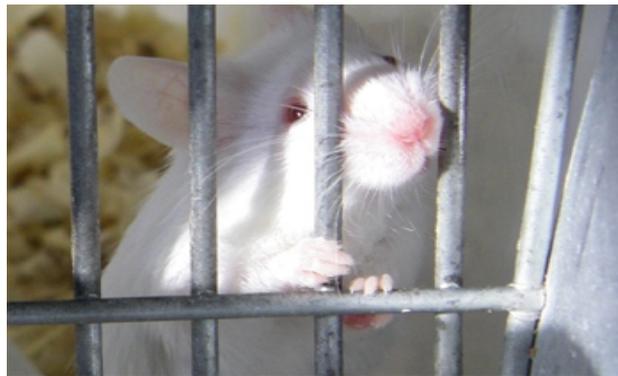


## Scientific and Ethical Implications of the Use of Mice as Model

The mouse is a small mammal which is used as a "model" in experiments in biology, medicine and psychology, primarily because they are easy to maintain and to handle. Worldwide billions of mice are bred and used by industry and scientists. It's a billion Dollar industry and mouse supplier "[The Jackson Laboratory](#)" had a operating revenue of \$229.6 million in the fiscal year 2012. Mice have been used as a fast and easy experimental tool that furthers scientific glory through publications. The system is running itself and people are told that we need to do this for mankind's progress.

Mice are very social and compassionate animals. May-be you have heard about the [mouse in Hangzhou](#) Zoo in China who attacked a snake trying to save his friend. Also, every lab technician can tell you that each mouse reacts different and has it's own personality. Some mice develop characteristics which resemble those attributed to human depression and because of this they have been used by scientists to study depression. In these studies scientists make connections to human disease in order to receive government funds. Many people do not have problems with sacrificing mice to better the lives of people.



*Foto: Ärzte gegen Tierversuche e.V.*

ETH Professor and Philosopher Michael Hampe wrote about the scientific use of mice:

If you can show that starving mice live longer and advertise that the reduction of calories leads to a longer life, you ideologize your knowledge. As a result in research that applies only to mice is less spectacular than one referring to all living creatures, including humans, scientists in a competitive situation might use this overstatement to get more money. (Science on the Market: What Does Competition Do to Research? Michael Hampe)

Most people don't understand the real world impact of scientific papers and to be honest, we don't want to read it. Here I would like to give a slight insight what they are doing to mice and why. For this I analyzed 65 recent publications of two renomnated universities. The Harvard University in Cambridge, USA, and one in Europe the ETH Zürich, Switzerland.

## Results

First I want to point out that this is just a small window of knowledge into what's been done to mice for scientific reasons. If you searched in July 2013 for "mice" in Google Scholar, you got 32800 results just for the year 2013. I will be discussing 65 of those papers.

Due to the overwhelming amount of research on mice I will not discuss the number of mice used or the money spent. A surprisingly low number of these 65 papers were about cancer research or about any approach to finding a cure for human illness.

Some studies were exceptionally cruel and useless like the studies with numbers 1, 2, 3 or 4. In study 3 there was no new finding, they repeated other experiments thereby extending the time mice were subjected to torture. This is called long-term effect and it is discussed that many mice have been lost during their experiments. Another cruel and useless experiment is study No 4, a so-called burning experiment.

One very useless paper was about interactions between environmental factors and neuropsychiatric disease in mice (5). Besides the fact that it is absolutely not clear why the human race needs a stress protocol for mice to progress, a fellow scientist has objected that the statistical analyses is inappropriate:

„Giovanoli *et al.* provided a detailed description of their methods (statistical test used, sample size per group, and degrees of freedom), which makes it clear that the analyses were inappropriate. Comment on "Stress in Puberty Unmasks Latent Neuropathological Consequences of Prenatal Immune Activation in Mice" by Stanley E. Lazic.

Among all this useless cruelty, only a fraction are related to cancer and its cures. Yes, there are some very good approaches like in number 6. Prof. Detmar's group isolated cells from bladder cancer and compared them to normal bladder tissue. The group generated very beautiful and useful results concerning bladder cancer. But the results were from human patients not from mice. Why did they use mice? They used mice to confirm some results *in vivo*. Why did they do this useless additional experiment? Because they needed to do it in order to publish their findings in a high profile paper. That's why they had to sacrifice mice.

Experiments that estimate lethal doses of any given chemical in mice are an easy and common method for generating prestige through published papers. Those scientists who would like to appear a bit more sophisticated can mimic number 7. This group combined the feeding of mice with intoxication of Paracetamol. Similar experiments in order to generate a paper have been to produce knock-out mice (the deletion of any gene) and then to watch what happens. A good example for this are 8, 9, 10 or 11. These experiments produced knock-out mice and analyzed exactly what happened. They didn't claim any progress for cancer or HIV but in mammalian neural development, phosphate homeostasis, arthritis or cardiac hypertrophy.

Although scientists know that each human and each mouse is completely different (12 "neither all humans nor mice harbor the same bacterial strains") they continue to do their tests anyway on mice or they talk about "humanized mice"<sup>13</sup>.

In some publications, the reason for using mice is absolutely unclear, like in 14. They generated [knockin mice](#) with human genes and found that, as in humans, hair thickness is slightly increased in some mice. This results seem to be very important news for the paper "Cell". They also claim that, "the laboratory mouse is an established tool for understanding pathological variants in the human genome".

