MHH
HBRS
Alumni

October 16th, 2006

1. Newsletter

Dear HBRS Alumni students,

Herewith, we proudly present the first HBRS Alumni newsletter. Since its foundation in 2003, Hannover Biomedical Research School (HBRS) has been extremely successful and has reached high international recognition. HBRS has integrated all postgraduate programs at MHH. Three classes of the MD/PhD program "Molecular Medicine", which started in October 2000, have already successfully graduated. You as one of the 36 Alumni are an ambassador for MHH in the world. We hope that you will enjoy this newsletter and will support our various activities towards excellence in research as well as teaching in Hannover further.

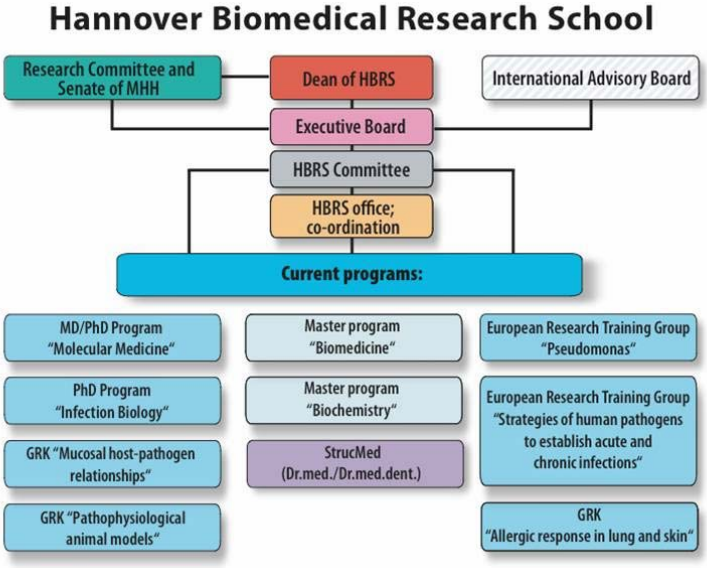
Reinhold E. Schmidt,
Dean of HBRS

Current status of HBRS and news

HBRS now comprises of **two international PhD programs** (the MD/PhD program "Molecular Medicine", the PhD program "Infection Biology" together with EU Marie Curie Early Stage Training Site MIDITRAIN "Molecular Interactions during Infection Training" at Helmholtz Centre for Infection Research Braunschweig) and **five DFG-funded research training groups**, two of which are joint European programs (GRK 745 "Mucosal host-pathogen interactions", GRK 705 "Characterization of pathophysiological animal models - functional and genomic analysis", GRK 1441/1 "Regulation of the allergic inflammatory response in lung and skin", EGRK "Pseudomonas: Pathogenicity and Biotechnology" and EGRK 1273 "Strategies of human pathogens to achieve acute and chronic infection").

More recently, a structured doctoral program for medical students was also successfully established (**StrucMed**; Dr.med./Dr.med.dent.), as well as an HBRS-associated new Master program "Biomedicine"

A joined HBRS Curriculum was developed in 2004.



Currently, the various programs of HBRS host ~170 PhD students. In addition, 30 medical students were accepted for StrucMed as well 20 new Master students this year. There are about 50% international and around 25% medical doctors doing their PhD (~50% women).

In June 2006, seven MD/PhD students successfully passed their final exams (Christoph, Diya, Linding, Krishna K., Manvendra, Vladka, Yijiang). The next ones are expected for November 10th (Anika, Anuhar, Georg, Gesa, Khaled, Rahul, Shipra, Shashi, Tammy). The first ten final exams in the PhD program "Infection Biology" will take place on February 16th, 2007.

This year, the PhD programs altogether received around 700 applications from all over the world (50% from India). The quality of candidates has increased enormously in past years.

HBRS orientation weeks started on October 4th. The joint opening ceremony will take place on October 16th. Outstanding scientists from HBRS International Advisory Board are invited.

3rd Intercultural Communication Workshop

June 2006; with M.Sc./PhD programs of Göttingen

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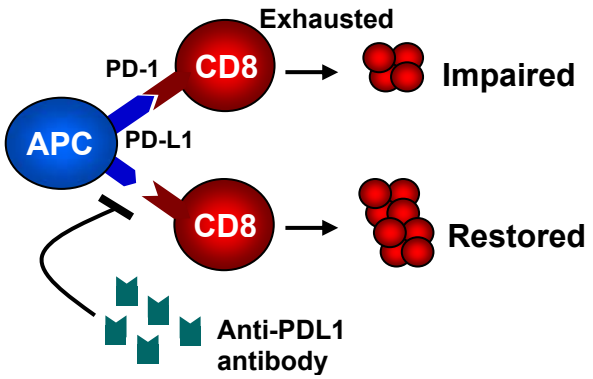
News in Research

In this section, we will regularly publish short reviews of important and recent achievements in selected research fields! Everybody is welcome to make contributions.

