



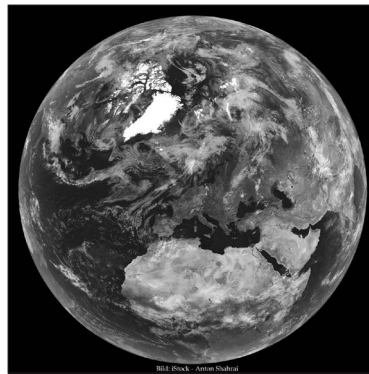
# ZIHP *News*

Zurich Center for Integrative Human Physiology

03-2018 • December 2018

## Editorial

Als wir klein waren, fanden alle Dinge Platz in zwei Kategorien: richtig oder falsch, gut oder böse, schwarz oder weiss. Wenn wir älter werden, wird es jedoch zunehmend schwieriger, klare Linien zu ziehen und wir müssen lernen, differenzierter zu denken. Trotzdem gibt es Situationen, in denen der Mensch auch als Erwachsener dazu tendiert, in schwarz/weiss Muster zu denken. Gerade Ergebnisse aus wissenschaftlichen Studien können zu solchen Gedankenmustern führen. So werden beispielsweise viele jungen Eltern verunsichert, wenn sie erfahren, dass Stress im sehr jungen Alter einen negativen Einfluss auf die Gehirnentwicklung von Mäusen hat. Auch weil ähnliche neurologische Veränderungen bei Kindern aus Waisenhäusern bekannt sind, übertragen diese Eltern die Studienergebnisse auf ihre Situation und denken, dass ihr weinendes Baby womöglich das gleiche Schicksal erleidet, wenn sie es nicht beruhigen können. Dabei vergessen sie, dass wissenschaftliche Resultate stark vom Kontext abhängig sind. Denn weder Mäusebabies noch Kinder aus Waisenhäusern können direkt mit Kindern aus einer intakten Familie verglichen werden.



*Weder die Welt noch die Wissenschaft ist schwarz und weiss.*

Zudem ist es wichtig, zu erkennen, dass wissenschaftliche Studien meist nur einen kleinen Teil der Wahrheit beleuchten und dass Zweifel weiterhin existieren. Mehr noch – Zweifel sind meist sogar die Grundlage neuer wissenschaftlicher Erkenntnisse. Dass es in der Wissenschaft Kontroversen gibt und dass Resultate in der Forschung im Kontext interpretiert werden müssen, kam beim diesjährigen ZIHP Symposium deutlich zum Vorschein. Lesen Sie mehr über das 14. ZIHP Symposium auf Seite 2.

Damit Laien wissenschaftliche Ergebnisse richtig einordnen können, ist es wichtig, dass sie richtig informiert sind und kritisch urteilen können. Dies hat sich das ZIHP zum Ziel gesetzt, indem es durch Publikationen auf Kommunikationsportalen und durch die Veranstaltungsreihe «Wissen-Schaf(f)t Wissen» der Bevölkerung Forschung näher bringt. Dieses Semester ist die Serie dem Thema «Zwischen Hoffnung und Risiko» gewidmet. Dass ein Pro oftmals auch ein Contra nach sich zieht, konnte man gut an den vergangenen Vorträgen sehen. Im nächsten Semester werden wir einige der hartnäckigsten Mythen des Alltags analysieren und zeigen, dass weder die Wissenschaft noch das Leben nur schwarz oder weiss ist.

When we were young, most things fell into either of two categories: right or wrong, good or bad, black or white. However, when we grow older it becomes more difficult to draw clear cut conclusions and we learn to differentiate. However, there are moments when adults still tend to think in black and white. Also scientific results can lead to such mind patterns. For example, many parents are unsettled when they learn that stress has a negative impact on the brain development of mice. Also since similar neurological changes are known in children from orphanages, these parents transfer the trial results to their situation and think that their crying baby may suffer the same fate if they can't calm him down. They forget that scientific results are often very context-dependent, as neither mouse babies, nor children from orphanages can be compared to children from an intact family.

Additionally, it is crucial to recognize that scientific studies only show a small part of the truth and that there can still be doubts. Science actually by its essence creates and is created by doubts. The fact that controversy often exists and that scientific results need to be interpreted within their context could be clearly seen at this year's ZIHP symposium (page 2).

