KIDNEY EXPERTS GATHER FOR ANNUAL RETREAT

On February 1 and 2, 2018, the NCCR Kidney.CH invited its members to its 8th retreat, at the SBB Centre Loewenberg in Murten. This annual event allows all NCCR members to meet and to exchange their ideas and research results with other renal experts from across Switzerland. This year, more than 80 participants took up the invitation.

After an informal welcome aperitif on February 1, the programme of the second day included numerous presentations, on topics ranging from oxygen to dietary impact as well as ion balance and calcification. Frank Eitner, Head of Cardiovascular II, Drug Discovery at Bayer AG in Wuppertal, Germany, had been invited as external guest speaker and gave the participants insights into 'Kidney Diseases Research @ Bayer'. As part of the programme, the NCCR's Junior Grant recipients—Johan Lorenzen, Alessandro Luciani, Carsten Scholz and Diane de Zélicourt—also presented their research.

This interesting and very lively retreat was brought to a close with a presentation from Christian Stockmann, professor at the Institute of Anatomy of the University of Zurich, entitled 'Hypoxia and myeloid cell-driven angiogenesis in tissue fibrosis'.

POSTER AWARD 2018

From left to right: Johannes Loffing, Joana Delgado Martins and Director François Verrey.

At the Retreat 2018, a jury consisting of members of the NCCR's Steering Committee and Advisory Board selected the three best from more than 40 posters. The directors of Kidney.CH—François Verrey and Johannes Loffing—awarded the first prize to Joana Delgado Martins (postdoc in the Hall lab, UZH). Second prize went to David Granjon (postdoc at the Junior Grant project of Diane de Zélicourt, UZH), and third prize went to Beatrice Paola Festa (PhD student at the Junior Grant project of Alessandro Luciani, UZH). Congratulations!

8TH INTERNATIONAL KIDNEY.CH SYMPOSIUM – 'SYSTEMS BIOLOGY AND PRECISION MEDICINE'

This year's symposium will take place at the University Hospital Bern (Inselspital, Hoersaal 7, Auditorium Langhans) on September 6, 2018. This centrally located hospital will be an inspiring venue for cutting-edge scientific presentations and fruitful discussions.

The main topics of the symposium will be the study of complex biological systems and the implementation of the systems biology approach in research and medical practice. The presentations will focus on areas of genome-wide association studies (GWAS), metabolomics, computational and experimental techniques, as well as clinical applications in nephrology and beyond.

We look forward to welcoming you to Bern. Programme and registration at www.nccr-kidney.ch.

ENROL IN THE FIRST SUMMER SCHOOL

The first Kidney.CH Summer School will take place at the University of Zurich from September 9 to 12, 2018.

It will be organized by Kidney.CH and members of TRENAL ('Translational kidney research – from physiology to clinical application'). TRENAL is an interdisciplinary association of various European kidney research networks. It unites nephrologists, physiologists, nephropathologists and basic researchers from Friedrich Alexander University Erlangen-Nuremberg, Charité - Universitätsmedizin Berlin, and Yale University, as well as University College London and the Max Planck Institute for the Physics of Light.

This international summer school will bring together experts in kidney research and diseases to discuss, in a stimulating and interactive setting, the basis of renal functions and their relevance for kidney disease. Small-group case discussions will highlight both common and rare forms of kidney disease. Participants are invited to present their research projects during a poster session.
For more information and registration, visit www.nccr-kidney.ch.

NCCR KIDNEY.CH GOES SOCIAL MEDIA

With the increasing use of mobile devices, Kidney.CH is adapting its communication strategy. You can now follow us on LinkedIn, Twitter and YouTube.
If you don't already have one, create a Twitter account and follow us on Twitter!

EVENTS

USZ – GRUNDLAGEN DER NEPHROLOGIE – NECROPTOSIS IN THE KIDNEY
June 25, 2018
Kurszimmer 1, Nord1 C301 USZ
Zurich, Switzerland

8TH INTERNATIONAL KIDNEY.CH SYMPOSIUM: SYSTEMS BIOLOGY & PRECISION MEDICINE
September 6, 2018
Inselspital Bern, Switzerland

NCCR KIDNEY.CH & TRENAL SUMMER SCHOOL 2018
September 9–12, 2018
University of Zurich, Switzerland

10. JAHRESTAGUNG DER DEUTSCHEN GESELLSCHAFT FÜR NEPHROLOGIE
September 27–30, 2018
Berlin, Germany

NEPHRO UPDATE EUROPE 2018
October 5–6, 2018
Budapest, Hungary

50TH ANNUAL MEETING OF THE SWISS SOCIETY OF NEPHROLOGY
December 6–7, 2018
Congress Center Kursaal
Interlaken, Switzerland

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KIDNEY
CONTROL OF HOMEOSTASIS
SWISS NATIONAL CENTRE OF COMPETENCE IN RESEARCH

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SWISS NATIONAL CENTRE OF COMPETENCE IN RESEARCH

KIDNEY
CONTROL OF HOMEOSTASIS

NEWSLETTER ::: NO. 16 ::: JUNE 2018

Kidney—Control of Homeostasis is a Swiss research initiative, headquartered at University of Zurich, which brings together leading specialists in experimental and clinical nephrology and physiology from the universities of Basel, Bern, Fribourg, Geneva, Lausanne, and Zurich, and corresponding university hospitals.