Translating basic research to clinics: A classical example

by Wahid Ansari, India
final exam Nov. 2005;
currently Imperial College, London, UK

The 9th February issue of this year's Nature featured an article that not only received special attention but follows a series of commentaries in high ranking journals including Cell, Nature, Nature Medicine and Nature Immunology. The article focussed on the role of inhibitory receptor programmed death -1 (PD-1) in chronic viral infection. CD8 T lymphocytes (CTL) play a major role in controlling the viruses. However, a function defect in CD8 T cell has been shown before in many chronic viral infections including hepatitis C virus (HCV) and human immunodeficiency virus 1 (HIV-1). PD-1 is an inhibitory molecule expressed on activated T lymphocytes and has been shown to maintain peripheral tolerance. However, their role in viral infection was not known until, very recently *Rafi Ahmed and colleagues*[1] described a novel role of PD-1 in Lymphocytic choriomeningitis virus (LCMV) mouse model of chronic infection. In this study they have nicely demonstrated a restricted surface expression of PD-1 on LCMV-specific exhausted (nearly dead) CD8 T cells during the chronic but not in acute phase of the infection. Moreover, when the mouse was treated with anti-PDL1 antibody to block the interaction of PD-1-PDL1, a restored CD8T cell effector function was achieved. In addition these exhausted CD8 T cell reversibly regain their function as shown by reduced viral load and production of effector cytokine IFN-γ. This study explained the critical role of PD-1 in the functional impairment of virus-specific CD8 T cells and has provided a platform for the scientists and clinicians working on chronic human viral infections. A schematic view of PD-1 in CD8 T cell function is illustrated.



Very recently three different laboratories (*Walker BD*[2], *Sekaly RP*[3] *and Koup RA*[4]) have simultaneously reported the association of PD-1 expression with HIV-1 specific CD8 T cell dysfunction. Using a large panel of HIV-1-specific MHC class I tetramers, they have elegantly demonstrated a strong association of PD-1 with the severity of the disease in chronically infected therapy naïve HIV-1 patients. Interestingly, patients who received anti-retroviral therapy displayed a lower PD-1 expression in the follow-up studies. Moreover, two clinical parameters that dictate the HIV-1 disease progression; CD4 T cell count inversely and viral load positively correlated with PD-1 expression on HIV-1-specific CD8 T cells. Off note, in vitro stimulation using HIV-1 specific peptides and PD-1/PDL1 blocking experiments restored the CD8 T cell expansion and IFN-γ production. These findings explain one of the unresolved issue of CD8 T cell functional defects in HIV-1 infection. Researchers are now implementing the above findings in other persistence human viruses such as HCV. The PD-1/PDL1 pathway can provide a potential therapeutic target to revert the CD8 T cell function in chronic viral infections. Researchers are considering it as one of the major findings of the year and an ideal example of how basic research can be translated into clinical sciences.

References:

1. Barber DL *et. al.* Restoring function in exhausted CD8 T cells during chronic viral infection. *Nature* 439, 682-687 (February 2006)
2. Day. CL *et. al*. PD-1 expression on HIV-specific T cells is associated with T cell exhaustion and disease progression. *Nature* Advance online publication (August 2006)
3. Trautmann. L *et. al.* Upregulation of PD-1 expression on HIV-specific CD8 + T cells leads to reversible immune dysfunction. *Nature Medicine* (September 2006)
4. Petrovas. C *et. al.* PD-1 is a regulator of virus-specific CD8+ T cell survival in HIV infection. *J. Exp. Med.* Advance on line publication (September 2006)

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News from MHH

MHH has recently applied for funding in the German "**Excellence Initiative**" by the Federal Ministry of Education and Research and DFG. Three applications successfully passed the first round: "Hannover Biomedical Research School", the Cluster of Excellence "Research for Infectious Diseases" and the Cluster of Excellence "From Regenerative Biology to Reconstructive Therapy". Decisions are expected on October 13th.

In addition, MHH applied for the future concept "Clinical Research Centre with Dual Career options (**DUO**)". This offers e.g. two parallel career paths including new positions: clinical or science track for both medical doctors as well as life scientists.

In 2006, the Helmholtz Centre of Infection Research in Braunschweig and MHH have founded the new Research institute "**Twincore**" located in the former Max-Planck building near MHH. Several outstanding research groups (including junior groups) will focus on clinical and experimental Infection Biology.

In summer 2004, MHH opened the Centre for Transplantation Research (**TPFZ**). There are around 3000 m^2 of research labspace (~35 rooms), which are primarily assigned to junior research groups.

Announcements

Marriages: Many of our students have married during their stay in Hannover. We know of Sonja Werwitzke & Andreas Tiede (both MD/PhD), Anuhar Chaturvedi & Sukhada, Diya Abraham, Meta Djojosubroto, Veit Erpenbeck, Christoph Happel, Anika Meyerholz, Harini Nivarthi, Prajeeth C.K., Leena Srivastava, Tibor Veres. *Congratulations!!*

Children ☺**:** There are quite a few "HBRS babies" by Yasmin, Masami, Linding, Erkhembulgan, Mathewos, Christoph, Sonja & Andreas, Gernot, Veit.