In order to enable also non-researchers to develop critical thinking it is important to inform them well. The ZIHP brings research to the general public by the popular lecture series «Wissen-Schaf(f)t Wissen». Various speakers this and upcoming semester will show, that neither science nor life is either black or white.

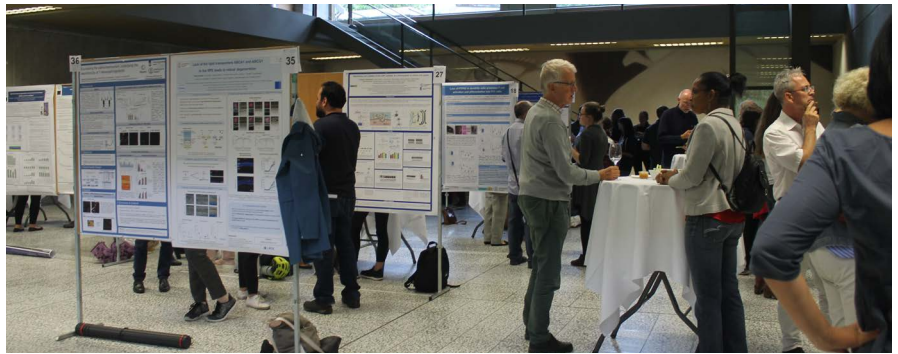
## The 14th ZIHP Symposium: Science is not black and white

Life Sciences are fascinating as each small research project helps understanding more and more how life works. But science is also controversial and conclusions from one study may not be generally valid. At the 14th ZIHP symposium renowned scientists and young researchers learned that the same enzyme causing blindness in diabetic patients is necessary for retinal development or that a treatment helping one patient may be harmful to another. It is crucial to recognize controversial data and to investigate the mechanisms behind them.

Sabina Huber-Reggi and Stefanie Maier

### Soluble epoxide hydrolase: Curse for diabetic patients, blessing for developing retinas

Scientific conclusions depend on the context. Our first keynote speaker Prof. Ingrid Fleming, from Goethe University, Frankfurt, showed this during the presentation of her research on damages to the retina, called retinopathies. In the adult, retinopathies are often caused by diabetes. Diabetic retinopathy is characterized by a loss of vascular cells in the retina, edema, and inflammatory events, which eventually lead to blindness. However, the mechanisms are largely unknown. Fleming's team discovered that the enzyme soluble epoxide hydrolase (sEH) is overexpressed in the diabetic retina of both human and mice. sEH generates from polyunsaturated fatty acids a dihydroxy metabolite, 19,20-DHDP, which accumulates in the diabetic eyes. 19,20-DHDP alters the localization of cholesterol-binding proteins in the cell membrane of blood vessels and compromises cell interactions, which results in vascular leakage and retinopathy. «Interestingly, an inhibitor of sEH successfully prevented the eye disease in diabetic mice», Fleming added. This is of outstanding interest for potential clinical applications.



Nevertheless, sEH and 19,20-DHDP are not only harmful. At low doses they are required for correct formation of new blood vessels during retinal development. Fleming and her team could demonstrate that in a mouse model, redox stress in the presence of an excess of oxygen during retinal development causes a downregulation of sEH and consequently an underproduction of 19,20-DHDP. As a consequence, blood vessels grow abnormally and then tend to leak and bleed, causing retinopathy. The same damages can be observed in the retina of very preterm infants, especially if they were exposed to oxygen supplementation. These infants are affected by the so called «retinopathy of prematurity», which can lead to blindness. Interestingly, supplementation with 19,20-DHDP in the mouse model could improve the phenotype. «Therefore, we hope that supplementation of formula for premature infants may help preventing the disease», Fleming concluded.

### Why some get high altitude sickness and some don't

Our next keynote speaker, Prof. Heimo Mairbäurl from the University of Heidelberg, continued by presenting his research on high altitude pulmonary edema (HAPE), a condition characterized by an excessive amount of fluid accumulation in the lungs and typically linked to an exposure to altitude above 3'000 m, where oxygen levels are low. For unknown reasons, however, it only appears in about 5% of the population.

