DBM FACTS

Periodisches Informationsblatt des Departementes Biomedizin
Universität Basel, Universitätsspital Basel und
Universitäts-Kinderspital beider Basel

Lymphoid tissue induction and innate immune regulation: progressive shift in space and time | The DBM PhD Club | Moscow sketches

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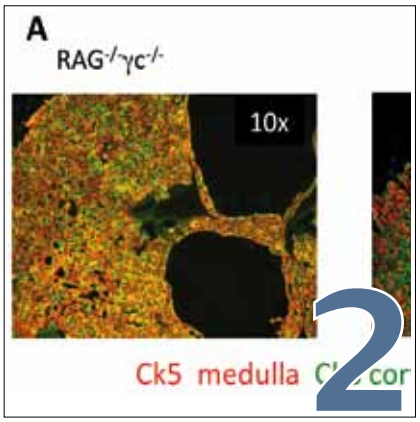
Departement Biomedizin Basel



Lymphoid tissue induction and innate immune regulation: progressive shift in space and time
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UNI BASEL

EDITORIAL

Radek Skoda
Leiter DBM

Liebe Leserinnen und Leser

Der Frühling ist da und auch das DBM erstrahlt in neuem Glanz. Der 2. Stock im ZLF ist bezogen und das Leben ist in die Labors und Büros eingekehrt. Nun geht es darum, auch die geplanten Umbauten im 3. und 4. Stock zu realisieren und den Bedürfnissen der DBM Forschungsgruppen anzupassen. An dieser Stelle nochmals herzlichen Dank an alle, die diesen Umbau möglich gemacht, mitgetragen oder einfach auch nur erduldet haben.
Erwähnenswert ist der Besuch des Advisory Boards, der im Januar 2014 im Rahmen des Research Days stattgefunden hat. Mit der Umsetzung der vielfältigen Anregungen haben wir begonnen.
Auch dieses Jahr erhält das DBM eine neue SNF-Förderprofessur: Roxanne Tussiwand wird am DBM Mattenstrasse ihre Tätigkeit aufnehmen und den Schwerpunkt Immunologie verstärken. Herzlichen Glückwunsch an dieser Stelle! Bereits begonnen haben am DBM die neuen SNF Professoren Mike Recher und Lukas Jeker sowie Christoph Berger mit einem Ambizione-SCORE.
Markus Heim und Gerhard Christofori vom DBM haben zusammen mit Mike Hall vom Biozentrum und Niko Beerenwinkel vom D-BSSE einen der begehrten Synergy Grants des Europäischen Forschungsrats (ERC) eingeworben. Sie erhalten rund 13,7 Millionen Franken für ein Projekt, das klären möchte, wie Tumore Resistenz gegen Medikamentenbehandlung entwickeln.
Yves Hartmann, bis dato Betriebsassistent am DBM Hebelstrasse und massgeblich am guten Gelingen des Ausbaus des 2. Stockes beteiligt, wechselt per 1. April 2014 als «Leiter Umweltschutz und Qualitätssicherung» in das USB. Wir bedauern seinen Weggang sehr, wünschen ihm aber bei der neuen Aufgabe viel Erfolg und Zufriedenheit!
In der neuesten Ausgabe der DBM Facts stellt uns Daniela Finke ab Seite 3 die aktuellsten Forschungsaktivitäten ihres Labors «Developmental Immunology» vor. Nicole Schaeren-Wiemers lässt uns an der Begeisterung teilhaben, PhD Koordinatorin am DBM zu sein (ab Seite 8). Ab Seite 13 folgen dann die aktuellsten Publikationen aus dem DBM.
Slawische Seele, chinesische Heil-, japanische Kochkunst und eine berüchtigte Bande aus Basel erwarten Sie im Weiteren. Da will ich Sie nicht weiter aufhalten ... Viel Spass bei der Lektüre!

Dear Readers

Spring has arrived and the DBM also shines like new. The offices and laboratories on the second floor of the ZLF have come to life. Now it is time to tackle the planned changes on the third and fourth floor to make them suitable to the requirements of the DBM research groups. Thanks again to everybody who made the changes possible and helped, or even just endured, the renovations.
Further mention must be given to the Advisory Board's visit within the programme of the Research Day. We have since begun to implement the various suggestions.
The DBM is receiving another SNF-grant-professorship this year: Roxanne Tussiwand will begin her work at the DBM Mattenstrasse and will reinforce the focus on immunology there. Congratulations are in order! The new SNF-professors Mike Recher and Lukas Jeker have already started, as has Christoph Berger with an Ambizione-SCORE.
Markus Heim and Gerhard Christofori of the DBM have, together with Mike Hall of the Biozentrum and Niko Beerenwinkel of the D-BSSE, successfully applied for and received one of the much sought after synergy grants of the European Research Council. They will be granted roughly 13.7 million Swiss Francs for a project to find how tumours develop resistance against medical treatment.
Yves Hartmann, currently technical assistant at DBM Hebelstrasse and heavily involved in the successful renovation of the second floor, will be moving to USB as "Head of Environmental Protection and Quality Assurance" on April 1st 2014. We will be sorry to see him go and wish him all the best in his new position.
In this issue of "DBM Facts", Daniela Finke will be introducing us to the latest research activity of her laboratory "Developmental Immunology" on page 3. Nicole Schaeren-Wiemers will let us join her in the joys of being a PhD-coordinator at the DBM (pages 8ff). The latest publications of the DBM follow from page 13 onwards.
Furthermore, Slavic souls, Chinese medicine, Japanese cuisine and a notorious gang from Basel await you - so I do not want to keep you any longer. Have fun!

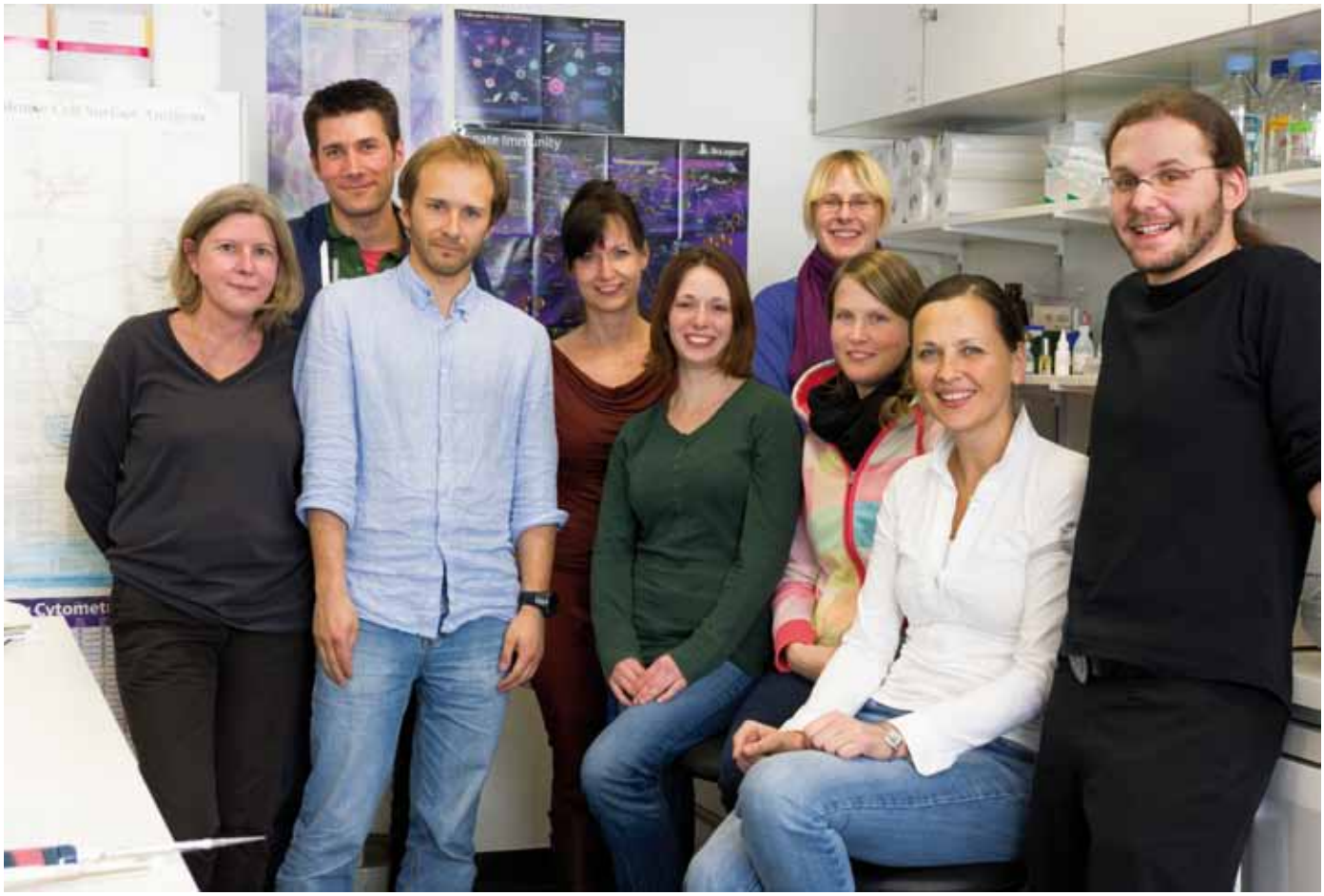
Lymphoid tissue induction and innate immune regulation: progressive shift in space and time

The immune system is localized in lymphoid organs: in primary lymphoid organs, lymphocytes are produced, whereas in secondary lymphoid organs they encounter antigens and differentiate into mature effector lymphocytes. The most extended secondary lymphoid tissue of the immune system is the mucosa-associated lymphoid tissue (MALT) covering the gastrointestinal and respiratory tract. From birth onwards, the MALT is exposed to a large number of microorganisms, nutritional compounds and foreign antigens. In the gut mucosa, lymphocytes must learn to tolerate harmless food antigens and to discriminate between the commensal microbiota and invasive pathogens. If this tolerance induction fails to develop, overshooting immune responses in the intestinal mucosa can result in the development of inflammation, food allergies and chronic autoimmune disorders. New subsets of functionally distinct innate lymphoid cells (ILCs) have been identified in recent years, which are essential for the development and homeostasis of lymphoid tissues, and have important roles in determining the outcome of infections and inflammation. Hence, understanding the molecular mechanism of lymphoid tissue development, homeostasis and immune regulation is essential to find potential targets for lymphoid tissue repair and prevention of chronic inflammatory diseases.

The major objective of the Developmental Immunology research group is to identify the molecular events underlying the growth and differentiation of ILCs and lymphoid organs from fetal to adult life. In particular, we focus on the mechanisms of ILC differentiation, the role for cytokines in development and maintenance of ILC compartments and the signals that regulate ILC immune functions under steady-state and proinflammatory conditions.

Lymphoid tissue induction in fetal and adult life

ILCs have emerged as important effector cells in innate immunity and lympho-organogenesis. In the last ten years we have studied a prototype of ILCs, the lymphoid tissue inducer (LTi) cell. These cells play a key role in secondary lymphoid organ formation during mouse and human ontogeny. LTi cells in mice are negative for leukocyte lineage marker (lin^-), and can be identified as lin^- $ROR\gamma t^+$ $CD127^+$ $CD117^+$ and $CD4^{+/-}$ cells. As early as day 12.5 they colonize developing lymphoid anlagen such as fetal spleen and intestine. LTi cells express tumor necrosis factor (TNF) family member molecules and integrins, which engage corresponding receptors on fetal mesenchymal cells. Using various genetically modified mouse models and adoptive transfer studies, we could identify $\alpha 4\beta 1$ integrin, CXCR5 and $LT\alpha\beta$ as key regulators for Peyer's patch development*(1)*. There is clear evidence that LTi cells are also required for the formation of lymph nodes (LNs), and contribute to the development of the thymic medulla in a critical time window during fetal life. In humans, LTi cells were first described in



Group foto:
From the left to the right: Annick Peter, Frank Lehmann, Gleb Turchinovich, Edit Horvath, Simone Neu, Anne Baerenwaldt, Nicole von Burg, Daniela Finke, Urs Kym

mesenteries of human embryos*(2)* and later also found in adult intestines and palatine tonsils. The remodeling of lymphoid tissues in adults requires inductive signals mediated by lymphoid cells. We described bone-marrow (BM)-derived adult $CD4^{+/-}$ lin- cells as counterparts of fetal LTi cells. Following adoptive transfer into recipient mice these cells were able to induce lymphoid follicle formation in the gut as well as regeneration of the splenic microarchitecture *(3, 4)*. The process on lymphoid tissue induction in adults depends on TNF family member signals, but also on innate signals through toll-like receptors and proinflammatory cytokines. In chronically inflamed tissues so-called 'tertiary lymphoid organs' can develop having a microarchitecture similar to secondary lymphoid organs. However, it is still unclear whether such TLOs contribute to the pathogenesis of chronic inflammation.

