SWISS NATIONAL CENTRE OF COMPETENCE IN RESEARCH

KIDNEY
CONTROL OF HOMEOSTASIS

NEWSLETTER ⁝ NO. 1 ⁝ DECEMBER 2010

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KEEPING THE BALANCE

Keeping the inner body environment in a homeostatic balance is essential for proper body function and thus for healthy life. The kidneys play a central role in controlling this homeostatic balance.

Kidneys are fantastic. Filtering and selectively reabsorbing nearly 200 litres of liquid from the blood every day, healthy kidneys precisely control body fluid volume and its salt and nutrient content and excrete waste products. As if this was not already enough to do, kidneys are also heavily involved in the regulation of red blood cell production, blood pressure, glucose metabolism, bone density and much more. To manage all this successfully, kidneys closely interact and cooperate with other systems like the cardiovascular, digestive and endocrine systems. "Over the past years important details have been elucidated in one or the other mechanism involved in body fluid homeostasis" says Prof. François Verrey from the University of Zurich. "However, how exactly this so vitally important homeostatic balance of the inner environment is controlled, remains largely unknown". And this is exactly what the newly established Swiss Centre of Competence in Research "Kidney Control of Homeostasis – Kidney.CH" hopes to throw light on.

As kidneys have so many vital functions, it is not surprising that impaired renal function has a tremendous impact on health. It is estimated that worldwide more than 50 million people suffer from chronic kidney disease (CKD) and that 850,000 people die from kidney failure every year. The death rate is likely to be even underestimated as most of the patients do not directly die from renal diseases but from complications such as cardiovascular diseases. Indeed, CKD patients are at risk for hypertension, atherosclerosis, heart failure, osteoporosis, neuropathy, anaemia and premature aging, to name but a few of them.

The costs for CKD treatment are enormous, currently estimated to account for 5% to 10% of all health-related expenses. In the US, CKD-related Medicare spending, including renal replacement therapy such as dialysis and transplantation, reached 57.5 billion dollars in 2007, accounting for 28% of the total Medicare spending. The already near-epidemic incidence of chronic kidney disease will likely further accelerate in the near future due to increasing life-expectancy

KIDNEY
CONTROL OF HOMEOSTASIS
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OF COMPETENCE IN RESEARCH

University of Zurich[UZH]

FNSNF
Swiss National Science Foundation

EDITORIAL

François Verrey

Kidney.CH stands not only for a web-based communication about kidney from Switzerland; it also means Kidney - Control of Homeostasis. The main aim of our new Swiss National Centre of Competence in Research (NCCR) is indeed to increase the understanding of how kidneys control the dynamic equilibrium of our body constituents. This control of homeostasis is achieved by a yet not well understood cooperative network that involves kidneys and other organs and systems. Similarly, our initiative is based on a cooperative network between research groups and individuals that contribute to kidney-centered homeostasis research at the Universities of Zurich, Basel, Bern, Fribourg, Lausanne and Geneva. With this Newsletter, the first of what we hope will become a tradition, our new Swiss-NSF supported NCCR Kidney.CH aims to establish a communication channel that will allow a wider audience to understand its aims and function as well as provide a medium to keep up-to-date with the activities of its members. The main news is of course that our Kidney.CH project started this summer on August 1, the Swiss National Holiday! Now that the celebrations are over, it's time to organise the functions and cooperations within Kidney.CH. In this first issue of our Newsletter you will learn more about the aims of our initiative and you will read about one Kidney.CH location: Geneva, our most westerly member.
Welcome to Kidney.CH!

François Verrey

and growing incidence of obesity and type-2 diabetes. Headquartered at University of Zurich, the Swiss research initiative "Kidney Control of Homeostasis – Kidney.CH" is supported by the Swiss National Science Foundation (SNSF) and combines over 20 research teams from all Swiss universities teaching medicine. Integrating leading Swiss experts in experimental and clinical nephrology, this initiative bridges the gap between basic and clinical research. The collaborative research projects are grouped in four modules around main homeostatic functions of the kidney. The goal is to advance knowledge and to provide a scientific and clinical basis for the development of novel preventive, diagnostic and therapeutic approaches. Practical support is provided to the research modules by platforms and reference centres in the field of rodent transgenesis, imaging, rodent phenotyping and human studies.