Mairbäurl and his team investigated the mechanisms triggering this disease and tried to answer the question why only a small number of people is affected. In both, hypoxic (low oxygen supply) and normoxic (adequate oxygen supply) conditions, the lung constantly produces water, which needs to be removed by reabsorption. This occurs by an osmotic gradient, generated by active reabsorption of sodium (Na). «Therefore, one could speculate that people with a higher susceptibility to HAPE might have a low capacity of sodium transport», Mairbäurl said. Indeed, administration of dexamethasone, a known Na channel expression stimulant, can successfully prevent the occurrence of this disease. The research team members could further support this theory as they measured an inhibited nasal Na-transport in HAPE-susceptible individuals. They further hypothesized that in hypoxic conditions, such as at high altitude, Na-transport may be naturally reduced. This would be manageable for most people but may cause HAPE in those, who already have low capacity of Na-transport. Indeed, Mairbäurl and his team found out that hypoxia decreases epithelial Na-transport in the lung by inhibiting synthesis of endothelial Na channel proteins as well as their transport to the apical plasma membrane. Moreover, they found out that hypoxia increases activity level of the  $\alpha$ -subunit of the transcription factor HIF-2, which controls the available amounts of epithelial Na channels in the apical plasma membrane, likely by con-

trolling its degradation. Therefore, it is possible that the reduced epithelial Na-transport in hypoxia, together with the already low capacity of Na-transport in normoxia in HAPE-susceptible individuals, causes the susceptibility to this disease.

### How the oxygen sensor PHD1 controls skeletal muscle mass

An increase in muscle mass promotes health. Amongst others, it leads to a lower risk of injury and an increased quality of life, especially in the elderly. Unfortunately, it is only poorly understood how muscle mass is regulated. However, the team around our next keynote speaker, Prof. Katrien De Bock from ETH Zurich and associated ZIHP member, has successfully identified a mechanism through which amino acid sensing mechanisms control skeletal muscle mass. Muscle mass is determined by the balance between protein synthesis and protein breakdown. The master regulator of this process is mTORC1, which, once activated, promotes protein synthesis, leading to muscle growth, explained De Bock. Protein synthesis is a highly energy -i.e. oxygen - demanding process. Therefore, protein synthesis needs to be adapted to oxygen availability, and oxygen sensing mechanisms need to integrate with the protein synthesis machinery. A main oxygen sensor in the muscle is Prolyl Hydroxylase Domain (PHD1). The team around De Bock could show that in the presence of oxygen PHD1 controls protein synthesis in response to the amino acid leucine, but surprisingly not in response to other anabolic stimuli such as insulin and contractions. Mechanistically, PHD1 interacts with the leucine sensor aminoacyl tRNA synthetase (LARS), which activates mTORC1 by promoting its recruitment to the lysosomal membrane. Thus, oxygen fine-tunes

## Awards for the best talk and the best four posters

Congratulations to the winners:

**Daria Vdovenko**, Center for Molecular Cardiology, UZH (best presentation)

**Anne Jomard**, Inst. of Food, Nutrition and Health, ETHZ

**Bettina Lanfranchi**, Inst. of Veterinary Anatomy, UZH

**Felix Scholkmann**, Biomedical Optics Research Lab, Dep. of Neonatology, USZ

**Fraser Simpson**, Inst. of Veterinary Physiology, UZH (best posters)

the anabolic response to amino acids and allows the increase in skeletal muscle mass.

### Precision medicine in psychiatry

«Psychiatry may be the field of medicine which is the most controversial», Prof. Paul Hoff introduced his presentation. The renowned psychiatrist and deputy director of the Department of Psychiatry, Psychotherapy and Psychosomatics of the University of Zurich presented how complex it is to diagnose psychiatric disorders. Today, diagnosis is mainly based on the presence of a defined number of clear, ideally observable, psychopathological symptoms. This approach allows universal definitions of mental disorders but it constraints patients into categories and may not help them getting cured. After all, treatments target symptoms and not disease categories as such. And the same symptom may occur in different psychiatric categories. «There are no clear boundaries for example between schizophrenia and bipolar disorder» – Hoff explained – «We need to move away from thinking in strictly distinct categories.» As a good starting point, instead of investigating mechanisms behind disease categories such as depression or psychosis, researchers have begun to focus on symptoms such as anxiety. «But this is not enough. Psychiatry should move towards taking into account the whole person, thus towards personalized precision medicine», Hoff added. Precision medicine in such a

broad sense may deconstruct traditional categories and, besides symptoms, may take into account several other heterogeneous aspects such as genetical analysis, measurements of brain activity and inflammatory markers, cognitive tests, life experiences and values. This mainly data-driven approach, labeled «qResearch Domain Criteria (RDoC)», aims at dissecting current clinical syndromes into more homogeneous clusters, finally making possible to develop more specific and effective therapies. However, Hoff stressed, this does not imply a diminished importance of subjective and interpersonal aspects in psychiatry.

