Universität Zürich[UZH]

ZIRPNews

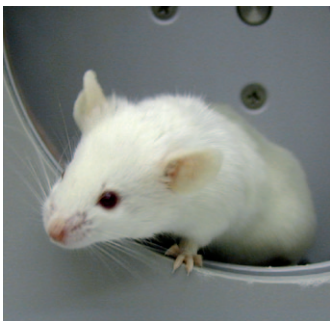
Zurich Integrative Rodent Physiology July 2014

Zurich Integrative Rodent Physiology (ZIRP): Bundled competences for research

Animal experiments are one of the key requisites for progress in medical research. Rodent models enable better insight into complex biological processes. Newly developed techniques and high-throughput phenotyping procedures – like imaging modalities, miniaturized implantable devices and laboratory analyses – enable investigations of many processes in living animals.

All of these techniques have in common that the acquisition of the equipment is costly, operation and servicing is technically demanding, and downscaling to small rodents is most often challenging. Skilled staff with appropriate know-how is needed for their optimal utilization. As a consequence, the individual researcher most often does not have the ability to acquire all necessary equipment, cover its running costs and pay technical staff for operation.

→ Zurich Integrative Rodent Physiology (ZIRP) provides infrastructure and equipment with a focus on analyses of rodent physiology on a shared resources basis, thus making complex techniques available at low cost to all researchers.



ZIRP's mission: facilitate and improve experimental work

ZIRP pools the researchers' needs and facilitates their work by organizing and maintaining key infrastructure, providing training and support, and offering a number of basic services.

ZIRP's services are organized to facilitate customized solutions. In addition to special technical platforms, a number of basic services are provided. For example,

- workspace, completely equipped «ready to use» or free space to build up own equipment
- sample collection
- administration of substances and
- surgical services.

ZIRP's strategy: flexible, research-driven approach - individually tailored solutions

ZIRP offers flexible solutions and individual strategies in close cooperation with researchers by adapting procedures or combining different techniques with respect to individual requirements. ZIRP's skilled staff utilizes a broad array of standard experimental procedures, adapted to the characteristics of small rodent models.

ZIRP's vision: one-stop - all services from one source

ZIRP seeks to offer all services from one common source with all experimental work performed within the ZIRP - from transferring the animals into ZIRP's animal housing facility and performing different experiments to having the data available ready for analysis. ZIRP continuously upgrades its services and the ZIRP staff members are permanently refining existing techniques – always considering the researchers' needs.

Imaging Platform

Non-invasive imaging modalities offer numerous options for morphologic analyses and tracking of biological processes like disease progression or metabolic pathways. The → ZIRP imaging platform provides a number of state-of-the-art imaging devices as well as associated services and support.

Micro CT

In vivo micro-computed tomography is a non-invasive tool to visualize the animal's morphology. Common applications include imaging of the skeleton or bone samples, lung, cardiovascular system, soft tissue and tumors.

For soft tissue imaging a multitude of contrast agents are available, e.g. for the depiction of vessels or organs (Figure 1).

High throughput imaging at low radiation doses is ideally suited for morphological phenotyping (Figure 2). High resolution scans are the method of choice for quantitative morphometric image analyses (Figure 1).

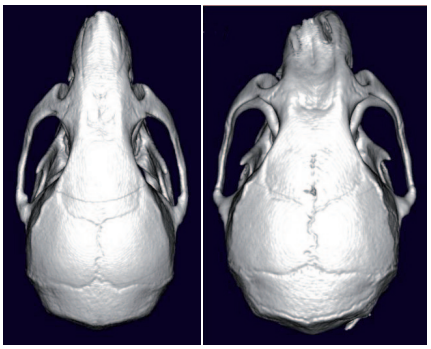


Figure 2: Skull phenotyping in mice: normal (left) versus malformed skull (right).

«Optical imaging of tumour cells is an invaluable tool for long term quantitative monitoring of cancer growth and spread in living mice.»

Prof. Ian Frew, ZIHP Assistant Professor
Institute of Physiology, University of Zurich

Optical Imaging

Bioluminescence and fluorescence imaging allow the visualization and quantification of biological processes in the living animal in real-time.

Bioluminescence imaging utilizes native light emission from bioluminescing organisms. The DNA encoding the luminescent protein (for example firefly luciferase) is incorporated into the laboratory animal. For light emission the corresponding substrate (for example D-luciferin) needs to be injected into the animal prior to imaging (Figure 3, left).

Bioluminescence imaging is commonly used for in vivo studies of cancer progression, development or cell migration, or infection.