INTEGRATIVE RESEARCH APPROACH

The aim of Kidney.CH is not only to integrate researchers from all Swiss medical universities working in basic and clinical research, but also to integrate results obtained at the level of molecules, cells, tissues and organs into the complex picture, to increase our understanding of how this multi-layered complex network of organs and regulatory systems control homeostasis. This challenging integrative approach makes our initiative unique.
The research module "Oxygen" for instance investigates the systems and mechanisms involved in the

PORTRAIT

WHEN GENEVA MET OEDEMA

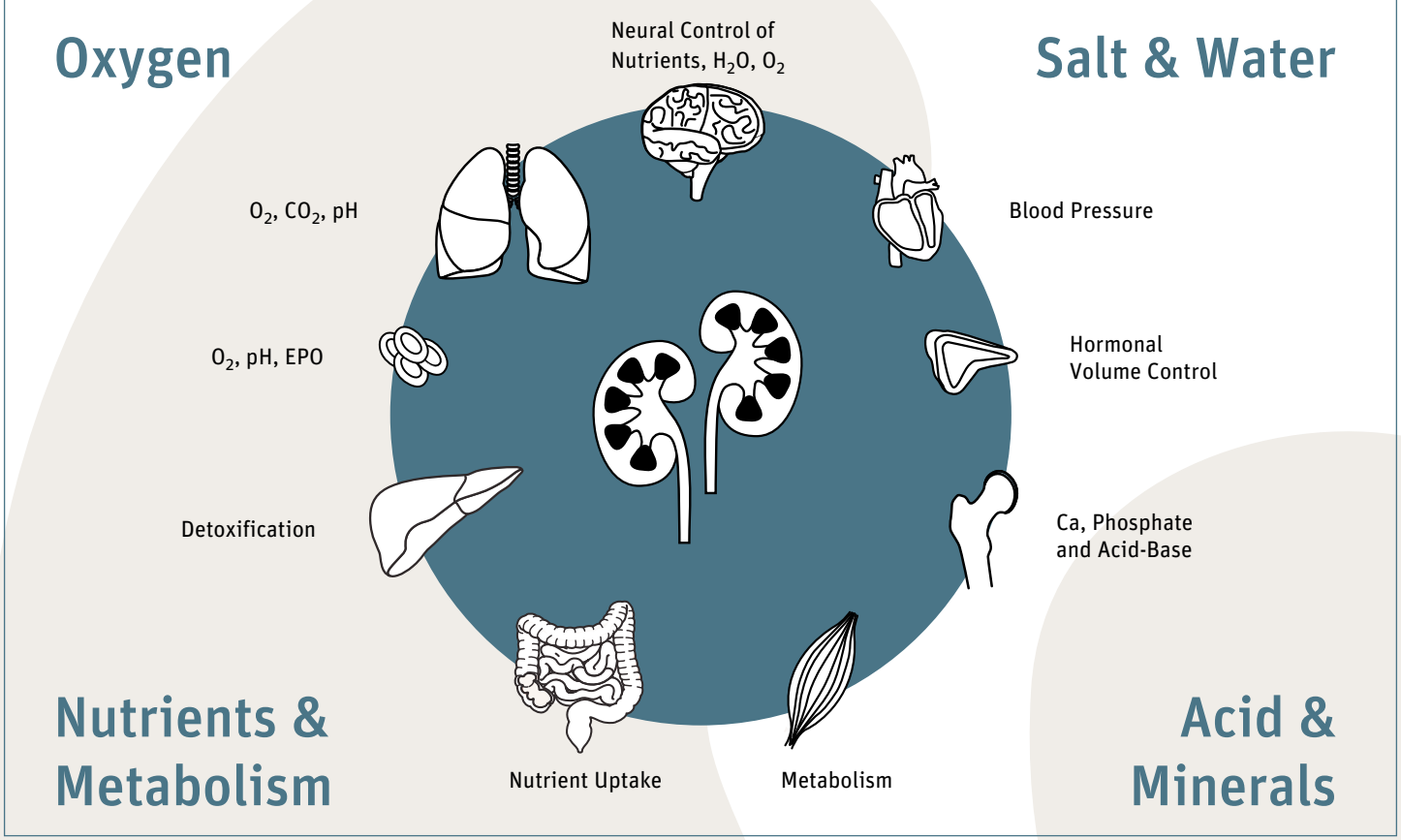
Geneva water fountain. © Geneva Tourism

The medical history of Geneva is intimately linked with the so-called renal clinical physiology. In the middle of the fifties, René Mach and his collaborators Alex F. Muller and Jean Favre did ground-breaking contributions to the understanding of the mechanisms of oedema and more specifically water and sodium retention in heart failure. They underlined the key role of aldosterone in this process and also contributed to the identification of the aldosterone escape phenomenon, that is important for limiting sodium retention in the presence of increased aldosterone levels. The leadership of Geneva in this field was honoured by the organization of the first meeting of the International Society of Nephrology in Geneva and Evian that was co-chaired by René Mach and Jean Hamburger in 1960. The creation of the Laboratory of Clinical Investigations by Alex F. Muller in the late sixties was the logical follow-up of this early interest in renal and hormonal mechanisms governing renal handling of sodium and water. In this stimulating context, the famous pharmacologist Bernard Rossier fell in love with aldosterone during his stay at the University Hospital of Geneva, before developing his research team in Lausanne. The follow-up of this initial breakthrough was taken up by two students of René Mach. First, the endocrinologist Michel Vallotton dedicated his scientific career to the translational study of the renin-angiotensin-aldosterone system, a hormone system regulating blood pressure and water fluid balance. It is worth to mention that it was him, who also developed the first radio-immunoassay to detect plasma angiotensin in humans as early as 1967. Second, the nephrologist Hervé Favre was fascinated by the potential role of the master enzyme Na,K-ATPase on sodium retention and hypertension. He did numerous clinical and laboratory studies tracking an inhibitor of Na,K-ATPase that was finally identified as endogenous ouabain in the nineties. He also made the original observation that an aldosterone-independent increase in Na,K-ATPase activity is the major contributor to sodium retention of nephrotic syndrome. More recently, Pierre-Yves Martin, who currently heads the service of Nephrology, did major scientific contributions in the fields of sodium and water retention in both, liver cirrhosis and cardiac failure.