Surprisingly there is one study that cares about the mice, because mice can't behave normally after implanting transponders, these scientists decided to develop a new method published in 15. In another study scientists complain about the [IACUC](#) (The Institutional Animal Care and Use Committee) because they would not approve their standard approach of torturing the animals (16). This gives us hope for the future.

## Discussion

Is progress being made by using mice as an animal model for humans? Today we are able to grow human skin, human cells and human tissues in large scale. The 3-D cell culture is still not advancing very much because it's much easier to use mice. Of course it's much easier to use the enduring protocols over and over again instead of using ones own brain. Is it too much for scientists to think about new methods without torturing animals? A mouse is not human and it will never become human. There is medicine for a mouse, medicine for a dog, medicine for a sunflower and there is medicine for a human. A mouse is a mouse and deserves respect as a mouse. It's time for the leading scientists to step forward and make progress towards the future.

The young scientists who are using animals today will do tomorrow clinical trials with humans. We know from history that there were many unethical human experimentations. Actually there are still ongoing human subject abuses in Asia, Africa and South America by [AstraZeneca](#), [Bayer](#), [Pfizer](#), [PPD](#), [Bristol-Myers Squibb](#), [Amgen](#), [Eli Lilly](#), [Quintiles](#), [Merck KGaA](#), [Sanofi-Aventis](#) and [Wyeth](#).

In [Wikipedia you will find](#) a list of uncovered unethical human experimentations.

We know today that most killers, rapist and child abuser started out with torturing animals. (Child abuse, domestic violence, and animal abuse: Linking the circles of compassion for prevention and intervention. FR Ascione, F Arkow – 1999).

This does not mean that all young scientists who use animals as a tool will end up as abusers, but they perform the first step in accepting cruelty for the sake of their career.

## Methods

To get an insight into what experiments are being performed I searched in July 2013 with Google Scholar for mice, ETH Zürich or Harvard since 2013 without books, patents or citations. Because some papers are licensed to Journals, I omit the abstracts in the table. The publications were analyzed with [NCBI PubMed](#) and this is also where the interested readers are referred to. In the column named “mice used“ you will find a brief overview of the methods used for the publication. The column with the “impact“ is giving the most important number for the scientists. This number is what's all about: Many high numbers equals funding, success and career.

\* you will find the green numbers in the first column of the table.

Due to content readers discretion is advised:

My thanks to [L.A. Watson](#) for her critical comments and helpful suggestions.

