

# Of researchers and rodents

The Phenomics Center keeps 25,000 laboratory mice under the most modern conditions. *Globe* visited the centre to discover why researchers still have to rely on animal models.

TEXT Samuel Schlaefli PHOTO Daniel Winkler

The six-storey Molecular Health Sciences Platform building on ETH Zurich's Höggerberg campus is a modern and elegant addition to the skyline. But to find out what makes the HPL building really unique you have to venture inside. Three floors down in the building's basement is an area that is accessible only to staff members who are wearing the right badge. We first meet Operations Manager Jonathan Ward in a changing room on the first basement level. "Please take off everything apart from your underwear," he says, handing us shirts and trousers made from a dark blue fabric.

## Air showers and overalls

At the heart of the Molecular Health Sciences Platform building – which was inaugurated in 2013 – is the Phenomics Center. This is where researchers working at the interface between biology, medicine and technology have access to cutting-edge laboratories and professional husbandry facilities for their mice. Ward takes us two floors further down into the bowels of the HPL building, passing through several locked doors on the way. Before we enter the cleanroom facility, we have to pass through another infection control barrier. We take off our blue shirts and trousers and pull on fine-checked, light blue synthetic overalls that have already been sterilised. Our cleanroom attire is rounded off with a mouth mask, hair-

net, rubber gloves and plastic shoes. But there's still one last step to go: we need to pass through an air shower to blow off any remaining particles that might still be clinging to our overalls. One by one, we spend a minute standing in a glass cabin while a howling blast of air gets us thoroughly clean. Finally, the glass doors on the other side of the barrier open and we are allowed to enter the cleanroom area.

"These rigorous infection control measures aren't just to protect us," says Claudine Blaser, who welcomes us to the cleanroom after our air shower.

"We need them to shield the mice against any micro-organisms that could be carried in by the animal care technicians or scientists as these could influence the research results." Blaser has spent the past six years setting up the Phenomics Center.

A qualified biologist with a PhD in immunology, she returned to the place where she took her degree in 2010 after several years working in industry. "I've always been someone who loves setting things up and getting projects off the ground," she says. The Phenomics Center was the perfect test of her



Claudine Blaser set up the Phenomics Center.



A 3,000 square metre cleanroom facility with space for 40,000 mice



Escape from the light: mice perceive the colour red as black.

skills, boasting a 3,000-square-metre cleanroom facility, space for 40,000 mice, 30 laboratories with cutting-edge analytical equipment and computer infrastructure, and an entire floor of technical facilities for ventilation, temperature regulation and steam generators. The Phenomics Center is used by a total of 40 research groups from six departments, primarily comprising doctors, immunologists, oncologists and biologists. What unites them is their search for a better understanding of diseases such as cancer, diabetes, inflammatory disorders and infections.

## Understanding the organism as a whole

Manfred Kopf is an immunologist and Professor of Molecular Biomedicine at the Institute of Molecular Health Sciences. His group's primary focus is on autoimmune and inflammatory diseases such as asthma, psoriasis and arteriosclerosis. Kopf's office is situated just a few floors above the Phenomics Center, and he relies on mouse models for 90 percent of his research. "We're trying to understand the role of the immune system as a function of the organism as a whole. That's why we need animal models to enable us to establish causalities between deviations in the genome and diseases," Kopf explains. He believes that a genetic and biochemical understanding of the organism is the basis for developing new therapies.

Opponents of animal experimentation argue that these kinds of experiments are unnecessary because they can now be replaced by computer simulations, but Kopf disagrees: “Nobody has ever launched a drug that was tested for efficacy solely on the basis of computer experiments. Higher organisms are much too complex for that.” He insists that his group carries out animal experiments only in cases where there is no in vitro or in silico alternative. Their motivation is both ethical and financial: “Animal experiments are time-consuming and very expensive.”

**First encounter with the rodents**  
Claudine Blaser leads us to an animal breeding laboratory in the cleanroom area. It smells like a pet shop. Some 1,500 mice are housed here, with three to five mice occupying each of the shoebox-sized plexiglass cages. The cages are neatly arranged in mobile metal racks. We immediately hear the monotonous drone of the ventilation system that supplies each cage with its own filtered supply of fresh air. This prevents the cross-contamination of pathogens between cages. The mice themselves don’t make a sound, and it would be easy to miss them at first glance. Many of them are holed up in