IT TAKES TWO TO TANGO

The kidney and the adrenal gland team up to control blood pressure

High blood pressure is very common. It is often triggered by chronic activation of the renin–angiotensin–aldosterone system (RAAS), which plays an important role in the regulation of blood volume and arterial pressure and interlinks the kidneys and the adrenal glands. Renal experts are currently exploring molecular mechanisms and environmental factors that cause chronic RAAS activation.

Depending on age group, 10 to 40 per cent of the population are affected by high blood pressure (hypertension), which can lead to fatal cardiovascular diseases. One major cause of hypertension is the chronic activation of the renin–angiotensin–aldosterone system (RAAS). This system regulates blood pressure, fluid volume and the vascular response to injury and inflammation. It also interlinks two main organs—the kidneys and the adrenal glands. Chronic RAAS activation leads to persistent hypertension, setting off a cascade of inflammatory, thrombotic and atherogenic effects eventually leading to end-organ damage.

Numerous studies have demonstrated that elevated renin and/or aldosterone levels are predictors of adverse outcomes in hypertension, and of heart failure, myocardial infarction and chronic kidney disease, and influence insulin resistance.

FINDING THE CAUSE

RAAS activation can be induced on several levels: for example, renal artery stenosis results in increased renin secretion, which leads to high aldosterone output from the adrenal zona glomerulosa cells, which are the source of aldosterone secretion. And there are other reasons for a dysregulated RAAS based on adrenal aldosterone, and one is—at least in part—independent of the upstream stimulation of renin and angiotensin. In fact, this condition—known as primary aldosteronism (PA)—is the most common secondary form of hypertension, with an estimated prevalence of between 4 and 12 per cent of hypertensives and 11 to 20 per cent of patients being resistant to combined antihypertensive medication. PA is currently acknowledged

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Edith Hummler
Edith Hummler is a professor at the Department of Pharmacology & Toxicology at the University of Lausanne. She is a member of the Steering Committee and future Gender Representative of the NCCR Kidney.CH.

Mentoring young researchers

The NCCR Kidney.CH offers researchers and students a platform via which to meet and collaborate with other scientists and clinicians in the renal field across Switzerland. In addition, it promotes the training of young scientists and monitors the integration of gender perspectives. For example, the NCCR Kidney.CH was among the first NCCRs to implement financial support for the continuation of research projects during maternity leave.

Supporting doctoral students and postdocs is essential: competition for tenured positions remains tough in both basic and clinical research, which means we risk losing valuable renal knowledge we have acquired. We may need to offer additional individual mentoring during the transition phase from working alongside a scientist as a doctoral student or postdoctoral fellow to becoming an independent researcher and principal investigator of one's own right. This holds true for both female and male candidates. One of the biggest challenges will be to enable young researchers to combine family and parental tasks with research and clinical duties.

For me, it is thus important to contribute by coaching and promoting young scientists of both sexes in order to support them in successfully pursuing their academic careers.

Edith Hummler

to be the most common curable form of hypertension. The two predominant causes of dysregulated aldosterone secretion are aldosterone-producing adenomas (APAs) and bilateral adrenal hyperplasia (BAH). Once a patient is diagnosed with PA, it is important to distinguish between the surgically correctable forms (APA and unilateral primary adrenal hyperplasia) and forms that should be treated pharmacologically (BAH).

TRACING MOLECULAR MECHANISMS

In the last decade, several mutations in channels, transporters and enzymes (KCNJ5, ATP1A1, ATP2B3, CACNA1H, CACNA1D and CLCN2) have been linked to the development of APA and familial forms of PA. These mutations are thought to trigger inappropriate shifts in intracellular ion content, which ultimately leads to an excess of aldosterone. Yet we still have only limited knowledge of the molecular mechanisms that link abnormal intracellular signaling and increased steroid production, and particularly adrenocortical cell proliferation.