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	Mice used	Cause	Journal	Impact	Titel	Authors	Published
	The animals were anesthetized and catheters were inserted into the right femoral artery and vein with the help of a stereomicroscope and securely fastened with ligatures. The animals were kept under anesthesia for all subsequent procedures.	Brain glucose metabolism in mice.	Journal of Nuclear Medicine	~ 6.3	Quantification of Brain Glucose Metabolism by 18F-FDG PET with Real-Time Arterial and Image-Derived Input Function in Mice.	Malte F. Alf, Matthias T. Wyss, Alfred Buck, Bruno Weber, Roger Schibli, Stefanie D. Krämer.	2013 January
	Mice were subcutaneously inoculated with human cervical carcinoma cells. When the average tumor volume had reached a value of 118–141 mm <sup>3</sup> mice were treated. Human endpoint criteria were defined as weight loss of more than 15% of the initial body weight, a tumor volume of more than 1,500 mm <sup>3</sup> , active ulceration of the tumor, and abnormal behavior indicating pain or unease. Mice were promptly removed from the study and euthanized on reaching one of the predefined endpoint criteria.	Cancer in mice.	Journal of Nuclear Medicine	~ 6.3	DOTA conjugate with an albumin-binding entity enables the first folic acid-targeted 177Lu-radiionuclide tumor therapy in mice.	Müller C, Struthers H, Winiger C, Zheronosekov K, Schibli R.	2013 January
	Livers from 6, 9, 11, 13, 15, 17 and 19 week old mice were harvested following four hours of fasting and one hour of refeeding.	Obesity and Diabetes in mice.	NMR in Biomedicine	~ 3.4	Longitudinal evaluation of hepatic lipid deposition and composition in ob/ob and ob/+ control mice.	Ye Q, Danzer CF, Fuchs A, Vats D, Wolfrum C, Rudin M.	2013 January
	Mice were given an intraperitoneal injection at 15 days of age. Mice were sacrificed at 1 year and examined for liver tumor formation.	Liver cancer in mice	Hepatology	~12	Disordered purinergic signaling and abnormal cellular metabolism are associated with development of liver cancer in Cd39/ENTPD1 null mice.	Sun X, Han L, Seth P, Bian S, Li L, Csizmadia E, Junger WG, Schmelzle M, Usheva A, Tapper EB, Baffy G, Sukhatme VP, Wu Y, Robson SC.	2013 January
	Mice were generated and backcrossed for at least 11 generations. To induce enterocolitis mice were pretreated with streptomycin and twenty-four hours later, mice received by gavage <i>Salmonella</i> . Differences in survival rates were evaluated.	Salmonella infection in mice.	Infection and Immunity	~4.0	Increased susceptibility of melanin-concentrating hormone-deficient mice to infection with <i>Salmonella enterica</i> serovar Typhimurium.	Karagiannis AK, Ziogas DC, Gras-Miralles B, Geiger BM, Nagel J, Trebicka E, Najarian R, Cherayil BJ, Kokkotou E.	2013 January
1	The mice were anesthetized for the surgical procedure. The bone flap was removed and mice were subjected to controlled cortical impact using a pneumatic impact device to yield a trauma. After recovery from anesthesia, the mice were returned to their cages. The neurological tests were based on the ability of the mice to perform 10 different tasks that evaluate the motor ability, balance, and alertness of the mouse. For the laser treatment mice were lightly anesthetized with isoflurane and immobilized by taping their paws to a plastic plate. Mice received active laser treatment for 12 minutes positioned centrally on top of the mouse head and delivered 4 hours post-injury. Group 3 received fourteen daily laser. Before sacrifice at 28 days mice were given seven consecutive daily intraperitoneal injections	Traumatic brain injury in mice.	PLoS ONE	~4.1	Transcranial low-level laser therapy improves neurological performance in traumatic brain injury in mice: effect of treatment repetition regimen.	Xuan W, Vatanserver F, Huang L, Wu Q, Xuan Y, Dai T, Ando T, Xu T, Huang YY, Hamblin MR.	2013 January
	Mice were generated and were backcrossed 5 generations. Mice were treated with insulin, glucose or sodium pyruvate by injection. Mice were implanted with catheters followed by a 5-day recovery. Glucose was infused to measure basal glucose turnover. A euglycemic-hyperinsulinemic clamp was conducted with a prime and continuous insulin infusion, coupled with a variable infusion of 40% glucose to maintain blood glucose high. Every 5 minutes, blood glucose was measured via tail bleed during the first hour to stabilize blood glucose levels and every 10 minutes thereafter until the end of the 2-hour clamp to maintain constant blood glucose levels.	Glucose level in mice.	Journal of Clinical Investigation	~14.2	Direct control of hepatic glucose production by interleukin-13 in mice.	Stanya KJ, Jacobi D, Liu S, Bhargava P, Dai L, Gangl MR, Inouye K, Barlow JL, Ji Y, Mizgerd JP, Qi L, Shi H, McKenzie AN, Lee CH.	2013 January
6	Transgenic mice were bred. Mouse ears were harvested from 24-week-old mice. 24 mice.	Bladder cancer in mice and humans.	Cancer Research	~7.9	Endocan is upregulated on tumor vessels in invasive bladder cancer where it mediates VEGF-A-induced angiogenesis.	Roudnicky F, Poyet C, Wild P, Krampitz S, Negrini F, Huggenberger R, Rogler A, Stöhr R, Hartmann A, Provenzano M, Otto VI, Detmar M.	2013 February
	Knockout mice and transgenic mice were generated. All experiments reported here utilized mice from the highest expressing line. For the lifespan studies males were mated with females and onset and survival was determined in F1 animals. End-stage was determined by the inability of the animal to right itself within 20 seconds when placed on its side. This is a widely accepted and published endpoint for life span studies in ALS-mice. Mice that were unable to right themselves within 20 seconds were euthanized immediately and recorded as dead for the purpose of life span studies.	Neurodegeneration in amyotrophic lateral sclerosis (ALS) mouse models.	PLoS ONE	~ 4.1	Absence of Nr2f2 or Its Selective Overexpression in Neurons and Muscle Does Not Affect Survival in ALS-Linked Mutant hSOD1 Mouse Models.	Marcelo R. Vargas, Neal C. Burton, Li Gan, Delinda A. Johnson, Matthias Schäfer, Sabine Werner, Jeffrey A. Johnson.	2013 February
	Female nude mice were obtained from Charles River. Twenty-five million tumor cells were injected subcutaneously and tumors grown for 4–6 days prior to the experiment. Radiolabeled fusion proteins were injected into the tail vein of tumor-bearing nude mice (5 mice per group). Mice were sacrificed 24 h after injection.	Imaging of tumors in mice.	Bioconjugate Chemistry	~4.6	Tumor-targeting antibody-anticalin fusion proteins for in vivo pretargeting applications.	Steiner M, Gutbrodt K, Krall N, Neri D.	2013 February
	Eight-to-twelve-week-old transgenic mice were inoculated by gavage with different <i>Salmonella</i> strains. At 10 days post infection mice were killed.	<i>Salmonella enterica</i> infection in mice.	Nature	~36	Stabilization of cooperative virulence by the expression of an avirulent phenotype.	Diard M, Garcia V, Maier L, Remus-Emsermann MN, Regoes RR, Ackermann M, Hardt WD.	2013 February
	Bone tissue was collected from growth hormone deficient inbred strains of mice and offspring. To test the high-throughput approach they used bone tissue from 1990 mice.	To develop an automated method to quantify murine femoral bone stiffness in mice.	Bone	~4.5	High-throughput quantification of the mechanical competence of murine femora - A highly automated approach for large-scale genetic studies.	Ruffoni D, Kohler T, Voide R, Wirth AJ, Donahue LR, Müller R, van Lenthe GH.	2013 February
	They generated a knockout mice strains. They isolated tissue from 2, 6 and 12 months old mice. Not a single mutant female has escaped leukemia.	Leukemia in mice.	Cell	~32	Xist RNA is a potent suppressor of hematologic cancer in mice.	Yildirim E, Kirby JE, Brown DE, Mercier FE, Sadreyev RI, Scadden DT, Lee JT.	2013 February
14	Overexpressing human genes in mice found an increase in gland size. Another human gene in mice produced thicker hairs.	Expression of a human gene in mice.	Cell	~32	Modeling recent human evolution in mice by expression of a selected EDAR variant.	Kamberov YG, Wang S, Tan J, Gerbault P, Wark A, Tan L, Yang Y, Li S, Tang K, Chen H, Powell A, Itan Y, Fuller D, Lohmueller J, Mao J, Schachar A, Paymer M, Hostetter E, Byrne E, Burnett M, McMahon AP, Thomas MG, Lieberman DE, Jin L, Tabin CJ, Morgan BA, Sabeti PC.	2013 February