View from abroad

In this section, we will regularly publish short reports of experiences of our Alumni students as Postdocs etc. abroad! Everybody is welcome to make contributions.

Claudia Karacsonyi, Argentina
final exam Nov. 2005;

currently NIH, Bethesda, USA

It has been a little more than one year since I left Hannover to start a Postdoc at the National Institutes of Health in Maryland, US, and since then my life has changed quite a lot. Being a Postdoc, especially at the NIH, demands a lot of time and work. Competition is very high here and it is essential to get publications as fast as possible and in high ranked journals. In order to achieve this level of efficient work it is crucial to have a good base during the PhD studies, and for that I have to truly thank the MD\PhD program of MHH. The three years I have spent in Germany have prepared me well for a Postdoc position at one of the most competitive research institutions, as is the NIH. Regardless of the pressure, working in USA is a great option for those wanting to do a Postdoc. They have economical resources to help you fulfilling your goals and there is basically no technique that one cannot do here because there is enough money to buy anything you need and more, plus core facilities for anything you can think of. In addition, collaborations within the NIH labs or even other US universities are highly accessible. Another advantage of working in the US is the possibility of attending meetings, seminars and talks. On a daily basis, NIH is hosting lectures from the most prominent people in every science field. Last, but not least, salaries are very good in US in comparison to Europe. Moreover, the social life at the NIH is great due to the great number of foreigners working there. You have the possibility to meet people from all over the world, and although you have to work very hard, there is always time to have fun afterwards. To sum up, coming to US to continue my career was a good decision, and although I will always miss and thank MHH for everything they gave me, it was time to move on and I believe US was the best option.

"If we knew what it was we were doing, it would not be called research, would it?"
Albert Einstein (1879-1955)

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Current list of HBRS Alumni students

MD/PhD program Molecular Medicine

year 2000 *(final exams 2003)*

1.) Masoumeh Attaran-Bandarabadi: Gastroenterology/Hepatology/Endocrinology, MHH

2.) Yasmin Dulkys: is expecting her third child

3.) Veit Erpenbeck: Pharmacology, MHH

4.) Masami Rudolph: Molecular Biology, MHH

5.) Gernot Sellge Institute Pasteur, Paris

6.) Julia Skokowa: Pediatric Hematology & Oncology, MHH

7.) Andreas Tiede: Hematology & Oncology, MHH

year 2001 *(final exams 2004/2005)*

8.) A. Wahid Ansari: Knoxville, USA; from end of 2006: Immunology, Imperial College London, UK

9.) Ferdinand Bahlmann: Nephrology, MHH

10.) Asha Balakrishnan: Molecular Oncology, Institute for Cancer Research and Treatment (IRCC), Turin, Italy

11.) Christian Bernreuther: Neuropathology, University Clinics Hamburg-Eppendorf

12.) Frank Bollig: Molecular Genetics, Institute for Molecular Biotechnology (IMB), Jena

13.) Marc H. Dahlke: Liver Stem Cell Group, Surgery, Regensburg

14.) Meta Djojosubroto: Gene Therapy & Stem Cell Biology, Jules Gonin Eye Hospital, Lausanne, Switzerland

15.) Julia Freise: Rheumatology, MHH

16.) Christoph Happel: Pediatrics, MHH

17.) Vladimira Jakubcakova: Genes & Behavior, Max-Planck-Institute for Biophysical Chemistry, Göttingen

18.) Tom Lüdde: EMBL Mouse Biology Unit, Monterotondo, Italy

19.) Yijiang Li: Thoracic & Cardiovascular Surgery, MHH

20.) Jianyun Liu: Beijing (V.R China)

21.) Ebru Serinsöz-Pfeiffer: mother, Hannover

22.) Frank Tacke: Medical Clinics III, Aachen

23.) Mathewos Tessema: Pathology, CRF 225, New Mexico, HSC, USA

24.) Sonja Werwitzke: Hematology & Oncology, MHH

year 2002 *(final exams 2005/2006)*

25.) Diya Abraham: Genes & Behavior, Max-Planck-Institute for Biophysical Chemistry, Göttingen

26.) Syed Raza Ali: Pharmacology, University of California, San Diego, USA

27.) Thomas Gebhardt: Microbiology & Immunology, The University of Melbourne, Australia

28.) Claudia Karasconyi: Cell Biology, NHLBI, NIH, Bethesda, USA

29.) Varsha Kumar: Theodor Kocher Institute, Bern, Switzerland

30.) Christina Nassenstein: Fraunhofer Institute, Hannover; from October 2006 six months in Baltimore, John Hopkins Allergy and Asthma Center, USA

31.) Axel Schambach: Hematology & Oncology, MHH

32.) Amar Deep Sharma: Gastroenterology/ Hepatology/Endocrinology, MHH

33.) Krishna K. Singh: Human Genetics, MHH

34.) Manvendra K. Singh: Genetics & Development, Columbia University, New York, USA

35.) Frank Traub: General, Visceral- and Transplant Surgery, Tübingen

36.) Linding Wang: Virology, MHH

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