ILCs: the innate counterpart of T helper lymphocytes

LTi cells and natural killer (NK) cells belong to a growing family of ILCs, that depend on cytokine signaling through the common γ chain (γc) and the inhibitor of DNA binding 2 (ID2) for their development*(5)*. ILC populations have distinct patterns of cytokine production that mirror the cytokine production of T helper cells. In analogy with Th1, Th2 and Th17 T cells, a new nomenclature of ILCs divided into 3 major families has therefore been proposed*(6)*: 1) IFNγ-and TNFα-producing ILC1, 2) IL-5, and -13-producing ILC2, and 3) IL-22 and -17-producing ILC3 (Figure 1). Whereas ILC3s contribute to the protection against mainly extracellular bacteria and inflammation, ILC2s were found to mediate resistance against helminth infection*(7) (8)*. ILC1s are, like NK cells, IFNγ producer but are devoid of any Th2 or Th17-cytokines.

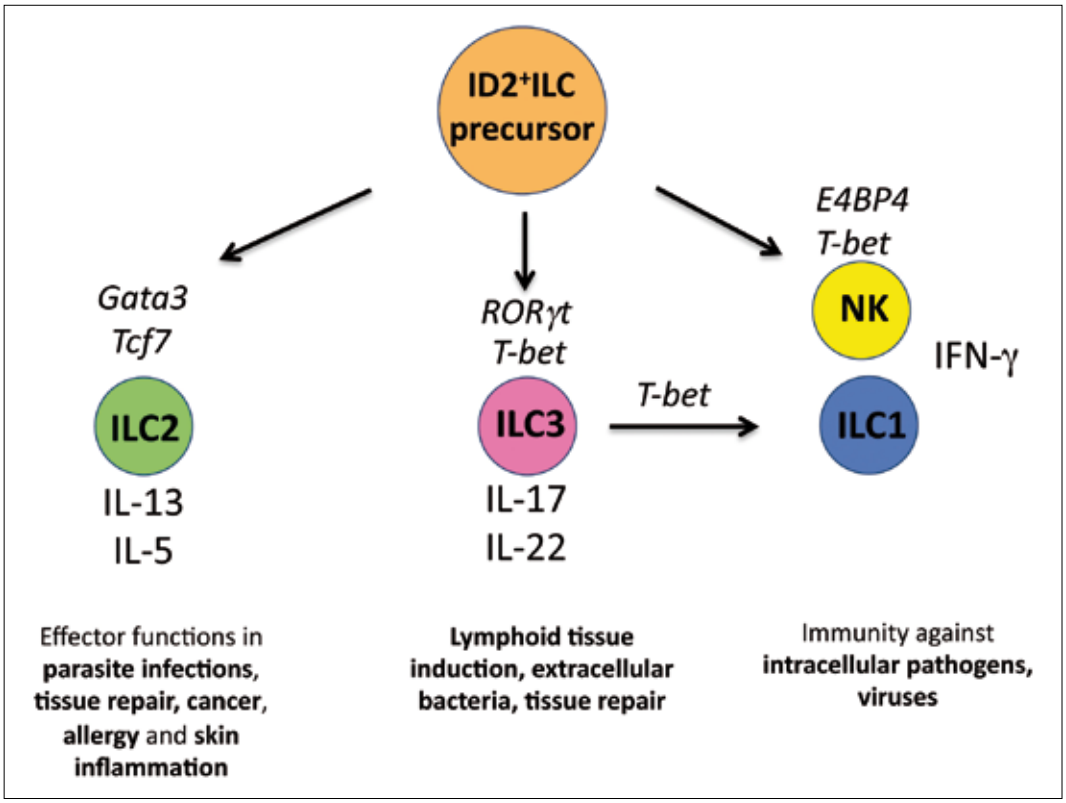


Figure 1:
Model of the innate lymphoid cell (ILC) family. ID2$^+$ progenitor cells give rise to 3 groups of ILCs that differ in transcriptional regulation and cytokine production. The ILC1 family is composed of natural killer cells (NK cells) and ILC1s, which are most likely derived from ILC3s. ILC2s depend on GATA-3 and Tcf7, whereas RORγt and T-bet is critical for the generation of ILC3 subsets.

Key players in ILC development

We have reported three critical cytokine receptor pathways involved in the life cycle and differentiation of ILCs and in their function to control lymphoid tissue generation. One is mediated by the interleukin 7 receptor (IL-7R, CD127) that binds IL-7, a survival factor for lymphocytes*(4, 9, 10)*. IL-7 stabilizes RORγ expression in ILC3s, which is instructive in determining cell fate and survival*(11)*. Another pathway is triggered by the engagement of thymic stromal lymphopoietin receptor (TSLPR), a cytokine receptor involved in allergic inflammation and T cell differentiation *(9, 12)*. Aryl hydrocarbon receptor (AHR) ligands control the expression of Kit (CD117) *(13)*, the third cytokine receptor involved in the expansion of ILC3s*(14)*. Importantly, we could show that IL-7R and Kit collaborate in establishing the pool of ILCs and in the generation of LNs. More recently, using Flt3L knockout and transgenic mice we found that Fms-like tyrosine kinase 3 ligand (Flt3L) controls the pool of ILC3 progenitors in the fetal liver (FL). The generation of fetal and adult ILC3s is dependent on the synergistic action of Flt3L and IL-7 independently of Flt3L-responsive dendritic cells. Flt3L transgene expression or treatment with recombinant Flt3L preferentially increases the pool of CD4$^+$ILC3s in the lamina propria indicating that Flt3L differentially regulates ILC3 subset development.

RORγt$^+$ILC3s can be heterogeneous in the expression of a number of surface markers, including CD4, CCR6, CD117 and NK cell receptors such as NKp46. The development of NKp46$^+$ILCs depends on T-bet*(15)*. A significant proportion of ILC1s appears to develop from ILC3s that downregulate RORγt and upregulate T-bet*(11, 16)*. This suggests that there is plasticity in type 1 and 3 ILCs, similar to the plasticity between Th1 and Th17 cells. Although recent work on ILC development identified key transcription factors controlling ILC development, these studies rarely provided means to identify successive stages of ILC development and the developmental relationship of different subsets. In order to address these questions, we use *in vitro* cultured BM hematopoietic stem cells (HSC) retrovirally transduced with the transcription factor HoxB4. In particular, we utilize an improved protocol employing HoxB4-Nup98 fusion construct*(17)*. We have been able to demonstrate that HoxB4-transduced HSC can reconstitute the ILC com-

partment when transferred into Rag2$^{-/-}\gamma_c^{-/-}$ mice. Cultured HSC from wild type or mutant mice are amenable to genetic manipulation by additional retroviral transduction, and enable us to study the role of specific factors and signalling pathways in the development of ILC subsets *in vitro* and *in vivo*.

ILC functions in tissue repair and protection

Immune cells have been proposed to contribute to epithelial and mesenchymal tissue repair through the release of factors that promote cell growth, defense and wound healing. ILC2s produce a panel of epithelial growth factors, and loss of ILC2s in the context of influenza infection leads to loss of epithelial cell integrity and impaired tissue remodelling*(18)*. ILC3s are the main producers of IL-22, a cytokine known to be involved in protection against bacteria, as well as the regeneration of epithelial and liver cells. ILC3s can help to restore and maintain the architecture of lymphoid tissues after virus-induced injury, suggesting a key function of this subset in tissue repair*(3)*. Moreover, IL-22 deficiency was shown to accelerate the mortality of graft versus host disease and apoptosis of epithelial stem cells*(19)* indicating that ILC3s may protect the intestinal stem cell niche. Altogether, IL-22-producing ILC3s may be important innate target cells for therapeutic strategies to reconstitute intestinal and lymphoid niches even in the absence of a functional adaptive immune system. In order to study this further, we generated K14 TSLPtg RAG$^{-/-}\gamma c^{-/-}$mice, which have an increased number of ILC2s and ILC3s, but lack T, B and NK cells. In these mice we found full restoration of LN numbers*(9)*, a partial segregation of medullary and cortical thymic epithelial cells with expression of Aire (indicated by arrows) (Figure 2A) and increased production of chemokines such as CCL25 that is required for regular trafficking and maturation of thymocytes (Figure 2B). This indicates that the TSLP tg expression induced maturation of the thymic microenvironment. In addition, we found that thymic and peripheral T cell restoration was significantly accelerated in K14 TSLPtg RAG$^{-/-}\gamma c^{-/-}$ as compared to RAG$^{-/-}\gamma c^{-/-}$ mice after BM transplantation (TSLPR$^{-/-}$ donor mice). This was not a result of a direct effect of TSLP on donor cells, since they were from TSLPR$^{-/-}$ origin. Custom RT profiler PCR array analysis of the intestine revealed that the production of IL-22, antimicrobial peptides (Reg3b and Reg3g) and other protective factors were significantly increased in K14 TSLPtg RAG$^{-/-}\gamma c^{-/-}$ mice. We conclude from these results that TSLP and IL-22^{+}ILCs may support the regeneration of stromal compartments in the thymus, LNs and intestine of immunodeficient hosts.

Environmental shaping of ILC diversity

There is growing evidence that the generation of ILC subsets depends on anatomical and microenvironmental signals. For example, commensal bacteria and

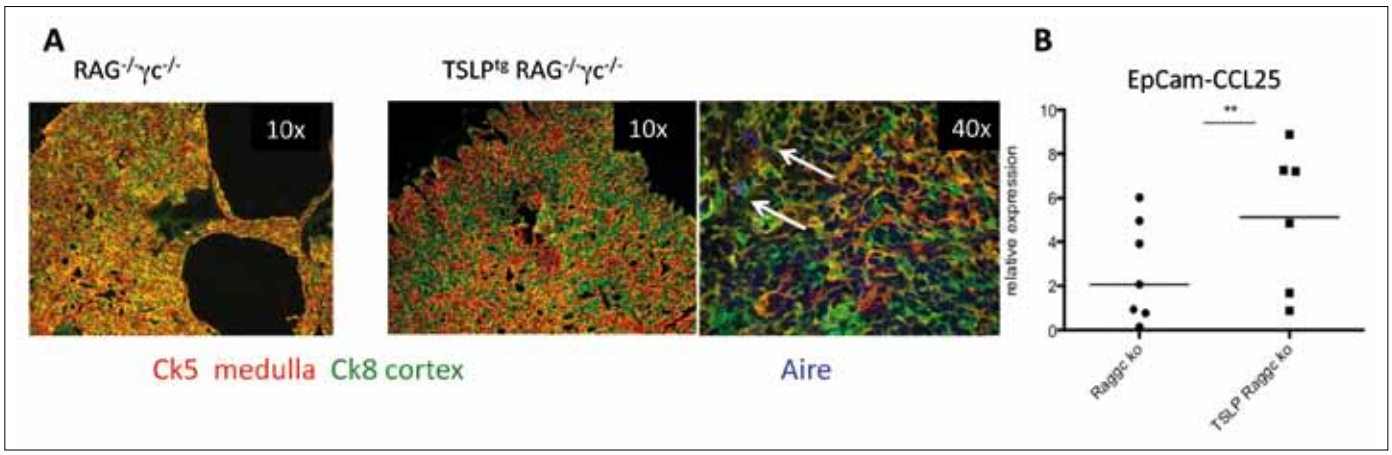


Figure 2:
(A) Immunohistochemistry of the thymus of adult RAG$^{-/-}\gamma c^{-/-}$ and TSLPtg RAG$^{-/-}\gamma c^{-/-}$ mice. Cytokeratin 5 (red) and 8 (green) and Aire (blue) expression is shown. (B) qRT-PCR analysis shows a relative increase in CCL25 transcripts in the thymus of TSLPtg RAG$^{-/-}\gamma c^{-/-}$ mice.

dietary factors can influence ILC development and cytokine responses. In a Sinergia project we currently investigate the influence of the microbiota and the impact of ILC subsets on recovery from colitis. The exposure of ILC3s towards pro-inflammatory cytokines modifies their cytokine secretion profile suggesting that either ILC3s have flexible responses towards environmental changes or alternatively, the proportion of ILC3 subsets depends on environmental signals. We found that upon IL-1β stimulation, FL-derived purified RORγt$^+$ ILC3s upregulate MHC class II, express co-stimulatory molecules, secrete cytokines (e.g. IFNγ, IL-2, GM-CSF) and gain the ability to present antigen to CD4$^+$ T cells. This cognate interaction induces T-cell activation and proliferation *in vitro* while deletion of MHC class II in RORγt$^+$ ILC3s (I-ab$^{\Delta ILC3}$) impairs T cell-mediated responses *in vivo*. In addition, we found that ILC3s can directly respond to particular toll-like receptor ligands. Interestingly, mucosal ILCs are far less responsive towards inflammatory stimulation than splenic ILC3s suggesting site-specific ILC effector functions. Altogether, our data show that under inflammatory conditions, ILC3s can trigger T cell responses, ascribing them with a novel function in connecting innate and adaptive immunity.