	Mice were vaccinated with adenovirus constructs and vaccine responses was measured.	Hepatitis C vaccination in mice	Clinical and Vaccine Immunology	~2.6	Hepatitis C genotype 1 mosaic vaccines are immunogenic in mice and induce stronger T-cell responses than natural strains.	Yusim K, Dilan R, Borducchi E, Stanley K, Giorgi E, Fischer W, Theiler J, Marcotrigiano J, Korber B, Barouch DH.	2013 February
2	Under anesthesia, a small borehole was drilled, and a microinjection needle was lowered into the right striatum. The mice were allowed to wake up and were put in a mouse restrainer under light restraint. After hemorrhage induction, various chemicals were continuously injected through a jugular vein catheter using an injection pump. One day after hemorrhage induction, mortality rate was determined. To prepare a chronic cranial window for imaging a 6 mm diameter bilateral craniotomy was performed over the parietal cortex. An 8 mm glass cover slip was then glued over the exposed brain using cyanoacrylate and dental cement. In another experiment mice were subjected to one to four microhemorrhages with a minimum of 1 mm spacing between hemorrhaged vessels.	Stroke in mice.	PLoS ONE	~4.1	Intravenous tPA therapy does not worsen acute intracerebral hemorrhage in mice.	Foerch C, Rosidi NL, Schlunk F, Lauer A, Cianchetti FA, Mandeville E, Arai K, Yigitkanli K, Fan X, Wang X, van Leyen K, Steinmetz H, Schaffer CB, Lo EH.	2013 February
5	Prenatal immune activation was induced. Offspring were then left undisturbed or exposed to variable and unpredictable stress during peripubertal development, a maturational period known to be highly sensitive to the disrupting effects of traumatizing events relevant to psychosis-related disease. The stress protocol included five distinct stressors: (i) electric foot shock, (ii) restraint stress, (iii) swimming stress, (iv) water deprivation, or (v) repeated home cage changes, applied on alternate days between postnatal days.	Neuropsychiatric disease in mice.	Science	~31	Stress in puberty unmasks latent neuropathological consequences of prenatal immune activation in mice.	Giovanoli S, Engler H, Engler A, Richetto J, Voget M, Willi R, Winter C, Riva MA, Mortensen PB, Schedlowski M, Meyer U.	2013 March
	Various mice strains were infected with one or two viruses. The virus titer in the spleen was determined on day 10 post-infection.	Virus (LCMV) infected mice.	European Journal of Immunology	~5.1	Reversal of chronic to resolved infection by IL-10 blockade is LCMV strain dependent.	Richter K, Perriard G, Oxenius A.	2013 March
	Mice were fed either a regular chow diet or a high-fat diet. To place the virus injections exclusively into the epididymal fat pad, the intra-abdominal cavity was opened and the epididymal fat pads were exposed. Subcutaneous adipose tissue was taken from the inguinal subcutaneous region while visceral adipose tissue was taken from the epididymal region.	Estrogen signaling in obese mice and humans.	Molecular Metabolism	n.a.	Transcriptional regulation of adipocyte formation by the liver receptor homologue 1 (Lrh1)—Small hetero-dimerization partner (Shp) network.	Nadja Mrosek, Bettina Meissburger, Chikage Matak, Eva Roeder, Jozef Ukropec, Iwar Klimes, Daniela Gasperikova, Peter-Paul Nawroth, Gottfried Rudolfsk, Johan Auwerx, Kristina Schoonjans, Christian Wolfrum.	2013 March
	All animals studied were 8- to 12-week-old male mice, purchased from Charles River. Various mice strains were injected with recombinant adenovirus and analyzed.	Obesity and Diabetes in mice.	Cell Metabolism	~ 17.8	Glucagon-Induced Acetylation of Foxa2 Regulates Hepatic Lipid Metabolism.	von Meyenn F, Porstmann T, Gasser E, Selevsek N, Schmidt A, Aebersold R, Stoffel M.	2013 March
	Generation of various mice strains. Embryos were obtained from intracrossed mice and cells were cultivated and analyzed.	Tumour suppressor in mice.	European Journal of Cancer	~4.8	Genetic deletion of the long isoform of the von Hippel-Lindau tumour suppressor gene product alters microtubule dynamics.	Frew IJ, Smole Z, Thoma CR, Krek W.	2013 March