As a logical consequence of this long research-tradition in Geneva on water and sodium retention, Eric Féraille from the University of Geneva leads the Kidney.CH research module "Salt & Water". He heads the renal research laboratory at the School of Medicine of the University of Geneva and contributes to Kidney.CH with specific projects on the role of Na,K-ATPase in normal and disturbed sodium homeostasis. The 2nd Kidney.CH member from Geneva is Udo Hasler, who studies the adaptive mechanisms of the organism to changes in extracellular salt content that usefully compliment work on sodium homeostasis. This laboratory work is strengthen by the head of the service of Nephrology, Pierre-Yves Martin, who brings in his large experience in clinical studies and investigates further the mechanisms of sodium retention in liver cirrhosis.

Pierre-Yves Martin

Eric Féraille

KIDNEY IN THE CENTRE OF HOMEOSTASIS NETWORK



START OF PROJECT:
1st of August 2010

DURATION OF 1ST PERIOD: 4 years

FINANCING:
CHF 16,5 M Swiss National Science Foundation;
CHF 3.5 M University of Zurich

NO OF PARTICIPANTS AND ASSOCIATED PARTICIPANTS: >20

HEADQUARTER: University of Zurich

PARTICIPATING SWISS MEDICAL UNIVERSITIES:
Basel, Bern, Geneva, Fribourg, Lausanne and Zurich

DIRECTOR: François Verrey

VICE DIRECTOR: Johannes Loffing

RESEARCH MODULE LEADERS:
Roland Wenger (Oxygen)
François Verrey (Nutrients & Metabolism)
Carsten Wagner (Acid & Minerals)
Eric Féraille (Salt & Water)

TECHN. PLATFORMS AND REF. CENTRES:
Imaging (Johannes Loffing)
Rodent Transgenesis (Edith Hummler)
Rodent Phenotyping (Carsten Wagner)
Human Studies (Felix Frey)

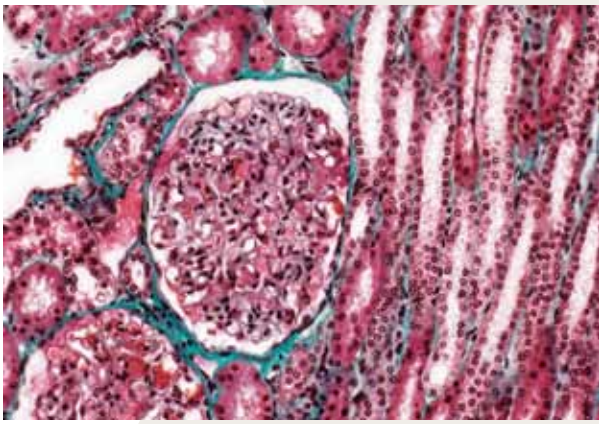
EDUCATIONAL PROGRAMMES:
Uyen Huynh-Do

control of oxygen supply to the organs. As lack of oxygen is the most acutely life-threatening situation, it is crucial to keep body oxygen levels in a homeostatic balance. Sensors in the kidney measure the level of oxygen in blood and produce as a response more or less erythropoietin (EPO), the hormone initiating red blood cell production. By looking at different stages of healthy and diseased kidneys, results may set a basis for novel approaches to protect kidneys as well as other organs from insufficient oxygen and blood supply (systemic hypoxia and ischemia).