Several questions remain as to how ILC subsets arise, including the mechanisms that control the generation of pro- vs. anti-inflammatory ILC subsets. Although it is likely that the mucosal microenvironment promotes tolerogenic ILC subsets the pathways that ultimately generate mature ILC subsets remain to be elucidated.

Conclusions and outlook

ILCs have received recent attention for their potential roles in early response to infection, autoimmune disorders, allergy, and tissue maintenance. The outcome of an infection/inflammation may be regulated not only by the number and type of ILCs producing various cytokines but also by the microenvironment, the time kinetic and the activation state of the cells. Research in our lab will help to elucidate which environmental and intrinsic signals regulate the development and immune function of ILCs. We hope that the in depth analysis of genetic and epigenetic control of ILC commitment as well as *in vivo* mouse models will help to elucidate the molecular mechanisms that control ILC functions. This is essential to better understand how cells of the innate immune system may support or prevent innate and adaptive immune responses in humans. Targeting either ILCs in immunodeficient patients (e.g. after chemotherapy or irradiation) with cytokines (e.g. TSLP, IL-7) or adoptive transfer of *in vitro* expanded autologous ILCs before BM transplantation may be essential for improving reconstitution of the adaptive immune system.

Daniela Finke

References

1. D. Finke, H. Acha-Orbea, A. Mattis, M. Lipp, J. Kraehenbuhl, *Immunity* **17**, 363 (Sep, 2002).
2. T. Cupedo *et al., Nat Immunol* **10**, 66 (Jan, 2009).
3. E. Scandella *et al., Nat Immunol* **9**, 667 (Apr 20, 2008).
4. S. Schmutz *et al., J Immunol* **183,** 2217 (Aug 15, 2009).
5. Y. Yokota *et al., Nature* **397**, 702 (Feb 25, 1999).
6. H. Spits *et al., Nat Rev Immunol* **13**, 145 (Feb, 2013).
7. P. G. Fallon *et al., J Exp Med* **203**, 1105 (Apr 17, 2006).
8. C. Wilhelm *et al., Nat Immunol* **12**, 1071 (Nov, 2011).
9. S. Chappaz, D. Finke, *J Immunol* **184**, 3562 (Apr 1, 2010).
10. D. Meier *et al., Immunity* **26**, 643 (May, 2007).
11. C. Vonarbourg *et al., Immunity* **33**, 736 (Nov 24, 2010).
12. S. Chappaz, L. Flueck, A. G. Farr, A. G. Rolink, D. Finke, *Blood*, (Aug 16, 2007).
13. E. A. Kiss *et al., Science* **334**, 1561 (Dec 16, 2011).
14. S. Chappaz, C. Gartner, H. R. Rodewald, D. Finke, *J Immunol* **185**, 3514 (Sep 15, 2010).
15. C. S. Klose *et al., Nature* **494**, 261 (Feb 14, 2013).
16. J. H. Bernink *et al., Nat Immunol* **14**, 221 (Mar, 2013).
17. C. Ruedl, H. J. Khameneh, K. Karjalainen, *Int Immunol* **20**, 1211 (Sep, 2008).
18. L. A. Monticelli *et al., Nat Immunol* **12**, 1045 (Nov, 2011).
19. A. M. Hanash *et al., Immunity* **37**, 339 (Aug 24, 2012)

Dissertationen

Am 18. Dezember 2013 konnte **Sabrina Köhli** von der Forschungsgruppe Transplantation Immunology (Departement Biomedizin Hebelstrasse) ihre Dissertation mit Erfolg beenden. Sie befasste sich in ihrer Dissertation mit dem Thema "T cell affinity and autoimmunity: What is the origin of autoimmune T cells?".

Ebenfalls seit dem 18. Dezember 2013 darf sich **Luigi Costa** von der Forschungsgruppe Pneumology (Departement Biomedizin Hebelstrasse) Herr Dr. nennen. Er befasste sich in seiner Doktorarbeit mit dem Thema: "The interaction of tiotropium with long lasting beta2-agonist on lung cell function".

Auszeichnungen

SNF- Förderprofessur für Roxanne Tussiwand

Dr. Roxane Tussiwand, momentan als Postdoc an der Washington University School of Medicine in St. Louis, USA, tätig, vormals Departement Biomedizin Mattenstrasse, hat eine SNF-Förderprofessur erhalten. Sie wird ans DBM Mattenstrasse zurückkehren. Ihr Projekt beschäftigt sich mit der Entstehung und Funktion von dendritischen Zellen, die bei der Immunabwehr eine zentrale Rolle spielen.

Venia docendi an François Duong, Jens Kuhle, Albert Neutzner und Oliver Bandschapp

In ihrer Sitzung am 5. März 2014 hat die Regenz der Universität Basel **François Duong** von der Forschungsgruppe Hepatology (Departement Biomedizin Hebelstrasse) die Lehrbefugnis für Experimentelle Medizin, **Jens Kuhle** von der Forschungsgruppe Clinical Neuroimmunology (Departement Biomedizin Hebelstrasse) für Neurologie und **Oliver Bandschapp** von der Forschungsgruppe Perioperative Patient Safety (Departement Biomedizin Hebelstrasse) für Anästhesiologie und Intensivmedizin verliehen. In der Sitzung vom 11. Dezember 2013 wurde **Albert Neutzner** von der Forschungsgruppe Ocular Pharmacology and Physiology (Departement Biomedizin Hebelstrasse) die Venia docendi für Experimentelle Medizin verliehen. Sie dürfen nun alle den Titel eines Privatdozenten führen.

Pfizer Forschungspreis 2014 an Reto Ritschard, Andreas Wicki und Christoph Mamot

Der diesjährige Pfizer Forschungspreis im Bereich Onkologie ging an **Reto Ritschard** und **Andreas Wicki** von der Forschungsgruppe Cancer Immunology (Departement Biomedizin Hebelstrasse) sowie Christoph Mamot (früher DBM nun Kantonsspital Aarau) für den zielgerichteten Einsatz von Medikamenten in der Onkologie. Die Preisträger erhielten den mit 15'000 CHF dotierten Preis am 6. Februar 2014 in Zürich.

Herzliche Gratulation an alle!

The DBM PhD Club

The DBM is a scary place. Only some time after we, the PhD students, join the DBM for a doctoral study, do we realize how big the DBM actually is, with close to 60 research groups divided into four focal research areas at five different locations. Numerous seminars and lectures are supposed to help us through this jungle of labs and people, but this is often tough and not easy. That is why there was a need to create a department-wide PhD students' club that facilitates knowledge transfer and communication among folks of our kind. In autumn 2012 the two existing student clubs at DBM Mattenstrasse and the ZLF merged to become the official DBM PhD Club. The merge was facilitated due to the fact that both clubs had very similar motivations and ambitions, which included the organization of a few high quality events each year that are focused on the presentation of research and career development.

This united DBM PhD Club enabled communication between students at the five different DBM locations in a unified form, and significantly simplified contact between the DBM directorate and Students' Clubs. Soon thereafter, one of our students created a logo, which highlights the connection of the students at the five DBM locations through the one students' club; keeping a similar style to the official DBM logo, the department we belong to.

The DBM PhD Club is coordinated by PhD students from the different locations and focal research areas:

Name (Doctoral Year)	Research Group	Location	Focal Area
Carlos Mayer (4th)	Pediatric Immunology	Mattenstrasse	Immunology
Frédéric Laurent (4th)	Developmental Genetics	Mattenstrasse	Stem Cell
Kea Martin (3rd)	Cancer Immunology	Hebelstrasse	Immunology
Maren Diepenbruck (4th)	Biochemistry and Genetics	Mattenstrasse	Oncology
Fabrizio Botindari (4th)	Cancer and Immunobiology	Mattenstrasse	Immunology
Anna Engler (2nd)	Embryology and Stem Cell Biology	Mattenstrasse	Neurobiology
Vincent Prêtre (2nd)	Medical Oncology	Hebelstrasse	Oncology
Konstantin Kletenkov (2nd)	Molecular Virology	Petersplatz	Immunology

Together with the DBM PhD coordinator (Nicole Schaeren-Wiemers) special activities have been established to support and promote the PhDs at the DBM in their scientific careers. The two major annual activities of the DBM PhD Cub are the Scientific DBM PhD Winter Retreat and the Career day. In addition, several smaller social activities are organized. Detailed information can be found on the DBM Education/PhD-website: http://biomedizin.unibas.ch/education/phd/phd-club/.

Scientific Winter Retreat

In 2012, the PhD students of the DBM Mattenstrasse had the opportunity to experience the first Scientific Winter Retreat in Saas Grund (VS). During the two days of the event, they had the possibility to interact with the other students in a scientific meeting-like atmosphere, presenting the contents of their own research projects and sharing common interests among the different topics. This has been a great opportunity for everyone to prac-

tice their own communication skills and to interact with people at the same level of experience and at the same stages of their scientific career.

In March 2013 the Scientific Winter Retreat was extended to all PhD students of the DBM. By increasing the number of participants we aimed to enhance the possibility for the students to interact with more colleagues in their respective fields and to get a comprehensive overview of the different scientific topics within the DBM. We strongly believe that the Scientific Winter Retreat is an outstanding opportunity for all students to actively present and promote themselves and their work within the student community. In that spirit we also invited Master students and MD/PhD students to participate.

Goals

The following goals were initially outlined: 1. Present own research in a talk or a poster; 2. Participate in scientific discussions, and 3. Get insights into less familiar research fields.

At our first retreat in March 2013, we were strongly focusing on providing all necessary means for every student to have an optimal opportunity to present her or his own research. The program included six presentation sessions grouped by the focal areas, each consisting of three to four 20 minutes-long presentations. In addition, two poster sessions offered all non-orally presenting students a platform to display and present their research. The oral presentations and posters, presented in various sessions throughout the retreat, created a stimulating environment that offered everybody the opportunity to participate actively by asking questions and discussing answers. We observed that many students felt much more comfortable to actively contribute with questions and comments as compared to other institutional events.

The DBM is a complex department that conducts research in a broad variety of research fields. As a young researcher it is not always easy to get a proper overview over the complete range of research activities at the department. Therefore, all presentations at the Winter Retreat included a more general introduction of that specific group's research activity, prior to presentation of the speaker's personal project. This broader introduction aimed to fill possible gaps in knowledge in order to facilitate everybody's contribution to the discussions. Most presentations followed this important structure.

Location

We found a location that fully met our requirements for the presentations (i.e. sufficient space and lighting for the projected presentations as well as for the poster sessions), and that was possibly located in the Alps near a winter sports area for the last day of the retreat. We were fortunate to find the Hotel Viktoria in Hasliberg (BE) that fully satisfied our requirements for the scientific presentations and offered twin (and few single) bedrooms for everybody to feel comfortable. In addition, the hotel personnel showed a professional, pro-active behaviour that supported the smooth realization of the planned program. The Hotel catered all food, which included all main meals (breakfasts, lunches, dinners) as well as the coffee breaks and the apéro on the last evening. Their varied buffet offered food for people with different diets to almost everybody's satisfaction.

After careful evaluation of the transportation options (i.e. train, bus or individual journey) with our criteria

(i.e. costs, travel time, possibility to transport material and luggage) we decided to rent two buses. This option was not only the cheapest one, but also gave us enough flexibility in the timing, as well as the number of persons and quantity of material transported. The two buses picked everybody up on Thursday at Petersplatz, transported us to the Hotel Viktoria at Hasliberg Reuti, and brought us back on Saturday in two punctual and unproblematic journeys.

Program

The presentations were based upon the abstract submitted by every student. 19 students were selected for an oral presentation of 15 minutes in 6 sessions, whereas the others presented their work on a poster. Usually, PhD students in their 3rd and 4th year were selected for an oral presentation. In addition, on each day a keynote speaker was invited. At the end of the 2-day scientific meeting all students were participating in voting for the best presentation and best poster prize.

Credit points

The scientific winter retreat is accredited for one day education of the postgraduate PhD program and for 1.5 days (in 2013) and 1 day (in 2014) continuous education for animal experimentation.

Finances

The aim of the organizing committee is to avoid having a financial contribution from the students as much as possible. We are convinced that the opportunity to present her or his own research by an oral presentation or by a poster would be sufficient to guarantee the necessary commitment expected from each participant. Therefore, we always aim to finance this retreat as far as possible by sponsorships from different sources (e.g. Pharma, University). The Nachwuchsförderungsfonds of the University of Basel kindly provided 10'000.- CHF that covered a substantial amount of the expenses of the Scientific Winter Retreat. Further, we obtained a financial contribution from a variety of private companies. In 2013, the DBM paid the deficit, whereas in 2014 we covered all expenses. We are very thankful for this support.