### Research of the ZIHP network presented by the young generation

In addition to the keynote lectures, we listened to 9 excellent oral presentations from young researchers of our network, most of them PhD students of the PhD Program imMed. The oral presentations as well as the posters in the main hall showed the broad range of topics covered by our research groups. These young researchers also experience in their daily work that science can be controversial. As for example Marianne Spalinger, who presented her research showing that the genetical background of patients may affect the beneficial effect of treatments for inflammatory bowel diseases.

The ZIHP Symposium is a great opportunity to gather experiences, initiate collaborations, and broaden networks. This year, graduates also had the opportunities to meet our sponsors – AstraZeneca, Kelly Services, and Microsynth, and to learn about job opportunities.

## Save the date: 15<sup>th</sup> ZIHP Symposium on August 23, 2019

Do not miss this opportunity to discuss your cutting-edge results and to build up your network! More information on the program will follow soon.



# WISSEN-SCHAFT WISSEN

## Laufende Herbstausgabe 2018

Zwischen Hoffnung und Risiko

SPECIAL



### Smiling Gecko für Kambodscha

Kambodscha ist noch immer eines der ärmsten Länder der Welt. In seinem Vortrag berichtete der berühmte Fotograf **Hannes Schmid**, warum und wie er sich in Kambodscha engagiert. Mehr dazu in den nächsten *ZIHPNews*.



### Vertikales Bauen für mehr Platz und Lebensqualität

Dr. **Paul Friedli** zeigte auf, wie in die Höhe gestapelte Stadtviertel eine Antwort auf den Platzmangel wäre und wie daraus eine neue Art des sozialen Zusammenlebens entstehen könnte. Mehr dazu in den nächsten *ZIHPNews*.



### Genforschung - Segen oder Gefahr?

Die Biosicherheitsexpertin Dr. **Ursula Jenal** diskutierte über den Umgang mit dem Missbrauchspotential von neuen hoffnungsvollen biotechnologischen Methoden, wie die Genschere CRISPR/Cas9. Mehr dazu auf dem → [Portal des Forums für Genforschung](#).



### Medizin und ihre Risiken

Dr. **Peter Kleist**, Geschäftsführer der Kantonalen Ethikkommission Zürich, zeigt am **10. Dezember 2018** auf, wie viel Wissen wir uns aneignen sollen, um kompetent Entscheidungen über medizinische Massnahmen zu treffen.

## Vorankündigung der Frühlingsausgabe 2019

### Mythen versus Realität

Verschiedene Redner werden einigen der hartnäckigsten Mythen des Alltags auf den Grund gehen.

Bereits festgelegte Redner:

#### 4. März 2019

Prof. Dr. **Martin Röösl**i, Professor für Umweltepidemiologie, über die Effekte von Handy- und WLAN-Strahlen auf die Gesundheit.

#### 25. März 2019

Prof. Dr. **Stephan Vavricka**, Facharzt für Innere Medizin und Gastroenterologie, über Mythen bei der Ernährung.

#### 27. Mai 2019

Prof. Dr. **Martin Meyer**, Titularprofessor in Neuropsychologie, über Gehirntrainings und Alternativen, um das Gehirn fit zu halten.

Mehr Informationen über weitere Redner, Themen und Daten werden in Kürze auf unserer Homepage veröffentlicht:

→ [Wissen-Schaf\(f\)t Wissen](#)

Wir freuen uns, Sie auch nächstes Semester an den Veranstaltungen wieder begrüssen zu dürfen.

## Welcome as a ZIHP member

**PD Elena Osto** was accepted as a **new ZIHP member**. She is an independent group leader at the Center for Molecular Cardiology of the University of Zurich and at the Laboratory for Translational Nutrition Biology of the ETH Zurich. She was recently granted with an own PRIMA grant from SNF. Her research focuses on cardio-metabolic diseases. The aim is to understand at the molecular level the communication between the cardiovascular system, the gut-liver and adipose tissue in the pathophysiology of immune-inflammatory and metabolic disarrangements such as diabetes type 2 and obesity.