	They engineered various knock-in mouse models to develop prostate cancer. Some male mice developed localized lesions that slowly progressed to prostate adenocarcinomas.	Prostate cancer in mice and humans.	Genes & Development	11.7	ETV1 directs androgen metabolism and confers aggressive prostate cancer in targeted mice and patients.	Baena E, Shao Z, Linn DE, Glass K, Hamblen MJ, Fujiwara Y, Kim J, Nguyen M, Zhang X, Godinho FJ, Bronson RT, Mucci LA, Loda M, Yuan GC, Orkin SH, Li Z	2013 March
	Mice were obtained from the Jackson Laboratory. Cutaneous inflammation was induced by injecting the ears of anesthetized mice every other day for ten days. Ear swelling was measured each day immediately before injection, starting on day 0.	Psoriasis in mice.	PLoS ONE	~4.1	IL-23 induces atopic dermatitis-like inflammation instead of psoriasis-like inflammation in CCR2-deficient mice.	Bromley SK, Larson RP, Ziegler SF, Luster AD.	2013 March
7	Mice were fed a diet based on fish oil or soybean oil followed by Paracetamol intoxication.	Drug-induced liver failure.	JPEN J Parenter Enteral Nutr.	~2.6	Dietary fish oil aggravates paracetamol-induced liver injury in mice.	de Meijer VE, Kalish BT, Meisel JA, Le HD, Puder M.	2013 March
	Mice were routinely back-crossed a minimum of five times prior to experimentation and were continued to be back-crossed routinely. For testing, the rod was accelerated from 4 to 40 rpm over 180 seconds and time to fall off the apparatus was recorded. Transgenic mice were tested with the following experiments: Rotarod Task, Grip-Strength Test, Open-Field Activity Test, Gait Dynamics, Beam Walk, Attention performance testing, Food restriction, Visual Discrimination Learning Procedure, Attention procedure, Preference for social novelty, Metabolic/24-hour Activity Test.	Nervous system morphology in mice	PLoS ONE	~4.1	Lack of tryptophan hydroxylase-1 in mice results in gait abnormalities.	Suidan GL, Duerschmied D, Dillon GM, Vanderhorst V, Hampton TG, Wong SL, Voorhees JR, Wagner DD.	2013 March
	For outflow measurements mice were anesthetized and treated with various chemicals. One- to 17-month-old female mice were euthanized and studied.	Glaucoma in mice.	PLoS ONE	~4.1	Soluble guanylate cyclase $\alpha$ 1-deficient mice: a novel murine model for primary open angle glaucoma.	Buys ES, Ko YC, Alt C, Hayton SR, Jones A, Tainsh LT, Ren R, Giani A, Clerf M, Abernathy E, Tainsh RE, Oh DJ, Malhotra R, Arora P, de Waard N, Yu B, Turcotte R, Nathan D, Scherrer-Crosbie M, Loomis SJ, Kang JH, Lin CP, Gong H, Rhee DJ, Brouckaert P, Wiggs JL, Gregory MS, Pasquale LR, Bloch KD, Ksander BR.	2013 March
9	They generated a mouse strain that transgenically overexpresses a protein by backcrossing transgenic mice for 9 generations. Transgenic mice died earlier and had more severe renal disease than wild-type mice.	Autoimmune disease in mice.	Arthritis&Rheumatism	~7.5	Brief report: increased expression of a short splice variant of CTLA-4 exacerbates lupus in MRL/lpr mice.	Ichinose K, Zhang Z, Koga T, Juang YT, Kis-Tóth K, Sharpe AH, Kuchroo V, Crispin JC, Tsokos GC.	2013 March
	They analyzed six mice groups: (1) surgery + anaesthesia (mice underwent anaesthesia and surgery without analgesic treatment) (2) surgery + anaesthesia + low dose analgesia (mice underwent anaesthesia and surgery with 5 mg/kg carprofen) (3) surgery + anaesthesia + high dose analgesia (mice underwent anaesthesia and surgery with 50 mg/kg carprofen) (4) anaesthesia only (5) anaesthesia + low dose analgesia (6) anaesthesia + high dose analgesia.	Postsurgical pain in laboratory mice.	Laboratory Animals	~1.2	Assessment of postsurgical distress and pain in laboratory mice by nest complexity scoring.	Jirkof P, Fleischmann T, Cesarovic N, Rettich A, Vogel J, Arras M.	2013 April
	Various mice strains were sacrificed by CO2 inhalation and organs and cells were cultivated and analyzed.	Blood glucose levels in mice cells.	Journal of Biological Chemistry	~4.7	Systematic proteomic analysis identifies beta-site amyloid precursor protein cleaving enzyme 2 and 1 (BACE2 and BACE1) substrates in pancreatic beta-cells.	Stützer I, Selevsek N, Esterházy D, Schmidt A, Aebersold R, Stoffel M.	2013 April