Career Day

Working in a University environment, students interact mostly with scientists whose experiences are mostly acquired in an academic environment. There are, however, many other options and potential working areas open to people with a PhD in Biology that students are generally not aware of, or do not consider, due to lack of

information. In order to offer them the possibility to discuss their future professional possibilities and to learn skills to prepare them for the work market, the DBM PhD Club organizes a Career Day that aims to focus on the post-graduation careers of the young researchers by providing students with practical knowledge through a combination of presentations and workshops.

On October 3rd, 2013 the DBM PhD Career Day took place at the Villa Wenkenhof in Riehen. 40 PhD students took the opportunity to listen to the following talks of Prof. Dr. **Regine Landmann** (Vice Dean Career Development, Medical Faculty, University of Basel) about *"Your career: What will you be? By which way, when and where?"*, of Prof. Dr. **Mike Hall** (Vice Director Biozentrum, Research Group Leader, and member of the SNF Scientific Board) about *"Funding schemes of the SNF"*, and of Dr. **Ulrich Mühlner** (Director Corporate Strategy, Novartis) *"From the lab coat to the business suit - how a PhD enables you to enter the business world"*.

Further the following four workshops were offered:

Scientific writing	Dr. Marie St-Pierre, Research Associate, Hepatology, Dept. Clinical Research, University of Bern
CV + Interview	Dr. Birgit Müller, Career Service Center, University of Basel
Grant Information	Dr. Caroline Peneff, International Grants Office, University of Basel
Stress Management	Dr. Markus Diem, Head Student Advisory Service, University of Basel

Acknowledgements

The DBM PhD Club with all its members wants to thank the DBM directorate for their great support of our activities. By helping to realize our projects, they allowed the formation of a PhD community within the DBM and promoted the inter-institutional contact among the students in the various research fields investigated at the DBM.

Nicole Schaeren-Wiemers
PhD Coordinator


The Editorial Team
of DBM Facts wishes
all its readers
Happy Easter!

Selected publications by DBM members

Below you can find the abstracts of recent articles published by members of the DBM. The abstracts are grouped according to the impact factor of the journal where the work appeared. To be included, the papers must meet the following criteria:

1. The first author, last author or corresponding author (at least one of them) is a member of the DBM.
2. The DBM affiliation must be mentioned in the authors list as it appeared in the journal.
3. The final version of the article must be available (online pre-publications will be included when the correct volume, page numbers etc. becomes available).

We are primarily concentrating on original articles. Due to page constraints, abstracts of publications that appeared in lower ranked journals may not be able to be included. Review articles are generally not considered, unless they appeared in the very top journals (e.g. Cell, Science, Nature, NEJM, etc.). The final decision concerning inclusion of an abstract will be made by the chair of the Department of Biomedicine.

If you wish that your article will appear in the next issue of DBM Facts please submit a pdf file to the Departmental Assistant, Manuela Bernasconi: manuela.bernasconi@unibas.ch

Deadline for the next issue is April 30, 2014.

The American Society of Hematology **Blood, 1 August 2013, Vol. 122, No 5** IF 9,060

Epithelial cytoprotection sustains ectopic expression of tissue-restricted antigens in the thymus during murine acute GVHD

Simone Dertschnig[1], Gretel Nusspaumer[1], Robert Ivanek[1], Mathias M. Hauri-Hohl[2], Georg A. Holländer[1,3], and Werner Krenger[1]

Development of acute graft-versus-host disease (aGVHD) predisposes to chronic GVHD with autoimmune manifestations. A characteristic of experimental aGVHD is the de novo generation of autoreactive T cells. Central tolerance is dependent on the intrathymic expression of tissue-restricted peripheral self-antigens (TRA), which is in mature medullary thymic epithelial cells (mTEC^{high}) partly controlled by the autoimmune regulator (Aire). Because TECs are targets of donor T-cell alloimmunity, we tested whether murine aGVHD interfered with the capacity of recipient Aire^{+}mTEC^{high} to sustain TRA diversity. We report that aGVHD weakens the platform for central tolerance induction because individual TRAs are purged from the total repertoire secondary to a decline in the Aire^{+}mTEC^{high} cell pool. Peritransplant administration of an epithelial cytoprotective agent, fibroblast growth factor-7, maintained a stable pool of Aire^{+}mTEC^{high},with an improved TRA transcriptome despite aGVHD. Taken together, our data provide a mechanism for how autoimmunity may develop in the context of antecedent alloimmunity.

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Arterioscler Thromb Vasc Biol. 2014; 34: 313–320 IF 6,338

Erythrocyte-Derived Microvesicles Amplify Systemic Inflammation by Thrombin-Dependent Activation of Complement

Daniel Zecher, Arun Cumpelik, Jürg A. Schifferli

Objective

Transfusion of aged blood has been associated with increased morbidity and mortality in critically ill patients. During storage, erythrocytes release increasing numbers of microvesicles (red blood cell–derived microvesicles [RBC-MV]). We hypothesized that RBC-MV mediate some of the deleterious effects of aged blood transfusions.

Approach and Results

We established a murine transfusion model using RBC-MV purified from aged mouse erythrocytes. Injection of RBC-MV into healthy mice had no effect. However, they aggravated pulmonary leukocyte sequestration and peripheral blood leukopenia induced by lipopolysaccharides. Lipopolysaccharide-induced proinflammatory cytokines were significantly increased in plasma after RBC-MV injection. These effects were not seen in C5aR-deficient mice. In vitro, RBC-MV bound C3 fragments after incubation with plasma but failed to bind immunoglobulins, C1q, or mannose-binding lectin. Preventing thrombin generation inhibited complement activation in vitro and in vivo and reversed the proinflammatory effects of RBC-MV in lipopolysaccharide-primed mice. Finally, the RBC-MV–induced phenotype was recapitulated using phosphatidylserine-expressing liposomes, suggesting that surface expression of phosphatidylserine by RBC-MV was mechanistically involved.

Conclusions

These results point toward a thrombin-dependent mechanism of complement activation by RBC-MV independent of the classical, lectin, or alternative pathway. Besides identifying RBC-MV as potential mediators of transfusion-related morbidity, our findings may be relevant for other inflammatory disorders involving intravascular microvesicle release, for example, sickle cell disease or thrombotic microangiopathy.

From the Department of Biomedicine (D.Z., A.C., J.S.), Department of Transplantation Immunology and Nephrology (D.Z.), and Department of Medicine (D.Z., J.S.), University Hospital Basel, Basel University, Basel, Switzerland.

Clin Pharmacokinet Springer DOI 10.1007/s40262-013-0115-0 IF 6,109

The Basel Cocktail for Simultaneous Phenotyping of Human Cytochrome P450 Isoforms in Plasma, Saliva and Dried Blood Spots

Massimiliano Donzelli[1,*], Adrian Derungs[2,*], Maria-Giovanna Serratore[3], Christoph Noppen[3], Lana Nezic[1], Stephan Krähenbühl[1], Manuel Haschke[1,4]

Abstract

Background and Objective Phenotyping cocktails use a combination of cytochrome P450 (CYP)-specific probe drugs to simultaneously assess the activity of different CYP isoforms. To improve the clinical applicability of CYP phenotyping, the main objectives of this study were to develop a new cocktail based on probe drugs that are widely used in clinical practice and to test whether alternative sampling methods such as collection of dried blood spots (DBS) or saliva could be used to simplify the sampling process.

Methods In a randomized crossover study, a new combination of commercially available probe drugs (the Basel cocktail) was tested for simultaneous phenotyping of CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4. Sixteen subjects received low doses of caffeine, efavirenz, losartan, omeprazole, metoprolol and midazolam in different combinations. All subjects were genotyped, and full pharmacokinetic profiles of the probe drugs and their main metabolites were determined in plasma, dried blood spots and saliva samples.

Results The Basel cocktail was well tolerated, and bioequivalence tests showed no evidence of mutual interactions between the probe drugs. In plasma, single timepoint metabolic ratios at 2 h (for CYP2C19 and CYP3A4) or at 8 h (for the other isoforms) after dosing showed high correlations with corresponding area under the concentration–time curve (AUC) ratios ($AUC_{0–24h\ parent}$/ $AUC_{0–24h\ metabolite}$) and are proposed as simple phenotyping metrics. Metabolic ratios in dried blood spots (for CYP1A2 and CYP2C19) or in saliva samples (for CYP1A2) were comparable to plasma ratios and offer the option of minimally invasive or non-invasive phenotyping of these isoforms.

Conclusions This new combination of phenotyping probe drugs can be used without mutual interactions. The proposed sampling timepoints have the potential to facilitate clinical application of phenotyping but require further validation in conditions of altered CYP activity. The use of DBS or saliva samples seems feasible for phenotyping of the selected CYP isoforms.

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International Journal of Neuropsychopharmacology CINP (2014), 17, 371–381 IF 5,641

Pharmacokinetic and pharmacodynamic effects of methylphenidate and MDMA administered alone or in combination

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Abstract

Methylphenidate and 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy') are widely misused psychoactive drugs. Methylphenidate increases brain dopamine and norepinephrine levels by blocking the presynaptic reuptake transporters. MDMA releases serotonin, dopamine and norepinephrine through the same transporters. Pharmacodynamic interactions of methylphenidate and MDMA are likely. This study compared the pharmacodynamic and pharmacokinetic effects of methylphenidate and MDMA administered alone or in combination in healthy subjects using a double-blind, placebo-controlled, crossover design. Methylphenidate did not enhance the psychotropic effects of MDMA, although it produced psychostimulant effects on its own. The haemodynamic and adverse effects of co-administration of methylphenidate and MDMA were significantly higher compared with MDMA or methylphenidate alone. Methylphenidate did not change the pharmacokinetics of MDMA and vice versa. Methylphenidate and MDMA shared some subjective amphetamine-type effects; however, 125 mg of MDMA increased positive mood more than 60 mg of methylphenidate, and methylphenidate enhanced activity and concentration more than MDMA. Methylphenidate and MDMA differentially altered facial emotion recognition. Methylphenidate enhanced the recognition of sad and fearful faces, whereas MDMA reduced the recognition of negative emotions. Additionally, the present study found acute pharmacodynamic tolerance to MDMA but not methylphenidate. In conclusion, the combined use of methylphenidate and MDMA does not produce more psychoactive effects compared with either drug alone, but potentially enhances cardiovascular and adverse effects. The findings may be of clinical importance for assessing the risks of combined psychostimulant misuse. Trial registration identification number: NCT01465685 (http:// clinicaltrials.gov/ct2/show/NCT01465685).

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Social Cognitive and Affective Neuroscience Advance Access Social Cognitive and Affective Neuroscience October 28, 2013 IF 5,042

MDMA enhances emotional empathy and prosocial behavior

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3,4-Methylenedioxymethamphetamine (MDMA, 'ecstasy') releases serotonin and norepinephrine. MDMA is reported to produce empathogenic and prosocial feelings. It is unknown whether MDMA in fact alters empathic concern and prosocial behavior. We investigated the acute effects of MDMA using the Multifaceted Empathy Test (MET), dynamic Face Emotion Recognition Task (FERT) and Social Value Orientation (SVO) test. We also assessed effects of MDMA on plasma levels of hormones involved in social behavior using a placebo-controlled, double-blind, random-order, cross-over design in 32 healthy volunteers (16 women). MDMA enhanced explicit and implicit emotional empathy in the MET and increased prosocial behavior in the SVO test in men. MDMA did not alter cognitive empathy in the MET but impaired the identification of negative emotions, including fearful, angry and sad faces, in the FERT, particularly in women. MDMA increased plasma levels of cortisol and prolactin, which are markers of serotonergic and noradrenergic activity, and of oxytocin, which has been associated with prosocial behavior. In summary, MDMA sex-specifically altered the recognition of emotions, emotional empathy and prosociality. These effects likely enhance sociability when MDMA is used recreationally and may be useful when MDMA is administered in conjunction with psychotherapy in patients with social dysfunction or post-traumatic stress disorder.

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Cellular Neuroscience | frontiers in CELLULAR NEUROSCIENCE | October 2013, Vol. 7, Article 176 IF 4,469

MARCH5 inactivation supports mitochondrial function during neurodegenerative stress

Lei Fang[1], Jia Li[1,2], Josef Flammer[2] and Albert Neutzner[1,3]

Neuronal cell death is accompanied by mitochondrial dysfunction with mitochondrial maintenance critical to neuronal survival. The mitochondrial ubiquitin ligase MARCH5 has dual roles in the upkeep of mitochondrial function. MARCH5 is involved in targeted degradation of proteins harmful to mitochondria and impacts mitochondrial morphology upstream of the fission protein Drp1. In a neuronal cell model, dominant-negative MARCH5 prevents mitochondrial fragmentation during neurodegenerative stress induced by the neuron-specific reactive oxygen generator 6-hydroxydopamine, the complex I inhibitor rotenone or Alzheimer's-related amyloid beta peptide. In addition, preservation of mitochondrial function in terms of membrane potential and lower reactive oxygen generation was observed following inactivation of MARCH5. Our findings connect MARCH5 to neuronal stress responses and further emphasize the link between mitochondrial dynamics and function.