## Press review

### → B-Zellen sind mitverantwortlich für Hirnschäden bei Multipler Sklerose

Ein von ZIHP-Mitglied Prof. Roland Martin geleitetes Forscherteam fand heraus, dass bei Multipler Sklerose (MS) nicht allein T-Zellen, sondern auch andere Abwehrzellen, die B-Zellen, für Entzündungen und Schäden im Gehirn mitverantwortlich sind. Dies eröffnet ganz neue Therapieoptionen im mühsamen Kampf gegen diese heimtückische Krankheit.

Medienmitteilung UZH, 4. September 2018

### → «Viele Probieren mal aus Neugier»

Das Bild einer Gesellschaft, die zu grossen Teilen ausschweifenden Sex praktiziert, stimmt nicht. Die grosse Mehrheit der Schweizerinnen und Schweizer verhalte sich gesund. Dies ist das Resultat einer gross angelegten Studie in der Schweiz rund um ZIHP-Mitglied und Sexualmedizinerin Prof. Brigitte Leeners. In diesem Interview gibt sie Aufschluss darüber, wie Herr und Frau Schweizer beim Thema Sex ticken.

Luzerner Zeitung, 7. September 2018

### → Ein Sonderfall in der Unileitung

Ein Interview mit ZIHP-Mitglied Prof. Beatrice Schimmer über sich selbst und ihre neue Position als Direktorin der Universitären Medizin Zürich.

Tages Anzeiger, 18. September, 2018

### → Warum haben Männer Brustwarzen?

Der Mensch ist mit Körperteilen ausgestattet, deren Funktion längst sekundär geworden sind: Weisheitszähne, Achselhaare, Steissbein, oder männliche

Brustwarzen. In der Sendung Treffpunkt erklärt Evolutionsmediziner und ZIHP-Mitglied Prof. Dr. Frank Rühli, warum die Evolution des Körpers den sich extrem schnell verändernden Lebensumständen hinterherhinkt. SRF Radio 1, Sendung «Treffpunkt», 18. September, 2018

### → Lösen Darmbakterien die multiple Sklerose aus?

Wie die Autoimmunkrankheit Multiple Sklerose (MS) genau entsteht, liegt weitgehend im Dunkeln. Forscher aus Spanien, Nordamerika und der Schweiz, unter ihnen Neurologe und ZIHP-Mitglied Prof. Roland Martin, haben nun aber entdeckt, dass bestimmte Bakterienarten im Verdauungstrakt eine Rolle spielen könnten. Weitere Untersuchungen sollen nun ihre genaue Wirkungsweise klären sowie neue Behandlungsmöglichkeiten prüfen.

NZZ, 11. Oktober, 2018

### → Zebrafischlarven helfen bei der Entdeckung von Appetitzüglern

Forscher der amerikanischen Harvard University und der Universität Zürich - unter Ihnen ZIHP-Mitglied Prof. Thomas Lutz - haben unter anderem mit Hilfe von Zebrafischen eine neue Strategie für die Suche nach psychoaktiven Medikamenten entwickelt. Dieser Artikel beschreibt, wie es ihnen gelungen ist, eine Reihe neuer Appetitmodulatoren zu finden. Um die Forschung voranzutreiben, hat Josua Jordi, Erstautor der Studie und ehemaliger Doktorand unseres PhD Programms, gemeinsam mit Kollegen das Start-up EraCal Therapeutics gegründet.

Medienmitteilung UZH, 1. November 2018

## Events supported by the ZIHP

Thursday April 4, 2019

**Sleep & Health Symposium 2019**

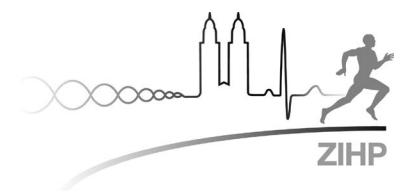
More information will follow soon.

Further events will be organized. An updated list can be found on our website: → [www.zihp.uzh.ch/en/events.html](http://www.zihp.uzh.ch/en/events.html)

## Recent publications

A list of publications of all ZIHP members can be found on the ZORA website

→ <http://www.zora.uzh.ch/view/subjectsnew/10076.html>





## Retreat 2018 of the PhD Program in Integrative Molecular Medicine (imMed)

Milica Bugarski

The annual imMed Retreat took place this year at the UZH Irchel Campus. Although being only a half-day event, it was warmly welcomed because it gave us a chance to nicely step out of our daily, ordinary routines.