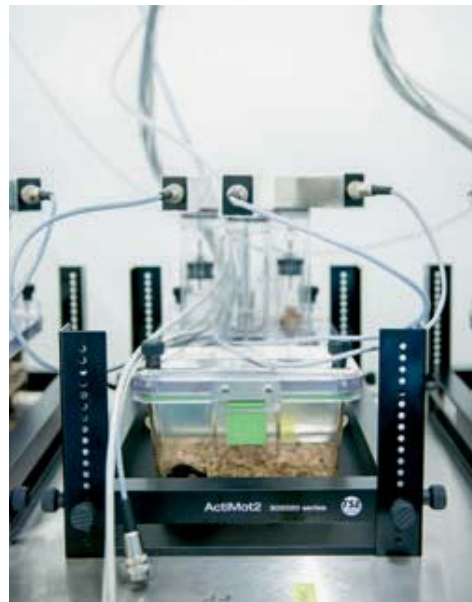
translucent red boxes, which provide the nocturnal animals with a hideaway to escape the light.

The Phenomics Center currently houses a total of 25,000 mice. These include 1,000 genetically distinct mouse strains or genotypes, which in many cases are indistinguishable just by their external features. Most of them were created by ETH researchers themselves through cross breeding and genetic engineering. Generally speaking, they are between one and six months old when they are first used in an experiment. An in-house animal welfare officer, two veterinarians and more than 20 animal care technicians are on hand to ensure the mice’s welfare.

Each of the cages is provided with a barcode, next to which are notes on the mouse strain, owner and genotype. To enable scientists to distinguish between the mice, they have small crescent-shaped markings stamped on the edge of their ear. The number and position of the crescents indicates whether you are dealing with animal one, two, three, four, etc. Any mix-up would be disastrous for the researchers and could potentially ruin years of research. But thanks to the ear markings and the information on each cage, each animal can be uniquely identified and registered in a central database.

**“Not another one who works with mice!”**

“The Phenomics Center is a fantastic facility for research because it allows us to standardise our models much more efficiently,” says Kopf. Recalling when he first came to ETH from Basel in 2001, he remembers the President sighing as they negotiated his initial funding and saying: “Not another one who works with mice!” At that time ETH simply had no space to keep large numbers of laboratory mice, so Kopf



A “metabolic cage” for metabolism experiments



Professors Manfred Kopf (left) and Markus Stoffel carry out research at the Institute of Molecular Health Sciences and rely on the infrastructure provided by the Phenomics Center.

moved into a building in Schlieren with various biotech companies and together they set up a new animal facility. Other researchers at ETH took a similar approach to tackling the situation, and over the years a number of separate mouse facilities sprang up in the area. This was certainly not the most economical solution, and it was ultimately not the best solution for the researchers either. In 2008, the Vice President of Research decided to centralise these facilities on the Hönggerberg campus. Today, Kopf has around 3,000 mice at the Phenomics Center, representing 100 different genetic strains. These provide him with a kind of library, which he uses to carry out promising experiments to gain insights into the causes of disease. The Phenomics Center also provides him and his colleagues with the specialist laboratories and equipment they need to conduct their experiments. One example is the photoacoustic laser system, which the researchers can use to observe the growth of a cancerous tumour in an animal over the course of several months without having to resort to surgery.

**Special cages for experiments**

Markus Stoffel’s group also makes regular use of these specialist laboratories. One of the few researchers at ETH to have studied medicine, he was appointed as a Professor at the Institute of Molecular Health Sciences in 2006. His group currently has 2,500 mice in the safe hands of the animal care technicians. Stoffel’s work focuses on metabolic disorders, in particular diabetes. Whenever he wants to discover what effect a certain genetic alteration will have on metabolism, he makes use of metabolic cages. These special cages have tiny light sensors embedded in the frame, allowing scientists to constantly monitor and record the animals’ physical activity. Additional sensors take measurements at ten minute intervals of the animals’ feed, water and oxygen consumption as well as their CO<sub>2</sub> production. By precisely measuring energy intake (feed) and energy expenditure (movement and heat loss) on a constant basis, Stoffel can detect even the slightest changes in metabolic processes.

During these kind of experiments the researcher works closely with the

animal care technicians. They support the researchers and ensure throughout the experiment that the animals’ basic needs are met and that they are not disturbed by external factors. The animal care technicians may also carry out a whole series of tasks on the scientists’ behalf, such as taking small tissue samples to determine the genome of new litters or taking blood samples to measure fat and sugar content. They also train less experienced researchers how to handle the animals and show them how to give injections as painlessly as possible. Stoffel greatly appreciates their contribution: “Without their help we would have to go to the basement several times a day, changing clothes twice and going through the air shower each time. You’ve seen for yourself how time-consuming that is!” ○

A short video on the Molecular Health Sciences Platform:  
→ [www.ethz.ch/youtube-phenomics](http://www.ethz.ch/youtube-phenomics)