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Cellular Neuroscience | frontiers in CELLULAR NEUROSCIENCE | September 2013, Vol. 7, Article 155 IF 4,469

cAMP promotes the differentiation of neural progenitor cells *in vitro* via modulation of voltage-gated calcium channels

Guilherme Lepski[1,2], Cinthia E. Jannes[1,3], Guido Nikkhah[1,4] and Josef Bischofberger[5,6]

The molecular mechanisms underlying the differentiation of neural progenitor cells (NPCs) remain poorly understood. In this study we investigated the role of Ca^{2+} and cAMP (cyclic adenosine monophosphate) in the differentiation of NPCs extracted from the subventricular zone of E14.5 rat embryos. Patch clamp recordings revealed that increasing cAMP-signaling with Forskolin or IBMX (3-isobutyl-1-methylxantine) significantly facilitated neuronal functional maturation. A continuous application of IBMX to the differentiation medium substantially increased the functional expression of voltage-gated Na^+ and K^+
channels, as well as neuronal firing frequency. Furthermore, we observed an increase in the frequency of spontaneous synaptic currents and in the amplitude of evoked glutamatergic and GABAergic synaptic currents. The most prominent acute effect of applying IBMX was an increase in L-type Ca^{2+}currents. Conversely, blocking L-type channels strongly inhibited dendritic outgrowth and synapse formation even in the presence of IBMX, indicating that voltage-gated Ca^{2+} influx plays a major role in neuronal differentiation. Finally, we found that nifedipine completely blocks IBMX-induced CREB phosphorylation (cAMP-response-element-binding protein), indicating that the activity of this important transcription factor equally depends on both enhanced cAMP and voltage-gated Ca^{2+}signaling. Taken together, these data indicate that the up-regulation of voltage-gated L-type Ca^{2+}-channels and early electrical excitability are critical steps in the cAMP-dependent differentiation of SVZ-derived NPCs into functional neurons. To our knowledge, this is the first demonstration of the acute effects of cAMP on voltage-gated Ca^{2+}channels in NPC-derived developing neurons.

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The Journal of Physiology | The Journal of Physiology | (2014) pp 125–140 IF 4,380

Functional properties of extrasynaptic AMPA and NMDA receptors during postnatal hippocampal neurogenesis

Charlotte Schmidt-Salzmann[1,2], Liyi Li[1] and Josef Bischofberger[1]

Abstract
In the mammalian hippocampus, new granule cells are continuously generated throughout life. Although it is well known that they rapidly form several thousand new glutamatergic synapses, the underlying mechanisms are not well understood. As extrasynaptic NMDA receptors are believed to support the generation of new spines, we have studied the functional properties of extrasynaptic ionotropic glutamate receptors in newborn granule cells in juvenile rats during and after synaptic integration. Using the fast application of glutamate to outside-out membrane patches, we show that all immature granule cells express functional AMPA and NMDA receptors. The density of AMPA receptors was small in cells starting to receive excitatory synaptic input (~30 pS μm^{-2}) but substantially increased during synaptic integration to finally reach ~120 pS μm^{-2} in fully mature cells. Interestingly, AMPA receptors showed a biphasic change in desensitization time constant which was slowest during synaptic integration and substantially faster before and afterwards. This was paralleled by a change in the non-desensitizing current component which was maximal during synaptic integration and about 50% smaller afterwards. Surprisingly, the NMDA receptor kinetics and density in young cells was already comparable to mature cells (~10 pS μm^{-2}), leading to an enhanced NMDA/AMPA receptor density ratio. Similar to somatic outside-out patches, iontophoretic application of glutamate onto dendrites also revealed an enhanced dendritic NMDA/AMPA ratio in young cells. These data indicate that prolonged AMPA receptor currents in newly generated

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American Society for Reproductive Medicine | 100 Issue 3, Sept 13, 770–776 IF 4,174

Histone deacetylase inhibitors down-regulate G-protein-coupled estrogen receptor and the GPER-antagonist G-15 inhibits proliferation in endometriotic cells

Patrick Imesch, M.D.[1], Eleftherios P. Samartzis, M.D.[1], Konstantin J. Dedes, M.D.[1], Daniel Fink, M.D.[1], and André Fedier, Ph.D.[1,2]

Objective: To investigate whether histone deacetylase inhibitors reduce the expression of the G-protein-coupled estrogen receptor (GPER) and whether the functional inhibition of GPER by the antagonist G-15 decreases the proliferation of endometriotic cells.
Design: In vitro study.
Setting: University hospital.
Patient(s): Immortalized epithelial endometriotic cells.
Intervention(s): Treatment with the histone deacetylase inhibitor romidepsin or suberoylanilide hydroxamic acid (SAHA), or with the GPER antagonist G-15.
Main Outcome Measure(s): Western blot analysis and quantitative real-time polymerase chain reaction (PCR) were used to monitor the expression of GPER in response to drug treatment. Effects of GPER stimulation and inhibition on cell proliferation were investigated by the 93-(4,5-dimethylthiazol-2-yl)2,5-diphenyl tetrazolium bromide (Sigma) (MTT) assay.
Result(s): Our results demonstrate that romidepsin and SAHA reduce GPER expression in a concentration-dependent manner. This reduction correlated with the accumulation of acetylated histones. No decreased expression of the estrogen receptor (ER)-a and ERb was found under comparable experimental conditions. Pretreatment of endometriotic cells with the GPER agonist G-1 stimulated cell proliferation accompanied by rapid Akt phosphorylation. G-15 reversed this stimulation and inhibited cell proliferation, which was accompanied by Akt dephosphorylation.
Conclusion(s): G-protein-coupled estrogen receptor is proposed as a potential therapeutic target in endometriosis. The downregulation of GPER and/or the impairment of its function may reduce the estrogen responsiveness in endometriosis, and therefore might be considered a possible treatment option of endometriosis.

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Monoamine transporter and receptor interaction profiles of a new series of designer cathinones

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Abstract

Psychoactive β-keto amphetamines (cathinones) are sold as "bath salts"or "legal highs"and recreationally abused. We characterized the pharmacology of a new series of cathinones, including methedrone, 4-methylethcathinone (4-MEC), 3-fluoromethcathinone (3-FMC), pentylone, ethcathinone, buphedrone, pentedrone, and N,N-dimethylcathinone. We investigated norepinephrine (NE), dopamine (DA), and serotonin (5-HT) uptake inhibition using human embryonic kidney 293 (HEK 293) cells that express the respective human monoamine transporter, the drug-induced efflux of NE, DA, and 5-HT from monoamine-preloaded cells, and binding affinity to monoamine transporters and receptors. All of the cathinones were potent NE uptake inhibitors but differed in their DA *vs.* 5-HT transporter inhibition profiles and monoamine release effects. Methedrone was a more potent 5-HT than DA transporter inhibitor and released NE and 5-HT similar to para-methoxymethamphetamine (PMMA), paramethoxyamphetamine (PMA), 4-methylthioamphetamine (4-MTA), and 3,4-methylenedioxymethamphetamine (MDMA). 4-MEC and pentylone equipotently inhibited all of the monoamine transporters and released 5-HT. Ethcathinone and 3-FMC inhibited NE and DA uptake and released NE, and 3-FMC also released DA similar to N-ethylamphetamine and methamphetamine. Pentedrone and N,N-dimethylcathinone were non-releasing NE and DA uptake inhibitors as previously shown for pyrovalerone cathinones. Buphedrone preferentially inhibited NE and DA uptake and also released NE. None of the cathinones bound to rodent trace amine-associated receptor 1, in contrast to the non-β-keto-amphetamines. None of the cathinones exhibited relevant binding to other monoamine receptors. In summary, we found considerable differences in the monoamine transporter interaction profiles among different cathinones and compared with related amphetamines.

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Tissue Engineering Mary Ann Liebert, Inc. publishers Vol. 19, Numbers 17 and 18, 2013 IF 4,065

Scaffold-Based Delivery of a Clinically Relevant Anti-Angiogenic Drug Promotes the Formation of *In Vivo* Stable Cartilage

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Standard cartilage tissue engineering approaches, for example, matrix-induced autologous chondrocyte implantation (MACI), consist of the implantation of cell-based constructs whose survival and further development first depend on the degree of graft maturity at the time of surgery (e.g., matrix production) and, subsequently, on initial host reaction. Indeed, blood vessel ingrowth and macrophage migration within the implant may endanger graft stability of immature constructs; so, control of angiogenesis was proposed as an adjuvant of cellular therapy for the treatment of cartilage defects. In this study, we hypothesized that engineered constructs with no *in vitro* precultivation, but functionalized to block angiogenesis right on implantation, might result in better survival, as well as superior long-term cartilaginous quality. Here, we propose a clinically compatible fibrin/ hyaluronan scaffold seeded with nasal chondrocytes (NC) and functionalized with an FDA-approved anti-angiogenic drug (bevacizumab; Avastin®), which sequestrates vascular endothelial growth factor from the surrounding environment. Our results show that the sustained bevacizumab release from NC-loaded scaffolds after subcutaneous implantation in nude mice efficiently blocked host vessels ingrowth (five times lower $CD31^+$ cells infiltration vs. control group, at 3 weeks after implant), and enhanced constructs survival rate (75% vs. 18% for the control, at 6 weeks after implant). *In vitro* assays, developed to elucidate the role of specific construct components in the *in vivo* remodeling, allowed to determine that fibrin degradation products enhanced the *in vitro* endothelial cell proliferation, as well as the macrophage migration; whereas the presence of bevacizumab was capable of counteracting these effects. The proposed pharmacological control of angiogenesis by a therapeutic drug released from a scaffold might enhance cartilage regeneration by MACI approaches, possibly allowing it to bypass the complex and costly phase of graft preculture to gain increased functionality.

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Angiogenesis Springer (2013) 16:795–807 IF 3,972

Paralemmin-1 is expressed in lymphatic endothelial cells and modulates cell migration, cell maturation and tumor lymphangiogenesis

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Abstract
The lymphatic system, the network of lymphatic vessels and lymphoid organs, maintains the body fluid balance and ensures the immunological surveillance of the body. In the adult organism, the de novo formation of lymphatic vessels is mainly observed in pathological conditions. In contrast to the molecular mechanisms governing the generation of the lymphatic vasculature during embryogenesis, the processes underlying pathological lymphangiogenesis are less well understood. A genomewide screen comparing the transcriptome of tumor-derived lymphatic endothelial cells with that of blood vessel endothelial cells identified paralemmin-1 as a protein prominently expressed in lymphatic endothelial cells. Paralemmin-1 is a lipid-anchored membrane protein that in fibroblasts and neurons plays a role in the regulation of cell shape, plasma membrane dynamics and cell motility. Here, we show that paralemmin-1 is expressed in tumor-derived lymphatic endothelial cells as well as in lymphatic endothelial cells of normal, non-tumorigenic tissue. Paralemmin-1 represses cell migration and delays the formation of tube-like structures of lymphatic endothelial cells in vitro by modulating cell-substrate adhesion, filopodia formation and plasma membrane blebbing. While constitutive genetic ablation of paralemmin-1 expression in mice has no effect on the development and physiological function of the lymphatic system, the loss of paralemmin-1 impaired tumor-associated lymphangiogenesis. Together, these results newly identify paralemmin-1 as a protein highly expressed in lymphatic endothelial cells. Similar to its function in neurons, it may link the cytoskeleton to the plasma membrane and thereby modulate lymphatic endothelial cell adhesion, migration and lymphangiogenesis.

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Variable Myopathic Presentation in a Single Family with Novel Skeletal *RYR1* Mutation

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Abstract
We describe an autosomal recessive heterogeneous congenital myopathy in a large consanguineous family. The disease is characterized by variable severity, progressive course in 3 of 4 patients, myopathic face without ophthalmoplegia and proximal muscle weakness. Absence of cores was noted in all patients. Genome wide linkage analysis revealed a single locus on chromosome 19q13 with Zmax = 3.86 at $\theta = 0.0$ and homozygosity of the polymorphic markers at this locus in patients. Direct sequencing of the main candidate gene within the candidate region, *RYR1*, was performed. A novel homozygous A to G nucleotide substitution (p.Y3016C) within exon 60 of the *RYR1* gene was found in patients. ARMS PCR was used to screen for the mutation in all available family members and in an additional 150 healthy individuals. This procedure confirmed sequence analysis and did not reveal the A to G mutation (p.Y3016C) in 300 chromosomes from healthy individuals. Functional analysis on EBV immortalized cell lines showed no effect of the mutation on RyR1 pharmacological activation or the content of intracellular Ca^{2+} stores. Western blot analysis demonstrated a significant reduction of the RyR1 protein in the patient's muscle concomitant with a reduction of the DHPRα1.1 protein. This novel mutation resulting in RyR1 protein decrease causes heterogeneous clinical presentation, including slow progression course and absence of centrally localized cores on muscle biopsy. We suggest that *RYR1* related myopathy should be considered in a wide variety of clinical and pathological presentation in childhood myopathies.