It began with 3 sessions of presentations from PhD students. The speakers gave insight into their research and covered many interesting topics. We have learned why a banana does not kill us and how close we are from male contraception pill (there were a lot of concerned questions about it from the audience). These sessions would not have been so well organized and we would not have been on time for our coffee break if there were no Katrin Klee, Amy Taheri and Twinkle Vohra chairing them. The excellent quality of all presentations for sure made committee's life difficult, but Prof. Dr. Thomas



Lutz, Dr. Lucia Rohrer and our student representative Urs Wegmann managed this challenge perfectly and the well-deserved best-presentation award was given to Twinkle Vohra. Congratulations Twinkle!

It was around 5 pm in the evening when we came to the end of the Minisymposium. The most helpful question/answer session with a PhD Program representative was followed by the walk to Wirtschaft Ziegelhütte. There is a funny saying - if you don't have pictures of it, it didn't happen! A half an hour

walk gave the participants the opportunity to relax in the sun and Adisa Trnjanin, our retreat photographer, to take some of the many pictures from this day. Thank you Adisa for making this year's retreat memorable!

Upon arriving at Ziegelhütte, we were served an apéro on their beautiful terrace – a perfect place to celebrate the hard day's work done. After dinner, most of us came to the end of the imMed Retreat 2018, whereas football lovers enjoyed the public viewing of the Football Worldcup at the Biergarten.

Success is a word that perfectly describes this retreat and a big thank you goes to all of the participants for contributing to this impression!

[→ Photo gallery](#)





## New students

Since July 2018 twelve new students who were accepted to the PhD Program in Integrative Molecular Medicine (imMed) started their work here in Zurich. Welcome!

Berber Mesut, Institute of Anatomy, UZH  
Gamakharia Salome, Institute of Veterinary Physiology, UZH  
Ging Kathi, Institute of Anatomy, UZH  
Krohn Patrick, Institute of Physiology, UZH  
Makris Georgios, Division of Metabolism and Molecular Pediatrics, Kispi  
Mamie Céline, Division of Gastroenterology and Hepatology, USZ  
Nieri Daniela, Institute of Physiology, UZH  
Pfefferlé Marc, Department of Internal Medicine, USZ  
Schraner Marissa, Institute of Veterinary Physiology, UZH  
van Cromvoirt Ankie, Institute of Veterinary Physiology, UZH  
Weber Lea, Institute of Physiology, UZH  
Weber Ronja, Division of Pulmonology, Kispi

## Vision 2020 - a personal perspective

**Current topic:** → «Industrial biotechnology»

December 13, 2018:  
→ **Insights into Roche Diagnostics - How we drive innovation in biotechnology**  
Dr. Lisanne Luks, Management Start up - Roche Diagnostics  
17:00 h UZH Campus Irchel, lecture hall Y03 G91

**Topic of spring semester 2019:** → **Disease diagnostics and therapy**

## Postgraduate courses

June 5/6, 2019 (2 full days)  
→ **Introduction to human physiology: Membrane transport / Signal transduction**

June 20/21, 2019 (2 full days)  
→ **Mouse physiology and pathophysiology**

September 12/13, 2019 (2 full days)  
→ **Introduction to human physiology: Sensory systems: How we hear and see**

September 18/19, 2019 (2 full days)  
→ **Introduction to human physiology: Regulation of cardiovascular function**

September 19 (2 full days)  
→ **Molecular Biology Methods**

Fall semester 2019 (2 full days)  
→ **Introduction to human physiology: Respiration and blood**

## imMed alumni event

**February 21, 2019**

→ **Academia, industry and more**

Dr. Martin Stucki, Sanofi Genzyme, Baar  
Dr. Josua Jordi, EraCal Therapeutics, Zurich  
17:30 h, UZH Campus Irchel, lecture hall Y16 G05

### Imprint

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Editorial staff: Stefanie Maier, Sabina Huber-Reggi, Heidi Preisig and Max Gassmann  
URL: <http://www.zihp.uzh.ch>, E-mail: [info@zihp.uzh.ch](mailto:info@zihp.uzh.ch), Tel +41 44 635 50 88/47