	Different mouse strains were interbred. Kidneys were dissected from 2-month-old mice. They cultured primary mouse renal epithelial cells from the various mouse strains.	Renal cell carcinoma in mice.	EMBO Mol Med	~10.3	Combined mutation of Vhl and Trp53 causes renal cysts and tumours in mice.	Albers J, Rajski M, Schönenberger D, Harlander S, Schraml P, von Teichman A, Georgiev S, Wild P, Moch H, Krek W, Frew IJ.	2013 April
	Spinal cords were removed from various mouse strains.	Spinal dorsal horns in mice.	The Journal of Neuroscience	~7.1	Genome-wide expression analysis of ptf1a- and ascl1-deficient mice reveals new markers for distinct dorsal horn interneuron populations contributing to nociceptive reflex plasticity.	Wildner H, Das Gupta R, Bröhl D, Heppenstall PA, Zeilhofer HU, Birchmeier C.	2013 April
	A tail loading model was used in mice. For this the caudal vertebra was subjected to cyclic mechanical loading through stainless steel pins inserted in the adjacent vertebrae, 3 times/week for 4 weeks at 10 Hz and 3000 cycles. A systemic, catabolic bone response was induced by ovariectomy of 15-week old female mice. In vivo scans were performed on the day of operation and consecutively every two weeks over a twelve-week period.	Imaging bone formation in mice.	PLoS ONE	~ 4.1	Local Mechanical Stimuli Regulate Bone Formation and Resorption in Mice at the Tissue Level.	Friederike A. Schulte, Davide Ruffoni, Floor M. Lambers, David Christen, Duncan J. Webster, Gisela Kuhn, Ralph Müller.	2013 April
	The popliteal lymph nodes in both hind legs of mice were removed. The surgery lasted 20–30 min. Wounds were closed with absorbable filament. Metamizol was added to the drinking water for 24 h after surgery. Lymphatic drain was imaged for a period of 4 weeks.	Lymphatic function in mice.	Breast Cancer Research and Treatment	~ 4.4	Dynamics of lymphatic regeneration and flow patterns after lymph node dissection.	Blum KS, Proulx ST, Luciani P, Leroux JC, Detmar M.	2013 April
	Mice were back-crossed for 10 generations and knockout mice were generated. Physiological and pathological studies of mice were performed at a time point of stable and moderate symptomatic severity. For all studies, animals were euthanized with carbon dioxide.	Myotubular myopathy in mice.	Human Molecular Genetics	~7.5	Enzyme replacement therapy rescues weakness and improves muscle pathology in mice with X-linked myotubular myopathy.	Lawlor MW, Armstrong D, Viola MG, Widrick JJ, Meng H, Grange RW, Childers MK, Hsu CP, O'Callaghan M, Pierson CR, Buj-Bello A, Beggs AH.	2013 April
	For these experiments 7-wk-old mice were placed in a stereotactic device under anesthesia, and a cannula was inserted into the right lateral cerebral ventricle. After 1 week of recovery, the mice received a single injection to induce diabetes. Twelve days later, the mice received three injections of insulin or the same volume of PBS through an internal cannula. Four hours after the last injection the hypothalami were collected.	Brains of type 1 and type 2 diabetic mice.	PLoS Biology	~12.7	Reduction of the cholesterol sensor SCAP in the brains of mice causes impaired synaptic transmission and altered cognitive function.	Suzuki R, Ferris HA, Chee MJ, Maratos-Flier E, Kahn CR.	2013 April
	Syngeneic colorectal cancer cells were injected to all groups of mice. The experiment was terminated when the tumor of at least one mouse reached the maximum allowable size of 1500 mm <sup>3</sup> .	Colon cancer in mice.	Gut	~10.7	Salutary effects of adiponectin on colon cancer: in vivo and in vitro studies in mice.	Moon HS, Liu X, Nagel JM, Chamberland JP, Diakopoulos KN, Brinkoetter MT, Hatziapostolou M, Wu Y, Robson SC, Iliopoulos D, Mantzoros CS.	2013 April
10	Transgenic mice (mixed background) were generated. Saline was infused in 8-wk-old male with the use of subcutaneously implanted miniosmotic pumps.	Cardiac hypertrophy in mice.	The FASEB Journal	~5.7	FHL2 prevents cardiac hypertrophy in mice with cardiac-specific deletion of ROCK2.	Okamoto R, Li Y, Noma K, Hiroi Y, Liu PY, Taniguchi M, Ito M, Liao JK.	2013 April
	Transplantation of bone marrow in mice.	Stem cell subset in mice.	Annals of Surgery	~6.3	CD39 Modulates Hematopoietic Stem Cell Recruitment and Promotes Liver Regeneration in Mice and Humans After Partial Hepatectomy.	Schmelzle M, Duhme C, Junger W, Salhanick SD, Chen Y, Wu Y, Toxavidis V, Csizmadia E, Han L, Bian S, Fürst G, Nowak M, Karp SJ, Knoefel WT, Schulte Esch J, Robson SC.	2013 April
8	They generated knock out mice. Mice showed a significant reduction in weight and length at birth, which persists over time. 75 % of pups died before reaching 2 months of age. They found that by making food more accessible, they could substantially rescue the early lethality, from 30% viability at 2 months of age without food access to 70% viability with food access. To investigate whether mice display learning and memory defects they used the fear-conditioning test. During training, mice demonstrated comparable low levels of freezing prior to shock application. When re-exposed to the conditioning chamber 24 hr later, mice displayed a 5-fold reduction in freezing compared to control mice.	Social behavior in mice.	Molecular Cell	~15.3	Altered social behavior and neuronal development in mice lacking the Uba6-Use1 ubiquitin transfer system.	Lee PC, Dodart JC, Aron L, Finley LW, Bronson RT, Haigis MC, Yankner BA, Harper JW.	2013 April
	Mice from each group were boosted intramuscularly with virus particles. Animals were bled weekly.	HIV vaccine.	Journal of Virology	~5.4	An attenuated Listeria monocytogenes vector primes more potent simian immunodeficiency virus-specific mucosal immunity than DNA vaccines in mice.	Im EJ, Borducchi EN, Provine NM, McNally AG, Li S, Frankel FR, Barouch DH.	2013 April
	Transgenic mice with skin-specific overexpression of amphiregulin displayed an enhanced size and density of lymphatic vessels in the skin. Mice were subcutaneously injected with growth factor-reduced Matrigel. After 15 days, tissues were excised.	Skin cancer in mice.	Journal of Dermatological Science	~3.6	Activation of the epidermal growth factor receptor promotes lymphangiogenesis in the skin.	Marino D, Angehrn Y, Klein S, Riccardi S, Baenziger-Tobler N, Otto VI, Pittelkow M, Detmar M.	2013 May
	Various mice strains were infected i.v. with virus doses and blood samples were obtained from infected mice.	Viral infection in mice.	PLoS Pathogens	~9.2	IL-21 Restricts Virus-driven Treg Cell Expansion in Chronic LCMV Infection.	Schmitz I, Schneider C, Fröhlich A, Frebel H, Christ D, Leonard WJ, Sparwasser T, Oxenius A, Freigang S, Kopf M.	2013 May
	Transgenic mice expressing the genes of the human papillomavirus. Mutant mice were observed weekly for the appearance of skin tumors and for progression of existing ones. Mice were euthanized if a single large tumor (>1 cm), more than one tumor of intermediate size (>0.5 cm), or an unfavorable localization required their elimination according to animal welfare regulations. For chemical skin carcinogenesis DMBA in acetone was applied topically to a shaved area on the back skin of 8- to 10-week-old female mice 2 days after shaving. One week later, TPA in acetone was applied to the same site once weekly for 24 weeks. After termination of TPA treatment, tumor observation was continued until the mice started to develop ulcerated tumors.	Wound-regulating in mice.	Cancer Research	~7.9	Dual Role of the Antioxidant Enzyme Peroxiredoxin 6 in Skin Carcinogenesis.	Roß F, Huber M, Gruber F, Böhm F, Pfister HJ, Bochkov VN, Tschachler E, Dummer R, Hohl D, Schäfer M, Werner S.	2013 May