Another module asks what impact reduced renal mass, e.g. only one instead of two kidneys has on the main metabolic functions of the body and the homeostasis of different organic compounds. That the metabolic syndrome (i.e. obesity, type-2 diabetes, and arterial hypertension) damages the kidney is well established. But does loss of renal tissue itself worsen or even induce a metabolic syndrome? And if so, what are the underlying mechanisms? Results from studies of this module, "Nutrients & Metabolism", will also contribute to assessing the long-term risk associated with removing one kidney.

Precisely controlled body levels of acid and minerals are critical for the function of our cells, bone metabolism and to avoid unwanted calcifications. Understanding the mechanisms sensing and controlling phosphate, calcium and magnesium is the main goal of the 3rd research module "Acid & Minerals". How does the healthy kidney adapt to and regulate changes in acid-base homeostasis? How do changes in mineral and acid excretion affect kidney stone formation? How does a high protein or high fat diet affect the acid and mineral body homeostasis?

The fourth module focuses on renal handling of water, sodium and potassium. Questions like how liver cirrhosis impacts on kidney function to induce oedema formation or how the intestine communicates with the kidney to control potassium homeostasis shall be clarified in the module "Salt & Water". Also novel insights into the pathogenic mechanisms of increased cardiovascular risk of a high salt diet shall be gained.



Micrograph of Human Kidney

Last but not least, a central aim of Kidney.CH is to support and teach the next generation of researchers in kidney-centered homeostasis. Kidney.CH will launch in 2011 a special PhD programme in renal physiology and pathophysiology. Additionally, a special programme is being launched to support subprojects submitted by junior researchers within the existing modules, and two Kidney.CH positions for assistant professors will be created at the University of Zurich.

OLIVIER DEVUYST JOINS KIDNEY.CH

Olivier Devuyst started as full professor in autumn this year at the Institute of Physiology at the University of Zurich, continuing his investigations on the pathophysiology of inherited kidney diseases, transport of salt and calcium by the kidney and the molecular mechanisms of water and solute transport across the peritoneal membrane.
He received his M.D. from the UCL Medical School in Brussels, Belgium and worked afterwards at the Technion Institute in Haifa, Israel (1989–1990) and from 1994 to 1996 as research fellow in the Department of Nephrology and Physiology at Johns Hopkins Medical School in Baltimore, USA. In 1997 he returned to UCL Medical School and has been elected into the Royal Academy of Medicine of Belgium in 2005. Since 1997, Olivier held a joint appointment with the Division of Nephrology at St.-Luc Academic Hospital of the UCL. He has received several international prizes and is leading the European Network for the Study of Inherited Nephropathies (EUNEFRON). He is associate editor of Peritoneal Dialysis International, Nephrology Dialysis Transplantation and member of the editorial board of Kidney International and Pflügers Archiv.
"Combining research data with genetic and clinical insights into a translational approach to better understand normal and diseased transport mechanisms and increasing international awareness for rare diseases affecting the kidneys are my priorities" he says.
Joining Kidney.CH he will be contributing to the research module "Acid & Minerals".

1ST KIDNEY.CH STUDENT'S DAY

On March 10, 2011, the official World Kidney Day, our first Kidney.CH Student's Day will take place in the beautiful Swiss capital of Bern. The Student's day is organised in two sessions. The morning session is open to all, while the afternoon session is reserved for students.
Invited key note speakers will talk in the morning session on selected topics around kidney control of homeostasis. Confirmed speakers are Prof. Uyen Huynh-Do and Prof. Felix Frey, both from the University Hospital Bern, Prof. Armin Kurtz from the University of Regensburg and Prof. François Verrey from the University of Zurich.
In the afternoon session PhD students as well as postdocs will present to each other their Kidney.CH projects.
The Kidney.CH Student's Day is part of the new Switzerland wide PhD programme in kidney physiology and pathophysiology, which will officially be launched later in 2011.

EVENTS

MECHANISMS OF SALT AND WATER HOMEOSTASIS IN THE KIDNEY
December 10, 2010
CHUV – Lausanne / Switzerland

OXYGEN 2011
January 8–12, 2011
Davos / Switzerland

RETREAT NCCR-KIDNEY.CH
January 21–22, 2011
Beatenberg / Switzerland

1ST NCCR-KIDNEY.CH STUDENT'S DAY
March 10, 2011
Bern / Switzerland

WORLD CONGRESS OF NEPHROLOGY – WCN 2011
April 8–12, 2011
Vancouver / Canada

OUTLOOK

1ST INT. SYMPOSIUM ON KIDNEY CONTROL OF HOMEOSTASIS
(to be announced;
May/June 2011)
Zurich / Switzerland

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NCCR-Kidney.CH
Institute of Physiology | University of Zurich
Winterthurerstrasse 190 | 8057 Zurich | Switzerland
Tel: +41 44 635 5216 | Fax: +41 44 635 6814
www.nccr-kidney.ch | info@nccr-kidney.ch