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Association between Low Levels of Mannan-Binding Lectin and Markers of Autoimmune Thyroid Disease in Pregnancy

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Abstract

Functional deficiency of mannan-binding lectin (MBL) has been associated with adverse pregnancy outcome. Adverse events during pregnancy have also been described in women with autoimmune thyroid diseases (AITD), and thyroid hormones have been shown to influence serum levels of MBL. Therefore, the aim of this study was to analyse the impact of MBL-deficiency on the outcome of pregnancy in relation to the presence of AITD. Almost one year after delivery, we assessed serum MBL levels and *MBL2*-genotypes in 212 women positively screened for AITD in pregnancy. In 103 of these women, we could also measure MBL levels in frozen serum samples from the 9-12th gestational week, obtaining 96 pairs of MBL values (pregnancy vs. follow-up). As controls, 80 sera of pregnant women screened negatively for AITD were used. *MBL2*-genotyping was performed using multiplex PCR. Women with thyroid dysfunction and/or thyroid peroxidase antibodies (TPOAb) had lower MBL levels during pregnancy than controls, (3275 vs. 5000 ng/ml, $p<0.05$). The lowest levels were found in women with elevated thyroid-stimulating hormone (TSH) levels in the absence of TPOAb (2207 ng/ml; $p<0.01$ as compared to controls). *MBL2* genotype distribution did not differ between subgroups. At a median follow-up period of 17 months (range: 3–78 months) after delivery, median MBL level had decreased further to 1923 ng/ml ($p<0.0001$) without significant changes in TSH. In an explorative survey, functional MBL-deficiency was neither linked to a history of spontaneous abortion, nor other obstetric complications, severe infections throughout life/pregnancy or antibiotics use in pregnancy. In conclusion, hypothyroidism during pregnancy is associated with decreased MBL levels, and the levels decreased further after delivery.

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Quantification of plasma carnitine and acylcarnitines by high-performance liquid chromatography-tandem mass spectrometry using online solid-phase extraction

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Abstract

Carnitine is an amino acid derivative that plays a key role in energy metabolism. Endogenous carnitine is found in its free form or esterified with acyl groups of several chain lengths. Quantification of carnitine and acylcarnitines is of particular interest for screening for research and metabolic disorders. We developed a method with online solid-phase extraction coupled to high-performance liquid chromatography and tandem mass spectrometry to quantify carnitine and three acylcarnitines with different polarity (acetylcarnitine, octanoylcarnitine, and palmitoylcarnitine). Plasma samples were deproteinized with methanol, loaded on a cation exchange trapping column and separated on a reversed-phase C8 column using heptafluorobutyric acid as an ion-pairing reagent. Considering the endogenous nature of the analytes, we quantified with the standard addition method and with external deuterated standards. Solid-phase extraction and separation were achieved within 8 min. Recoveries of carnitine and acylcarnitines were between 98 and 105 %. Both quantification methods were equally accurate (all values within 84 to 116 % of target concentrations) and precise (day-to-day variation of less than 18 %) for all carnitine species and concentrations analyzed. The method was used successfully for determination of carnitine and acylcarnitines in different human samples. In conclusion, we present a method for simultaneous quantification of carnitine and acylcarnitines with a rapid sample work-up. This approach requires small sample volumes and a short analysis time, and it can be applied for the determination of other acylcarnitines than the acylcarnitines tested. The method is useful for applications in research and clinical routine.

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α_1-Adrenergic Receptors Contribute to the Acute Effects of 3,4-Methylenedioxymethamphetamine in Humans

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Abstract

Preclinical studies implicate a role for α_1-noradrenergic receptors in the effects of psychostimulants, including 3,4-methylenedioxy-methamphetamine (MDMA, ''ecstasy''). The present study evaluated the effects of the α_1-noradrenergic receptor antagonist doxazosin on the acute pharmacodynamic and pharmacokinetic response to MDMA in 16 healthy subjects. Doxazosin (8 mg/d) or placebo was administered for 3 days before MDMA (125 mg) or placebo using a randomized, double-blind, placebo-controlled, 4-session, crossover design. Doxazosin reduced MDMA-induced elevations in blood pressure, body temperature, and moderately attenuated positive mood but enhanced tachycardia associated with MDMA. The results indicate that α_1-adrenergic receptors contribute to the acute cardiostimulant and to a minor extent possibly also to the thermogenic and euphoric effects of MDMA in humans.

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Meningothelial cells as part of the central nervous system host defence

Jia Li[1,2], Lei Fang[1], Hanspeter E. Killer[3], Josef Flammer[1], Peter Meyer[1] and Albert Neutzner[1]

Background Information.

Meningothelial cells (MECs) are the cellular components of the meninges protecting the brain and as such provide important barrier function for the central nervous system building the interface between neuronal tissue and the cerebrospinal fluid (CSF). MECs were previously shown to be involved in the clearance of waste products from the CSF and in maintaining the optic nerve microenvironment. In addition, MECs are involved in immunological processes in the brain by secretion of pro-inflammatory cytokines in response to various pathologically relevant stress conditions.

Results.

In this study, we analysed the uptake of latex beads as well as bacteria by human MECs using flow cytometric analyses. We found that MECs are highly active phagocytes able of ingesting large amounts of latex beads, as well as Gram-positive and Gram-negative bacteria. Phagocytic activity of MECs was sensitive to nocodazole and cytochalasin D treatment to a varying degree depending on particle composition. Interestingly, Gram-positive bacteria such as *Staphylococcus aureus* are more readily taken up compared with Gram-negative *Escherichia coli.* In addition, pre-treatment of MECs with lipopolysaccharide (LPS) or phorbol-12-myristate-13-acetate (PMA) enhanced *S. aureus* uptake, whereas PMA but not LPS was effective in enhancing *E. coli* uptake.

Conclusions.

Thus, MECs are highly active facultative phagocytes likely important for the maintenance of CSF homeostasis and host defence in the central nervous system especially against Gram-positive bacteria.

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Wenn ihr mich sucht, sucht mich in euren Herzen.
Habe ich dort eine Bleibe gefunden, lebe ich in euch weiter.
Rainer Maria Rilke

It is with great sorrow that we have taken notice of the death of Erika Fluri who passed away in December after suffering from one of those malicious illnesses that we still fail to obliterate by our research. Erika has been a laboratory technician at the DBM Mattenstrasse and a dear colleague to all of us. We commemorate and miss her for her dedicated contributions to many successful projects, her remarkable community spirit, her enduring social commitments and her continuous support of the ones in need inside and outside of the laboratory. Our thoughts are with her, and we offer her family our sincere condolences.
Gerhard Christofori

Congratulations

Das DBM gratuliert ganz herzlich!

Johanna Sesiani Gentner
Geboren am 05.03.2014

Victor Fachet Bour
Geboren am 11.11.2013

Herzlich willkommen, allerseits!

Karl Tilman Karow
Geboren am 22.01.2014

Mare Ross Keck
Geboren am 04.03.2014

Moscow sketches

Borovitskaya (Naberesnaya)

When Heidi suggested to me that I write about Moscow, I was excited, no secret. To have an opportunity to say a few words about my native city, so dearly-beloved in my childhood and youth! The city where such names as Clean Ponds or Arbat say so much to my heart! The city where we, happy students of our adored alma- mater, Moscow University, explored step-by-step the pathways and favourite places of great Russian poets – Alexander Pushkin, Mikhail Lermontov, Marina Tsvetaeva, Boris Pasternak... Then I realized, how demanding my task was. Moscow has changed a lot since I was young and has acquired a new look. An enormous city, so eclectic, whirling, ever-changing, agitated, like the restless Russian soul, incomprehensible to other nations. Sometimes seeming hostile, insecure, full of problems... What can I say in a short article? I was bewildered, I must admit. So please forgive me if my narration appears fragmentary, as notes on margins and as eclectic as the city itself.

White-stoned capital. The first record of Moscow appeared in a chronicle from 1147 when Prince Yuri Dolgorukiy, the founder of Moscow, invited his brother, Prince Sviatoslav to visit him. In 1156 Moscow, being a remote frontier settlement, got its first fortress walls and became a town.

The end of the fourteenth century. A new époque for Moscow was coming – the new white-stoned Kremlin was erected during time of Prince Dmitri Donskoi. This event impressed his contemporaries so greatly, that since then Muscovites still call their capital (Belokamennaya, white-stoned).

Lion and unicorn. Do you know that the existing Kremlin's walls and towers were build by Italian architects during the Renaissance period? And that their construction was finished in the seventeenth century by English masters? Spasskaya Tower was decorated with figures of wonderful animals, among them the lion and the unicorn, indispensible attributes of a king's power, which also were represented on the Emblem of London. Sitting humbly, they hold the globe in their paws. Every Kremlin tower of the 20 remaining has its own history, its own role and fate. "The castle on Borovitsky Hill" still keeps many historical secrets.

Time passed. Peter the Great left Moscow where he barely escaped death in his youth and built a new capital on the banks of river Neva – sinking in fogs, splendid and tragic Saint-Petersburg. Moscow was abandoned by court. In the beginning of nineteenth century it was a big provincial city, "unique in a strange mixture of ancient and up-to-date ar-

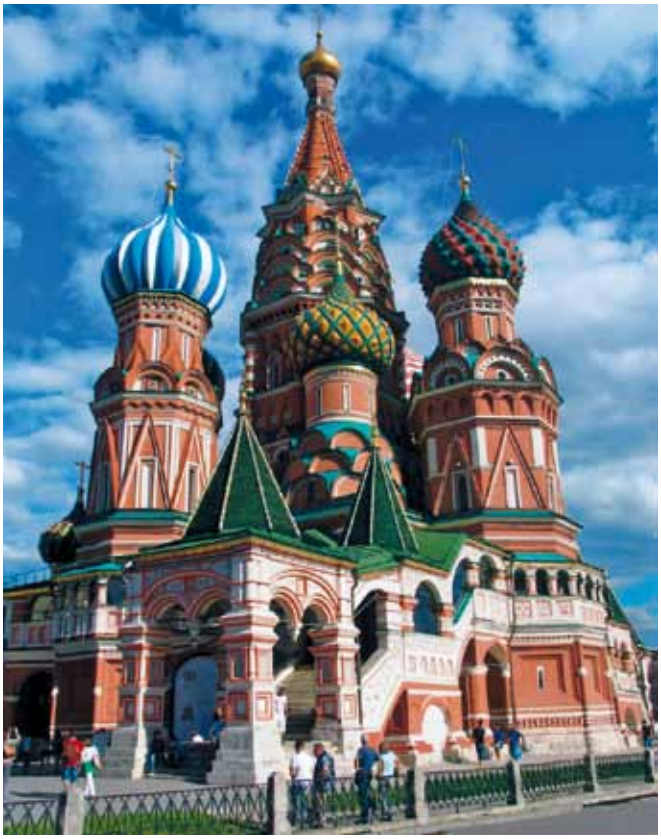
chitecture, poverty and wealth, European manners and oriental customs" (Konstantin Batushkov). The words of the poet are as true now as ever. Such is contemporary Moscow – luxury and misery, religious devotion and disbelief, ignorance and culture, conservatism and frivolity. Ever-lasting, baffling contrasts. Melting pot. Everything changes, but Moscow always remains strikingly diverse.

Kuskovo

Moscow rings. Reflecting the turbulent life of melting pot and historical perturbations, many different architectural styles are mingled in Moscow. The Fire of Moscow (1812) destroyed many beautiful historical buildings, churches, palaces and wooden mansions, but the old capital rose from the ashes like a phoenix. As with many other cities, such as Vienna, London, or Basel, Moscow has been encircled by rings since olden times. The Garden Ring in medieval times was an earth rampant, protecting the city from enemy raids. The Boulevard Ring, constructed in 1820, enclosed the former medieval White City. Oh, these Moscow boulevards! Muscovites like to stroll along them, especially in summer. They remind me the words of one Moscow song: "Love is a ring and ring has no beginning, no end"...

Novodevichy Convent (winter)

Москва хлебосольная (Hospitable Moscow). What Europeans call lunch, Russians call dinner. And this Russian dinner is not as strictly time-framed as in Europe. Basically it could occur any time from 1 to 4–5 pm, depending on your time opportunities and preferences, afterwards it would be called 'supper'. If you are invited to somebody's place, and Muscovites like to invite people for dinner, be well prepared. The main mottos are: "The best – on the table!" and "The more – the better!" Right, Muscovites pay a lot of attention to food. Of course many of them still remember the time when it was hard to get any. But anyway, Muscovites have always liked to eat well and to eat a lot. A table must be crammed with different kinds of dishes. Several salads, hot pies ("pirogi") with cabbage/fish/meat, pickled cucumbers, sauerkraut, smoked foods, and some-



Vasily Blazenniy Cathedral

times caviar, are served as starters. Then it is time for the soup or the main course (or sometimes even both of them). I remember that my Bernese friend gave up after soup. He simply said "I cannot eat anymore".