Current hypotheses regarding these molecular mechanisms have been inferred from the physiological action of stimulators of steroidogenesis. Remarkably, the signaling pathways of aldosterone secretagogues include the regulation of the activity of protein kinases, ultimately promoting hormonal output. Aldosterone stimulating factors, such as AngII and K^+, depolarise the membrane voltage of zona glomerulosa cells, triggering intracellular Ca^{2+} signaling that is thought to activate several members of the calmodulin kinase family. Moreover, AngII also promotes the release of Ca^{2+} from intracellular stores via IP3 and stimulates the protein kinase C and D families via the production of diacylglycerol.
Calcium signaling activates the steroidogenic acute regulatory protein (StAR), which translocates cholesterol from the outer towards the inner mitochondrial membrane and is regarded as one of the rate-limiting steps for adrenocortical steroid production. Members of the calmodulin kinase family that are activated by Ca^{2+} further regulate several transcription factors, ultimately promoting the expression of CYP11B2 (coding for aldosterone synthase), the terminal enzyme involved in the biosynthesis of aldosterone.
The genetic and molecular contributors of around 50 per cent of all APA cases can currently be delineated. Despite these achievements, there has been only minor progress in translating this knowledge into clinical practice. Moreover, somatic mutations causative of APAs have also been identified in a high proportion of adrenal glands from healthy kidney donors and from autopsy series. Due to the lack of animal models closely resembling the human phenotype, questions such as why some adrenal cells carrying APA-related somatic mutations develop into APAs while others do not, or what are the effects of aldosterone overproduction on the renal and cardiovascular system in this particular context, remain understudied.

DIET INFLUENCES BLOOD PRESSURE

Various environmental factors including salt intake effect both the kidney and the adrenal gland, which collectively dictate blood pressure control. Another such factor is dietary potassium intake. This effects kidney function directly as well as through modulating adrenal zona glomerulosa cells, which are very sensitive to changes in extracellular potassium concentration. In fact, high dietary potassium intake in wild type mice is associated with robust changes in the transcriptional profile of their adrenal glands. Potassium excretion from the kidney is also further increased through aldosterone, which results in a feedback loop in addition to that of the RAA system.
To improve blood pressure control it is important to further study mechanisms in a suitable experimental setting that takes into account the multiple layers of regulatory networks. It is clear that insights into the physiology and pathophysiology of blood pressure control will remain incomplete if they do not consider environmental factors and molecular mechanisms or if research is restricted to an organ-centric view. After all, it needs at least two—the kidney and the adrenal gland—to tango.

Felix Beuschlein is an endocrinologist and Clinic Director of the Department of Endocrinology, Diabetology and Clinical Nutrition at the University Hospital Zurich. He is currently a member of the Executive Committee of the European Society of Endocrinology. His research focus is the diseases of the adrenals and the pituitary gland.

PORTRAIT

FROM A SPARK TO A FLAME

For eight years François Verrey has served as the director of the NCCR Kidney.CH. The physiologist, who was instrumental in the founding of this Swiss-wide research platform, looks back to its beginnings and gives an outlook on what the NCCR wants to achieve in the future.

Ten years ago, the idea of a Swiss-wide network on kidney research was born. The igniting spark was an upcoming call from the Swiss National Science Foundation (SNSF) for new Centres of Competence in Research (NCCRs). Many scientists working in kidney research at competing Swiss Universities and their hospitals felt the need to build a platform to share their knowledge. Jan Loffing—from the Institute of Anatomy in Zurich—and I were among those who were strongly convinced that it was time to bring our experience together to achieve faster progress in renal and homeostasis research for the benefit of kidney disease patients.

OFFICIAL LAUNCH IN 2010

In 2008, a number of renal researchers from various Swiss universities met several times in Bern at the Nephrology Department of Inselspital then headed by Felix Frey. This was the foundation stone upon which we built what was to become our successful application to the SNSF. To our great pleasure, the Swiss NCCR Kidney.CH was able to begin its activities in August 2010 with headquarters in Zurich. The focus of our NCCR was, and is, advancing the knowledge and understanding of renal homeostatic mechanisms controlling body composition (milieu intérieur) in health and disease.
Over the past eight years, I have had the honour and great pleasure to lead—together with Jan Loffing—the NCCR Kidney.CH. Throughout this time, we have had the support of a strong management office led originally by Matthias Meier and for the past four years by Jens Selige with the help of Katharina Thomas, who managed the accounting side perfectly from the outset.

TRANSITION TO PHASE 3

In August 2018, the third phase of the NCCR will start. Jan Loffing is taking over the leadership of Kidney.CH and Carsten Wagner, who joined the management team last summer, will function as co-leader. With these changes, we want to introduce new impulses to further advance kidney research and to ensure the continuation of the Swiss kidney research network's activities beyond the end of SNSF financing, which is scheduled for 2022. It is essential that the NCCR Kidney.CH keeps alive its Swiss-wide dynamics and roots (CH stands not only for 'control of homeostasis' but, of course, also for Switzerland). This is also one of the major reasons why the NCCR is supported by a steering committee consisting of nine members that represent the different participating Swiss universities.