In addition, bioluminescence tomography allows the quantitative analysis of volumes and therefore, the precise three-dimensional follow up of disease progression. This is useful for the growth and spread of a tumor (Figure 3, left).

Fluorescence imaging requires a specific fluorescing agent able to absorb and emit light of a certain wavelength which needs to be injected

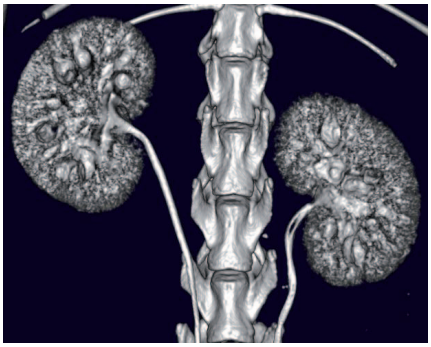


Figure 1: Visualization of kidney cysts in a rat using contrast agent, kidneys are cut longitudinally to better visualize the cysts.

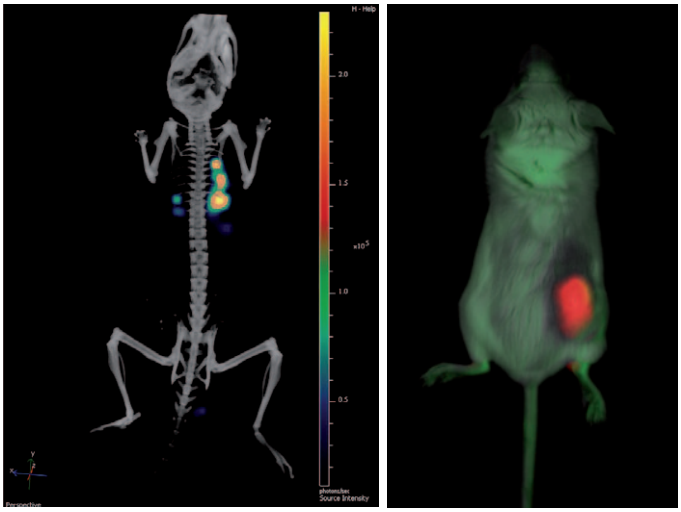


Figure 3: Bioluminescence imaging of a mouse lung tumor, co-registration of 3D micro CT and bioluminescence data (left) and visualization of subcutaneous tumor vascularization with fluorescence imaging using a targeted fluorescent agent (AngioSense 680, Perkin Elmer, right).

prior to imaging. Targeted fluorescent markers actively bind to target structures, thus allowing the selective visualization of specific tissues or processes like tumor vascularization or inflammatory processes (Figure 3, right).

The ZIRP imaging platform is equipped with the following instruments:

- IVIS Spectrum optical imaging system (bioluminescence and fluorescence, Perkin Elmer)
- Quantum Fx micro CT (Perkin Elmer)
- Body composition analyzer (EchoMRI) for the measurement of whole body fat, lean, free water, and total water masses in living awake rodents.

Additionally, ZIRP offers solutions for contrast agent application, e.g. catheter placement and perfusion pumps for continuous intravenous infusion.

Corresponding image analysis software and server space for data exchange and storage is offered in cooperation with the Center for Microscopy and Image Analysis (ZMB) of the University of Zurich.

«MicroCT imaging gave us a wealth of phenotypic information about our mice - including new aspects that we didn't even realise.»

Prof. Steven A. Brown
Institute of Pharmacology and Toxicology, University of Zurich

Telemetry Platform

Radiotelemetric transmitters enable the continuous and contact-free collection of physiological data in conscious and freely moving animals. For example respiration rate, body temperature, activity, pressure or biopotential signals can be monitored (Figure 4). The implanted telemetry device transmits the digitalized data via radio frequency signals to a nearby receiver plate.

«ZIRP's telemetry platform allows us to match in vitro organ chamber experiments with in vivo blood pressure measurement.»

Dr. Elvira Haas, Research Unit, Div. of Internal Medicine, University Hospital Zurich

The advantages are multifaceted: Since the miniaturized transmitter and all catheters and leads are completely internalized, the risk of wound infection is eliminated, animals can be group housed in their home cage directly after implantation and handling of animals is minimized in order to avoid stress related artefacts.

«Telemetry is a key technology in hypertension research. ZIRP provides not only the equipment but also the skills and the know-how for successful telemetry.»

Dr. Branko Simic
Center for Molecular Cardiology, University Hospital Zurich

Telemetric measurements can be combined with other techniques like running wheels, climate chambers etc. Furthermore, instrumented animals can serve as their own controls.