Every meal is traditionally followed by black tea. Muscovites are used to drinking tea 4–5 times a day. Tea must be very good, that means strong, fresh, and with a spicy flavour. Teabags are only accepted in exceptional circumstances (for instance while travelling). Tea break is a holy ceremony. Tea is usually served without milk, and is always accompanied by lemon, jam, pies, pastry, biscuits, "barankas" or honey cakes. All this: a teapot, porcelain cups, fresh tea, delicious sweets dispose you to unhurried friendly chat. Without evening tea at the end of the day, the day seems to be incomplete. And now, a good sign, there are so many places in the centre of Moscow, where you could nestle for a while at any time of the day, enjoy freshly baked pie with a cup of hot tea. Watch, how the hectic life of this sleepless monster is passing by...

Some curious facts about Moscow. How many fountains are in Basel? About 170 and the water from most of them is potable. In contrast there are more than 700 fountains in Moscow, but there is only one with drinking water. It is located at Nikitsky Gate near the Church of Great Ascension where poet Alexander Pushkin and Natalia Goncharova had their wedding ceremony. This fountain-rotunda known as "Natalie and Alexander" was constructed in 1999 to mark the 200th anniversary of Pushkin's birth.

The tallest building in Europe is currently the "Mercury City" tower located in the Moscow City International business complex. It is 339 meters high and has 5 stories. Moscow is a very green city. More than 40 percent of its territory consists of parks, garden and forests. For each Muscovite there are about 16 square meters of greenery considerably more than you would find in other major cities. In New York, for example there is about 8.6m^2 per New Yorker and for Londoners and Parisians there is 7.5m^2.

The name of the biggest bell in the world is "Tsar Bell". It weighs more than 200 tons with a height of 6.14 meter. The bell was cast by Ivan and Mikhail Motorin in 1730s during the reign of the empress Anna Ioanovna. The Tsar Bell has never rung; it was broken during its casting. How did that happen? The bell was almost completed when a fire broke out in the Kremlin in 1737. The wooden support structure caught fire, and the guards threw cold water on it. As a result it caused 11 cracks and a huge piece (11 tons) fell off. It would have been impossible to restore the bell. Only a century later the Tsar Bell was lifted from its pit and placed on a stone pedestal.

A few lyrical words. To finish let me say a few words of love dedicated to the street where I lived in my childhood, a very famous and charismatic Moscow street, called Arbat. Now it is a central and prestigious place (I hate the word, but it is very commonly (and adequately) used to attribute some Moscow districts). It is one of the oldest of the existing Moscow streets (this name was first

Arbat, 1966

mentioned in 15th century). Its name is believed to have an oriental origin due to the frequent attacks of the Golden Horde. Streets, you know, they are like human beings: they are born, look with curiosity at the world in their childhood, sow their wild oats in the youth. They have their best time, their golden age, and they die. Arbat has a similar spiritual meaning for Muscovites as Montparnasse does for Parisians: the street and surroundings, curved and charming side-streets inspired many painters, writers, poets. Now, it is touristic and kitschy, the street Arbat has almost completely lost its charisma, its special savour.

But I still hear in my ears low captivating voice of the Moscow poet, a bard of Arbat, Bulat Okudzhava. He dedicated several songs to the street, where he lived. The street, which in its peculiar to Russian intelligentsia meaning exists now only in verse, novels, memoirs, old photos...

You flow like a river, a weird name
And asphalt is transparent, like water in a river.
Oh Arbat, my Arbat! You are my vocation.
You are my joy, you are my trouble.

Your pedestrians, they are not great people.
Their heels clatter, they hurry to do business.
Oh Arbat, my Arbat! You are my religion.
Your roadways lie underneath me.

There is no cure from your love,
Even when one loved forty thousand of other roadways.
Oh Arbat, my Arbat! You are my fatherland.
To the very end I would never pass you.
(Word for word translation T.P.)

I wish for you to recall for a few moments your most beloved place on this earth: a street, a town, a village or city, that which you can call your motherland. It is not necessarily the place, where you were born or spent your childhood. It could be a place, which revives inside you some special, intimate and deep feelings. Sometimes you cannot even express and comprehend them. And now, let these special feelings stay with you for your whole life.

Tatiana Pochechueva
Photos Alexander Gusev

Novodevichy Convent (summer)

11 FINGER UND 1 MUG

ÜBER DAS WILD BUNCH DRUM & FIFE CORPS BASEL

Pfeifen und Trommeln hat in Basel schon lange Tradition. Dass es da einige wilde Vögel gibt, die nicht nur Piccolo und Basler Trommeln benützen, liegt auf der Hand. Und tatsächlich findet man neben der «klassischen» Fasnacht auch einige Formationen, die Neues ausprobiert haben. Aber zuerst von Anfang an...

WIE WIR WURDEN, WAS WIR SIND

Gegen Ende des Jahres 1986, als die Tage merklich kürzer und die Nächte bedeutend länger wurden, hat sich ein wilder Haufen zusammengefunden, um die ersten Gehversuche im Bereich der «Ancient Fife & Drum»-Musik zu unternehmen. Vielleicht noch ein wenig unsicher und musikalisch nicht ganz lupenrein, aber mit inbrünstiger Überzeugung und immensem Pioniergeist ging man ans Werk. Und am 12. Juli 1989 war das «Wild Bunch Drum & Fife Corps» offiziell gegründet.

Der Name des «Corps» leitet sich von einer berüchtigten Bande von Gesetzeslosen aus den USA ab. Angeführt wurden sie von Butch Cassidy und Sundance Kid. Diese haben vor über hundert Jahren für längere Zeit den wilden Westen von Mexiko bis hinauf nach Kanada unsicher gemacht. Von ihrem Hauptversteck «Robber's Roost» raubte die damalige «Wild Bunch» Banken und Züge aus und stahlen Vieh!

Ganz so wild sind wir nun aber doch nicht, aber mit unserem bewusst verlumpten «Outfit» versuchen wir, doch einen, diesen abenteuerlichen Zeiten entsprechenden optischen Eindruck zu hinterlassen.

Die Entwicklung des «Corps» ging schnell voran. 1992 nahmen wir zum ersten Mal am legendären «Deep River Ancient Muster» teil. Es folgten unzählige weitere Auftritte im In- und Ausland und mittlerweile kamen auch acht eigene Konzerte hinzu. So haben wir an den beiden ersten «Yyshalle Tattoo's» in Basel teilgenommen und sind seit Jahren an der offiziellen «Basel Tattoo Parade» dabei. Im 1997 formierte sich aus den eigenen Reihen die «Wild Bunch Singing Group». Sie verfügt über ein beachtliches Repertoire von irischen Songs und sorgt an den Konzerten für interessante Abwechslung und stimmt zu später Stunde oft ein Lied an. Heute zählt das Corps über 30 aktive und 60 Passiv-Mitglieder.

UNSERE INSTRUMENTE

Die Melodie wird von sogenannten «fifes» gespielt. Eine «fife» ist eine (meist) 10-Loch Holzflöte, welche von der Haltung her ähnlich dem Basler Piccolo gehandhabt wird. Die «fife» hat aber keine Klappen und ist etwas länger. Der Klang ist weicher als beim Piccolo.

Untermalend kommen die «snare drums» dazu. Ähnlich der Basler Trommel besteht das amerikanische Gegenstück aber generell aus Holz und ist vorwiegend mit Kalbfell bestückt.

Den Rhythmus und die Akzente setzen schliesslich die «bass-drums» (phonetisch: «bejss-drums»), grosse Pauken aus Holz und mit Kalbfellen.

«Snares» und «basses» werden sowohl in den USA als auch in der Schweiz hergestellt. Die «fifes» werden ausschliesslich aus den USA importiert.

Nebst Instrumenten und Musikern gibt es noch die «Colour Guard» – eine Art Vortrab, der (meist) die 1776 US-Flagge trägt. Nebst dieser Hauptflagge werden noch mehrere andere Flaggen mitgeführt. Sowohl die Corps-Standarten als auch State- oder Town-«flags».

DIVERSES UND WAS ES SONST NOCH SO GIBT

Gerne treffen wir uns mit anderen in Basel und Umgebung ansässigen Corps, um die Freundschaft zu pflegen. Dann und wann, ob in Amerika oder Basel, treffen wir uns auch mit Corps aus den USA.

Selbstverständlich kommt es vor, dass man uns vor oder nach einem Auftritt oder einer «parade» auch mal mit gefülltem oder auch bereits wieder leerem Mug (=Bierkrug) antrifft. Wir können ja nicht unablässig musizieren!

AMERICAN FIFE & DRUM DICTIONARY

(für diejenigen, die mitreden wollen)

Color Guard = Unser Vortrab. Hat nichts mit dem Koller zu tun, welchen wir manchmal bekommen, wenn sie in die falsche Richtung laufen. Marschieren

mit möglichst vielen Fahnen voraus, wobei das wichtigste Requisit die amerikanische Flagge ist.

Fife = Kurzquerflöte aus Holz ohne Klappen. Es gibt sie in 6-, 10- oder 11- Lochausführung. Je mehr Löcher desto mehr Finger braucht man logischerweise. Die Frage nach dem elften Finger ist nicht ganz einfach zu beantworten und lässt sich auf dem Papier nicht sehr gut erklären. Die modernen Ausführungen sind der Regel zweiteilig, wobei es auch schon Varianten mit Stimmenzug gibt wie beim Basler Piccolo. Betreffend Holz, Farbe und Formen gibt es unzählige Arten. Bei den WB spielen wir alle auf dem 10-Loch McDonagh Fife, weil schliesslich niemand von uns einen elften Finger hat.

Snare = Trommeln aus Holz, in der Regel mit Kalbfellen versehen. Diese müssen relativ viel aushalten, da unsere Polteris in so kurzer Zeit so viel draufschlagen und dann erst noch heftig. Der Ausschmückung hinsichtlich Grösse und Trommel, Farbe des Holzes und Bemalung sind keine Grenzen gesetzt.

Bass = Pauken aus Holz und ebenfalls in der Regel mit Kalbfellen versehen. Auch auf diesen Fellen wird kräftig herumgehauen. Darum brauchen unserer «Basser» entsprechende Oberarme und gehen regelmässig ins Krafttraining. Auch bei dem Bass gibt es unzählige Grössen und Varianten hinsichtlich Aussehen und Verzierungen. Der Bass ist das Grundrhythmusinstrument und aus der amerikanischen «Fife and Drum Music» nicht mehr weg zu denken.

Mug = Wertvoller und sehr wichtiger Gegenstand. Wird während den Pausen bei Auftritten und Konzerten gebraucht und sollte immer gut mit Bier gefüllt sein. Der Bierkrug aus «Armtale» – eine Art Zinn – wird am Hosengurt oder ähnlichem auch von den Frauen immer mitgetragen.

Muster = Hat absolut nichts mit einem Gratis«muster» oder Ähnlichem zu tun. Dieses Wort ist ursprünglich mit der militärischen «Musterung» gleich zu setzen. Schon im Mittelalter in Europa und während den Bürgerkriegszeiten war dies so. In der heutigen Form ist ein Muster ein gemütliches Zusammentreffen von verschiedenen Corps. Dies besteht aus einem Tattoo, einer Parade und dem Muster selbst, d.h. die Auftritte von jedem Corps. Die bekanntesten und grössten Muster sind diejenigen von Deep River und Westbrook. Während des Sommers finden in New England an jedem Wochenende grössere und kleinere Muster statt.

APROPOS AUFTRITT...

JA!!! Man kann uns auch mieten, anheuern, engagieren nur nicht kaufen. Gerne treten wir «open air» auf – oder auch in geschlossenen Räumen. Zum Beispiel an Firmenanlässen, Hochzeiten, Scheidungen, Stadtfesten, Vereinsjubiläen, Gala-Abenden, Geburtstagen etc.

Wer noch mehr wissen will, kann den Wissensdurst auf unserer Website www.wildbunch.ch stillen.

Niklaus «Niggi» Vogt

Let's try to make Sushi

Sushi is a well-known cuisine in Japan. It can be served at parties with friends, at special family occasions, or it can be eaten rather casually like a kind of fast-food. Sushi is consisting of cooked vinegared rice (referred to as "shari" or "sumeshi") combined with other ingredients, usually raw fish or other seafood. Ingredients and forms of sushi presentation vary widely, but the ingredient which all sushi have in common is vinegared rice.

There are many types of sushi, such as nigiri-zushi (variety of toppings served on a small bed of rice), chirashi-zushi (sashimi and other ingredients arranged on top of a bowl of rice), oshi-zushi (fish and rice pressed in a box then sliced), inari-zushi (rice stuffed into pouches of deep-fried tofu), and maki-zushi (served in a seaweed roll).

