM supports 8 – 11 per year. 317000 €
- CNRS – DFG (German Research Council) (funding quota 25 %) 244000 €
- ARC (funding quota 30 %) 30000 €
- 5 collaborative fundings from the Ministry of higher education 97000 €
- 1 collaborative funding from the CNRS (PICS – Canada) (funding quota 25 %) 45000 €

* the sums shown above represent exclusively the support for my research team. Further 280000 € were obtained as subventions for the start-up since 2010 (sum exclusive industrial contracts).

Supervision in France

Aside of eight students during their first year of Master studies I supervised eight students in their second year during their practical training. I further supervise(d) eight PhD students; actually also two students in collaboration with other Universities (Tsukuba, Japan, co-supervisor: Kyosuke Nagata; Jyvaeskylae, Finland, co-supervisor: Majia Vihinen-Ranta). Of note, the graduate school of Bordeaux allows the supervision of just one PhD student at the same time. Exceptions are made if one student is already in his last year allowing to accept a second one or, if a student does his thesis in collaboration with a University outside France. The same rule excluding a second student is applied for Master students.

Teaching/training

My current teaching duty is c. 80 h/year, which comprise teaching in medicine but also in life sciences. I basically explain the disease by molecular mechanisms but with a focus on the branch of the study. For medical students this approach opens a perspective for understanding molecular processes and why these processes cause disease. Students of life sciences in contrast understand the medical background driving their mostly fundamental research. Evidently, this teaching is held on an advanced level of their studies.

Teaching in Bordeaux:

- Lectures for students in life sciences: 1st year of Master studies (40 h), basic Virology
- Lectures for students in life sciences: 2nd year of Master studies (5 h), infection processes of the cell
- Lectures for students in medicine: 3rd and 4th year of Master studies (12 h), replication of viruses, viral hepatitis, parvoviruses
- Training of MDs in hepatitis B (4 h)
- Lectures in scientific English for students in life sciences: 1st year of Master studies (9 h)

Teaching at the University Andres Bello, Santiago de Chile:

- Lectures for students in life sciences, medicine and veterinary medicine (12 h), basic virology

Responsibilities in teaching

Organization of teaching in Virology, Parasitology and Immunology for students in life sciences during their 1st year of Master studies.

Medical activities

The diagnostic services at the University Hospitals of Bordeaux are organized in technical platforms, which are in the cross responsibility of the different services. This means that e.g. PCRs – also those for bacteria - are performed under supervision of the virology service, while serological analyses are done on another platform, which is supervised by the service of biochemistry. Validation of the results, irrespectively of the platform, is done by the respective specialized service.

Mu current activity comprises the routine validation of the results but also the interpretation of the results in discussion with the clinicians. Further, I took the responsibility for HBV and HIV PCRs and I participate in the ongoing accreditation of the service activities concerning HBV and HIV. Organizational activities as the rotation of technicians are performed as well as special training for BSL4 pathogens as Ebola.

Evidently, hospital activities also affect my research activities allowing easier access to clinical samples and data. This is crucial as HBV infections with high viral loads are rare in France and mostly found in immune suppressed patients.

Other administration and responsibilities

Local

- Board member of the Federal Research Structure "Fundamental Biology applied to Medicine" (Biologie fondamentale et appliquée à la Médecine, UMS 3427, accredited by Inserm, CNRS, University of Bordeaux). This transversal structure comprises c. 500 staff members of 10 laboratories and coordinates science between basic and applied research.
  http://www.transbiomed.u-bordeaux2.fr/pages/anglais.html
- Board member of the Medical Research Council (Direction de la recherche clinique et de l'innovation, DRCI) of the Hospitals in South-West France and the French oversea territories.

National

- Member of several boards at the ANRS (National Agency for Research on HIV and hepatitis) including the scientific board giving recommendations for hepatitis B and hepatitis D clinical trials.
- Board member of the CNRS (National Centre for Scientific Research, section Microbiology – Immunology) for hiring and evaluating permanent scientists in these domains nationwide.
- Member of the national evaluation committee of the Foundation on Cancer (Fondation ARC pour la recherche sur le cancer).
- Member of the national commission for the evaluation of French research structures (AERES/HCERES).

International

- Member of the International Committee on Taxonomy of Viruses (ICTV), division hepatitis B and D viruses.
- Invited professor at the University of Tsukuba, Japan.
- Head of a so-called "International Laboratory" on Virology, consisting of the department I am chairing, the Department of Immunology at the University of Bordeaux and the Heinrich-Pette-Institute for experimental Virology, Hamburg, Germany. The laboratory is accredited by the CNRS, France, and the Leibniz Association, Germany.
- Member of evaluation committees for different German research structures and institutions (Helmholtz Gesellschaft, DFG).
- Expert for various journals and funding agencies of different countries (France, Germany, UK, Belgium, Hong Kong); editor of the Journal of General Virology (UK), associated editor on Virology Journal (USA).
- Member of the scientific advisory board of the International Meetings on the Molecular Biology of Hepatitis B Viruses.
- Member of the organization committee of the 2016 International Workshop on Parvoviruses, Ajaccio, Corsica, June 19 – 23
- Organization of several conferences, including the co-organization of the 2014 International Meeting on the Molecular Biology of Hepatitis B Viruses 2014, Los Angeles and the International Workshop on Parvoviruses, which I organized in Bordeaux in 2014.