The → ZIRP telemetry platform offers four different transmitter types for the acquisition of pressure and biopotential signals, body temperature and activity in mice and rats as well as the relevant hard- and software system for data acquisition and analysis. Other transmitters can be implanted on request. ZIRP's entire service includes transmitter refurbishment, surgical implantation and postoperative care with the animal handed over «ready to use».

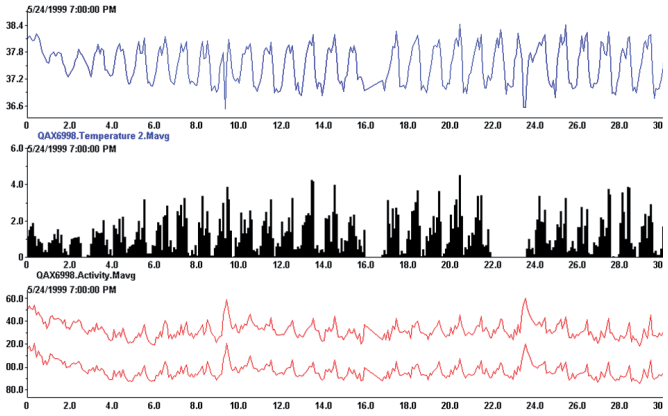


Figure 4: Course of body temperature, motor activity and blood pressure in a rat during 30 days after transmitter implantation.

Laboratory Platform

Biochemical analyses of biological fluids offer insight into the function of various organ systems. Animal models can be assessed by analyzing a multitude of different parameters in one sample.

In rodents such an evaluation is often hampered by the small volume of their body fluids – a limitation which is even more critical in case of repeated measurements during longitudinal studies or the analysis of a large number of parameters in one sample.

High quality analyses of small samples

The →ZIRP laboratory platform offers high quality analyses for a wide range of biochemical and toxicological parameters in small volumes of any biological fluid. All analyses are tailored to the researcher's specific needs. Consistency, high accuracy and technical attention to precious samples are the essential priorities.

All methods are ideally suited for the analysis in rodent models. Additionally, the laboratory platform has the capacity for high-throughput analysis of human samples from large population cohorts where small sample size could be also a limitation (e.g. genotype-phenotype correlations).

Figure 5: Automated analysis of serum samples

The platform utilizes liquid chemistry technologies, which allow the acquisition of a large array of reliable biochemical analyses in minimal volumes (usually < 10-15 µl) with a high throughput (> 200 analyses per hour) in combination with an automated calibration system.

The platform provides the following equipment:

- biochemical analyser (Beckman UniCel DxC 800 Synchron)
- osmometers (Advanced Osmometer 2020)
- Mettler-Toledo T50 microtitrator
- Radiometer ABL 80 CO-OX blood gas analyzer

The platform also offers a series of special protocols such as those for quantification of bicarbonate, uromodulin, cyclic AMP, vasopressin, ammonium as well as the possibility to develop new assays.

Challenging sample collection

Sample collection can be challenging in small rodents. Pre-analytical errors occurring during sample collection or post-processing are a major source of missed or wrong diagnoses. Therefore, ZIRP not only offers help with any type of sample collection but also a collection of tubes suited for optimal processing of small amounts of different types of biological fluids.

«This platform enables analyses of numerous parameters in small sample volumes with high accuracy.»

Prof. Olivier Devuyst
Institute of Physiology, University of Zurich

Zurich Integrative Rodent Physiology (ZIRP)

Zurich Integrative Rodent Physiology (ZIRP) is an interdisciplinary core facility at the Irchel campus of the University of Zurich. Its mission is to support and strengthen research activities in the field of integrative physiology by providing infrastructure and know-how for the advanced analysis of rodent physiology.
ZIRP is open to all researchers from the University of Zurich, the ETH, other research institutions and companies. ZIRP is currently supported by the ZIHP, the NCCR Kidney.CH and the Institute of Physiology, UZH.

General contact
→ www.zirp.uzh.ch 044 635 50 95
Dr. P. Seebeck → petra.seebeck@uzh.ch
Winterthurerstrasse 190, 8057 Zürich

Imaging and Telemetry Platform
S. Pfundstein → svende.pfundstein@uzh.ch
Laboratory Platform
N. Nägele → nadine.naegele@uzh.ch

«ZIRP's mission is to facilitate and improve experimental work in rodent models.»

Dr. Petra Seebeck , ZIRP Manager