In Japan, people enjoy eating these different kinds of sushi anytime during the day or night at their home or at a restaurant. I guess that nigiri-zushi is the most popular one of the different kinds of sushi. But, I don't recommend that you try to cook it yourself, because it requires a special technique. When making Nigiri-zushi, the formation of bite-sized mounds of rice is the highlight for a sushi chef to show his technique, and there are various techniques. From this reason, people in Japan generally enjoy eating the nigiri-zushi in sushi restaurants. I found a cool iPhone application called "SUSHI BOOK How and Where to Enjoy Sushi". It's a visual guidebook application which introduces you basic knowledge of Sushi with information on the seafood toppings. It might be useful if you have a chance to go to Japan.

People in Japan enjoy cooking and eating chirashi-zushi, inari-zushi or maki-zushi as home-made Sushi at home. In this article, I'd like to introduce you to a recipe for chirashi-zushi. I hope it will be helpful for your cooking.

Section 1.

"How to Prepare Vinegared Rice"

Ingredients (serves 2 or 3 persons, about 24 1/2 oz)
300g of rice (Sushi rice or California rice), 400cc of hot water, about 2 inches konbu kelp, 3 Tbsps vinegar, 2&1/2 Tbsps sugar, 1 tsp salt. (Tbsp; Tablespoon, tsp; teaspoon)

Directions
1. Wash the rice 30 min before cooking, and drain on a sieve. Place the rice in a rice cooker, add hot water and *konbu* kelp, and cook.

2. Put the vinegar, sugar and salt in a small pot, and heat until the sugar and salt dissolve. Don't boil the solution.

3. Put the cooked rice in a wooden sushi bowl, and sprinkle over the vinegar dressing prepared in step 2 in a circular motion. Use a flat wooden spoon to mix it quickly in a cutting motion. (Photo. 1)

4. When the rice is loosened without any lumps left and evenly mixed with the vinegar dressing, continue to mix the rice further with the wooden spoon quickly in a sideways slicing motion, which cools it and allows excess vinegar to evaporate. When the rice cools down to body temperature, it's ready. Cover the rice with a clean damp cloth.

Photo 1. Vinegared rice preparation

Section 2.

"How to cook chirashi-zushi"

Ingredients (serves 2 persons)
Vinegared rice, cooked with 300g of rice.
1 ½ inches carrot, {Solution A; 80cc of Japanese-style soup stock, 1 tsp sugar, small quantity of soy sauce and salt}, 3 dried *shiitake* mushrooms, {Solution B; 100cc of Japanese-style soup stock (mixed with the water the *shiitake* has been soaked in), 2 tsps soy sauce, 1 Tbsp sugar, 1/2 Tbsp sake, ½ Tbsp *mirin* sweet cooking sake}, About 1 inch lotus root, {Solution C; 1 Tbsp vinegar, 1 Tbsp sugar, Pinch of salt, 3 Tbsps water}, 2 eggs, 6 shrimps, 2 Tbsps salmon roe, 6 snow peas, 1 Tbsp white sesame seeds.

Directions
1. Make vinegared rice. (Previous section)

2. Peel the carrot and cut into 3/4 inch strips, and cook in solution A.

3. Soak dried *shiitake* mushrooms in cold water to soften. When softened, cook the shiitake in solution B. When cool, cut the *shiitake* into narrow strips.

4. Peel the lotus root, and thinly slice. Boil the lotus root in salty water, and marinate it in solution C, while hot to make sweet-vinegared lotus root.

5. Mix beaten eggs with small quantity of salt and sake. Make paper-thin omelets, and cut into julienne strips when cool.

6. Devein the shrimps, and boil them in their shells in salty water. When cool, shell the shrimps.

7. String the snow peas, and boil them in salty water.

8. While the vinegared rice is still warm, add the drained carrot prepared in step 2, cut the *shiitake* mushrooms from step 3, and white sesame seeds, and then mix them.

9. Place the mixed vinegared rice on a plate, and scatter over the sweet-vinegared lotus root from step 4, strips of omelets from step 5, boiled shrimps from step 6, boiled snow peas from step 7, and salmon roe. You can also additionally use other raw fish (e.g. salmon, tuna, and so on). (Photo 2)

Photo 2. Picture of chirashi-zushi

Please feel free to contact me if you would likemore detailed information. Enjoy your cooking!

どうぞ召し上がれ

Yukiko Shimizu

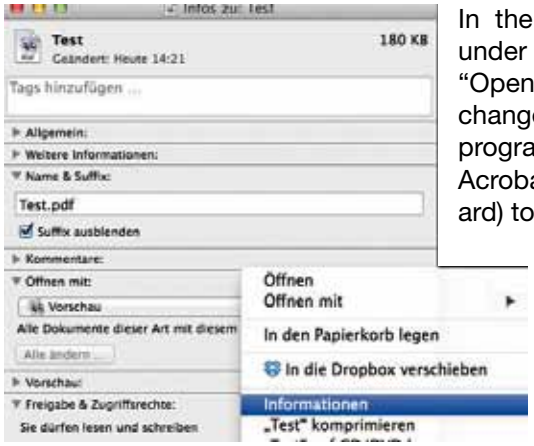
+ IT News +++ IT News +++ IT News ++

Today's theme is "printers and printing"!

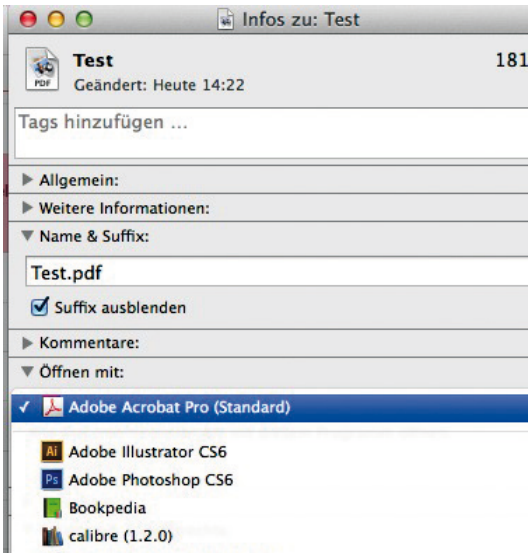
There are many printers in the DBM. Some of these are for individual groups, others only for hospital computers and others still are available for whole floors to use. Printers will definitely run out of paper and toner from time to time. DBM-iT is not responsible for the changing or replacing of toner or the refilling of the printer with paper. In the interest of our planet and it's ever dwindling resources one should really only print what is absolutely necessary. With OSX on the Mac everything can be viewed as a pdf before it is printed.

Using these pdfs one can quickly check if there are perhaps blank pages to be printed that once could delete before printing, or if it is possible to reduce the print area. Once something is sent to the printer then one should go directly to the printer! There are several reasons for this: firstly so that you can collect your document immediately before you have perhaps forgotten that you have printed something and more importantly in case there is a problem with the printer - for example if it is only printing "hieroglyphs" then the paper cassette should be immediately removed and we should be notified of the problem. We can then delete the print job form the server and the printer will not continue to spit out 500 or more pages that can only be recycled.

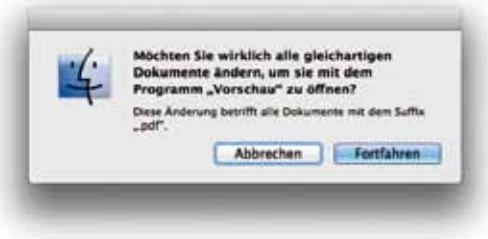
But we are happy to help when you cannot print out a document, or when only hieroglyphs appear when you try to print something. This latter problem often occurs when the pdf is created with an unknown pdf creator (not programs such as Acrobat Professional or Acrobat Distiller). When such documents are then printed via Acrobat problems can arise. It is therefore a good idea when using a Mac with OSX to use the program Preview to print such documents.
One tip we recommend, to ensure that pdfs are always opened with the program Preview, is to change the default application that is associated with pdfs. To do so click on any pdf with the mouse while holding down the ctrl key. Select "Information" from the menu that appears.



In the Info window, under the section "Open with:" you can change the standard program from Adobe Acrobat Pro (Standard) to Preview.



You then click on the button at the bottom "Change all..." and then verify this by clicking on "Continue". All pdfs will then be opened with Preview. Most pdfs will print without problems.



Today: Sanwei Guo, Oncology Surgery

I was born and grew up in North-East China, a middle-sized but nice city named Jilin. In 1998 when I was 18 years old, I started my college life in Shanghai. After an 8 year programmed study in Shanghai Jiaotong University medical school, I graduated in 2006 with an M.D. degree.

Luckily, I found a position in one of the Uni-Hospitals affiliated to the university where I studied, the Shanghai Jiaotong University First People's Hospital, and then my surgical career began there.

Nowadays, the standardized training program of residency has been carried out for almost a decade in University Hospitals in mainland China. As a surgical resident in University Hospital, I spent 18 months in surgical rotation, more than half of which was in General Surgery. In the 6 months following the rotation, I undertook a half-year training as a Chief Resident in General Surgery. It was hard time for me, being on-call every other day and always running between Emergency, ward and OR. There was an examination at the end of my Chief Residency, after which I entered my specialty, Urology, and earned more. It was at that time that I bought an apartment in a suburb of Shanghai and got married.

In 2008, I became a resident in Urology and then the Chief Resident in 2009. My full residency training then came to an end and after surviving several complicated final exams, I started my career as an attending urologist in 2010. Since then I do not need keep the first line and ER pagers anymore and remain as second in line during on-call days.

There are 4 classifications for surgeons in China: resident, including Chief Resident, attending doctor, assistant chief doctor, and chief doctor. From my observations it is my understanding that a resident is the equivalent of the "Assistenzarzt" in Switzerland. Both attending doctor and assistant chief doctor are similar to "Oberarzt", and chief doctor may be the same as "Leitender Arzt" or even professor in Switzerland. However, it is worth noting that the Chief Doctor is not an administrative concept, meaning that there could be more than one chief doctor in any one department, one of whom should be the Professor and of course the director of that department.

In order to be promoted to a class above that of attending doctor, one must carry out research work and this plays a more and more important role in promotion. That is why I am currently at the DBM.

Serving a giant population in China, young surgeons carry a very heavy clinical load. In turn, we too benefit from this. I feel that a young urologist in a University Hospital of China has more opportunities to perform surgeries than their Swiss colleague of a similar age could have. Interestingly, there are almost no secretaries in clinical departments in mainland China, the work carried out by secretaries in Switzerland is done by the doctors and nurses themselves in China.

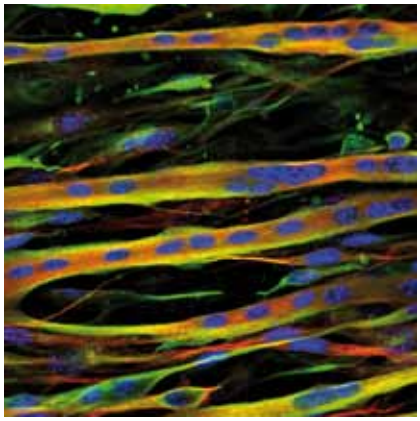
It is probably a worldwide fact that a surgeon has very limited free

time. I like to participate in domestic congresses and meetings on Urology and with these opportunities I have been to more than 80% of the provinces in mainland China. As to my free time in Shanghai, I prefer to stay at home, planting and taking care of my plants on the balcony, and reading the relative literature. Although my plants do not grow very well, growing them is my hobby.

Basel and Shanghai are twin cities. Medical students and interns in Basel University and Shanghai Jiaotong Univeristy visit each other from time to time. Whether in Basel or in Shanghai, the host hospitals need good tutors to teach the guests during their short visits. It could be done better on both sides and I am willing to contribute to this teaching when I return to Shanghai.

VORSCHAU PREVIEW

In der nächsten Ausgabe . . .



. . . erfahren wir von Michael Sinnreich mehr über Neuromuscular Research

. . . stellt uns Werner Krenger die GMP Facility vor

. . . entführt uns Elin Ellertsdottir nach Reykjavik

. . . bereiten wir die besten Rezepte für laue Sommerabende zu

. . . durchschwimmen wir mit Artem Kalinichenko den Bosporus

Maler Frühling

Der Frühling ist ein Maler,
er malet alles an,
die Berge mit den Wäldern,
die Täler mit den Feldern:
Was der doch malen kann!

Auch meine lieben Blumen
schmückt er mit Farbenpracht:
Wie sie so herrlich strahlen!
So schön kann keiner malen,
so schön, wie er es macht.

O könnt ich doch so malen,
ich malt ihm einen Strauß
und spräch in frohem Mute
für alles Lieb und Gute
so meinen Dank ihm aus!

August Heinrich Hoffmann von Fallersleben
(1798 – 1874)