	Transgenic mice lacking cutaneous lymphatic vessels were used. Female mice were shaved on their back skin in isoflurane anesthesia at 8 weeks of age. Two days later, mutations in DNA were induced by topical application of 50 µg of the tumor initiator DMBA in acetone on the back skin of anesthetized mice. Subsequently acetone was applied once per week on the back skin of anesthetized mice. The mice were shaved under isoflurane anesthesia two days before TPA treatment. In a first long-term study, tumor growth and malignant transformation were observed in 35 transgenic and 35 wild-type mice. Mice were sacrificed by overdose of anesthetic 6 weeks after SCC development.	Skin cancer in mice.	Cancer Research	~7.9	VEGF-C and VEGF-D blockade inhibits inflammatory skin carcinogenesis.	Alitalo AK, Proulx ST, Karaman S, Aebischer D, Martino S, Jost M, Schneider N, Bry M, Detmar M.	2013 May
	To produce trauma-induced neuropathic pain models, they performed chronic constriction injury sciatic nerve transection, and spinal nerve ligation under isoflurane anesthesia. To produce streptozotocin-induced diabetic neuropathy, mice received a single intraperitoneal injection. Heat sensitivity was tested by radiant heat. A portion of the lumbar spinal cord was removed from mice under urethane anesthesia. For the behavioral tests mice were placed in a box with access to both chambers and the behavior was recorded daily for 15 min. Autotomy score was assessed and a half point was assigned to a bleeding or lost nail. One point was added for each distal half digit attacked, and an additional point was added for each proximal half digit attacked. Animals reaching 5 points were euthanized.	Neuropathic pain in mice.	Annals of Neurology	~11.2	Neuroprotectin/Protectin D1 protects neuropathic pain in mice after nerve trauma.	Xu ZZ, Liu XJ, Berta T, Park CK, Lü N, Serhan CN, Ji RR.	2013 May
	Mice exhibited unaltered nociceptive pain and morphine-induced acute analgesia. Heat sensitivity was tested by radiant heat and expressed as paw withdrawal latency. The heat intensity was adjusted to prevent tissue damage. Tail-flick test was performed by immersing the tail into 52 °C hot water, and the response latency was recorded after removal of the whole tail from the water.	Inflammation-induced persistent pain and morphine tolerance.	Neuroscience	~3.1	Tissue plasminogen activator contributes to morphine tolerance and induces mechanical allodynia via astrocytic IL-1β and ERK signaling in the spinal cord of mice.	Berta T, Liu YC, Xu ZZ, Ji RR.	2013 May
	Ischemia was induced in mice. At the end of 48 hours of reperfusion, mice were euthanized.	Limb ischemia in mice	Journal of Vascular and Interventional Radiology	~2.1	Reduced hind limb ischemia-reperfusion injury in Toll-like receptor-4 mutant mice is associated with decreased neutrophil extracellular traps.	Oklu R, Albadawi H, Jones JE, Yoo HJ, Watkins MT.	2013 May
11	They generated double mutant mice and analyzed them.	Phosphate homeostasis in mice.	Contributions to nephrology	~1.3	FGF23-induced hypophosphatemia persists in Hyp mice deficient in the WNT coreceptor Lrp6.	Uchihashi K, Nakatani T, Goetz R, Mohammadi M, He X, Razzaque MS.	2013 May
	Deletion of Tace is lethal shortly after birth in mice; therefore, they utilized special mice and induced a tamoxifen injection. Tace conditional deletion mice and wild-type mice were exposed to HNE via nasal instillation three times at 3-day intervals, and the lungs were harvested on day 11 after initial HNE exposure. Mice were purchased from Jackson laboratory.	Chronic airway diseases in mice.	Lung Cellular and Molecular Physiology	~3.5	Human neutrophil elastase-mediated goblet cell metaplasia is attenuated in TACE-deficient mice.	Park JA, Sharif AS, Shiomi T, Kobzik L, Kasahara DI, Tschumperlin DJ, Vovnow J, Drazen JM.	2013 May
	Using tumor-bearing mice on imaging studies.	Imaging of tumors in mice.	Molecular Imaging and Biology	~3.8	Improved PET Imaging of Tumors in Mice Using a Novel 18 F-Folate Conjugate with an Albumin-Binding Entity.	Fischer CR, Groehn V, Reber J, Schibli R, Ametamey SM, Müller C.	2013 June
	The kidneys were excised from sacrificed mice.	Imaging of mouse kidneys.	Journal of Instrumentation	~ 1.9	Preliminary comparison of grating-based and in-line phase contrast X-ray imaging with synchrotron radiation for mouse kidney at TOMCAT.	J. Sun, P. Liu, S. Irvine, B. Pinzer, M. Stampanonib, L.X. Xua.	2013 June
	The effect of a dopamine releaser amphetamine in mice.	Cognitive functions of mice.	Psychopharmacology	~4.1	SSR504734 enhances basal expression of prepulse inhibition but exacerbates the disruption of prepulse inhibition by apomorphine.	Singer P, Zhang W, Yee BK.	2013 June
	For chemical skin carcinogenesis DMBA in acetone was applied topically to a shaved area on the back skin of 8- to 10-week-old female mice 2 days after shaving. One week later TPA in acetone was applied to the same site once weekly for 24 weeks. Tumor number and size were documented every 2 weeks. After termination of TPA treatment, tumor observation was continued until the mice started to develop ulcerated tumors. Seventy-two hours after the last of 3 TPA treatments, animals were euthanized with CO2.	Skin carcinogenesis in mice and human skin.	Cancer Research	~7.9	Dual Role of the Antioxidant Enzyme Peroxiredoxin 6 in Skin Carcinogenesis.	Rolfs F, Huber M, Gruber F, Böhm F, Pfister HJ, Bochkov VN, Tschachler E, Dummer R, Hohl D, Schäfer M, Werner S.	2013 June
	Social interaction of mice after systemic administration of Peptide YY.	Depression in mice.	Neuropsychopharmacology	~ 8	Administration of the Y2 Receptor Agonist PYY3-36 in Mice Induces Multiple Behavioral Changes Relevant to Schizophrenia.	Stadlbauer U, Langhans W, Meyer U.	2013 June
	Mice strains were generated and backcrossed eight generations. Mice were sensitized using a high dose of house dust mite protein extract. Three doses of protein extract were delivered by the in-tranasal route at weekly intervals, twenty-four hours after the last challenge mice were anesthetized.	Airway inflammation in mice.	Journal of Immunology	~5.5	Adam8 limits the development of allergic airway inflammation in mice.	Knolle MD, Nakajima T, Hergrueter A, Gupta K, Polverino F, Craig VJ, Fyfe SE, Zahid M, Permaul P, Cernadas M, Montano G, Tesfaigzi Y, Sholl L, Kobzik L, Israel E, Owen CA.	2013 June
15	New system compared to mice with implanted transponders.	New system to measure polysomnographic biopotentials in mice.	Journal of Neuroscience Methods	~2.1	A novel telemetric system to measure polysomnographic biopotentials in freely moving animals.	Zielinski MR, Gerashchenko L, Karpova SA, Gerashchenko D.	2013 June
4	A full-thickness thermal injury of 30% of the total body surface area was produced by shaving the dorsal surface. The animals were then placed in molds exposing 30% of the dorsum followed by exposure of the open area to a 90°C water bath for 9 seconds. After the procedure, the mice were caged individually. In the time course study, the liver specimens were collected 6, 12, 24, 72, and 144 hour after thermal injury.	Burn injuries in mice.	Annals of Surgery	~6.3	Simvastatin protects hepatocytes from apoptosis by suppressing the TNF-α/caspase-3 signaling pathway in mice with burn injury.	Zhao G, Yu YM, Kaneki M, Tompkins RG, Fischman AJ.	2013 June
		Thrombosis in mice.	J Thromb Haemost.	~5.7	Hypoxia, such as encountered at high altitude, promotes deep vein thrombosis in mice.	Brill A, Suidan GL, Wagner DD.	2013 June