MORE RESEARCH INVOLVING HUMAN SUBJECTS

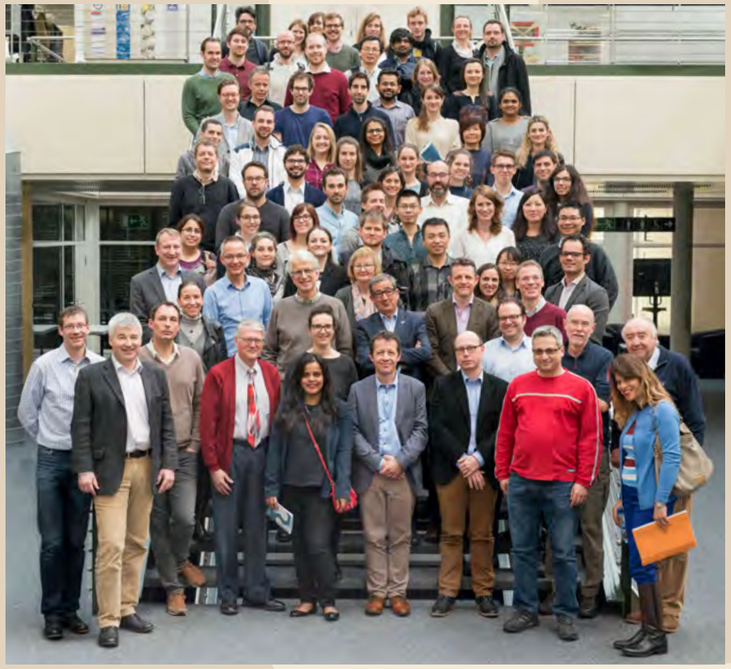
During its first two phases, the NCCR Kidney.CH has continuously strengthened the human and clinical aspects of its research portfolio—for instance by initiating a funding vehicle for human/clinical projects (HCPs) at the beginning of phase II. So far, 26 HCPs supported with a combined total of nearly CHF 2 million have been funded. Most of these projects were strongly collaborative, thus further strengthening the exchange of knowledge within Switzerland. Half of the allotted budget went to studies involving human subjects, while another substantial part supported human-genome-wide association studies (GWAS), with all of them complementing ongoing work-package projects.

COLLECTING DATA ACROSS SWITZERLAND

One of the most important initiatives supported by Kidney.CH is the Swiss Kidney Stone Cohort (SKSC), initiated in 2013. It was originally led by Reto Krapf, a clinician scientist working in Lucerne and Basel, and is now being managed by Olivier Bonny, MD–PhD, who works in Lausanne at the university and its hospital, and Carsten Wagner, from the Institute of Physiology in Zurich. This Swiss-wide cohort collects data from patients suffering from kidney stones and analyses and stores samples under identical conditions. With broad phenotyping, biobanking and longitudinal organization, this unique resource aims at enabling groundbreaking scientific research into this widespread and clinically very important disease.

FOSTERING A NEW GENERATION

A central endeavour of Kidney.CH is to foster the next generation of kidney researchers. One of the important initiatives of the NCCR is the national translational nephrology blended e-learning teaching program. It has become a CAS/DAS (Certificate/Diploma of Advanced Studies) at the University of Bern and will be endorsed by the University of Zurich, and probably in the future also by those of Lausanne and Geneva.
Another very successful initiative is the Junior Grant programme. It aims at filling a funding gap in the career of many young kidney research scientists, just before they qualify for a first independent group leader position. Remarkable success stories of this programme include the Assistant Professorship of Sophie de Seigneux in Geneva and the Associate Professorship of David Hoogewijs in Fribourg—both former Junior Grant awardees.



NCCR Kidney.CH Retreat 2018 in Murten

STRENGTHENING SWISS KIDNEY RESEARCH

Naturally, I can only mention certain important cornerstones of the NCCR Kidney.CH in this overview. With all our activities we aim to strengthen the Swiss kidney research network. And we are doing this by supporting renal researchers and by bringing them together at retreats, symposia and teaching events, and by attracting new kidney researchers to Switzerland, including group leaders such as Olivier Devuyst, Andrew Hall and Vartan Kurtcuoglu.
I wish all the very best for the future of Kidney.CH.

François Verrey works at the Institute of Physiology of the University of Zurich and is the director of the NCCR Kidney.CH from August 2010 until July 2018.