16	A total of 47 transgenic mice were studied. Animals were given gel-packs when their limbs became too weak to reach food. They were sacrificed with an intraperitoneal dose of Fatal Plus® at the point that their hind limbs became completely paralyzed and they could no longer successfully reach the gel-pack for feeding.	Treatment of ALS animal models.	PLoS ONE	~4.1	Electrophysiologic Biomarkers for Assessing Disease Progression and the Effect of Riluzole in SOD1 G93A ALS Mice	Li J, Sung M, Rutkove SB.	2013 June
13	Transmission of HIV in „humanized mice“	HIV in humanized mice.	Molecular Therapy	~6.8	Durable Knockdown and Protection From HIV Transmission in Humanized Mice Treated With Gel-formulated CD4 Aptamer-siRNA Chimeras.	Wheeler LA, Vrbanc V, Trifonova R, Brehm MA, Gilboa-Geffen A, Tanno S, Greiner DL, Luster AD, Tager AM, Lieberman J.	2013 July
12	They examined pathogen-free, gnotobiotic altered colonized mice and germ-free mice. Mice were treated for 21 days with various chemicals in the drinking water. T cells were injected into 6-8 week old recipients. Mice were monitored weekly for weight loss and morbidity for 6-9 weeks. At the conclusion of the experiment, mice were removed from isolators and processed immediately.	Intestinal inflammation in mice.	Science	~31	The Microbial Metabolites, Short-Chain Fatty Acids, Regulate Colonic Treg Cell Homeostasis.	Smith PM, Howitt MR, Panikov N, Michaud M, Gallini CA, Bohlooly-Y M, Glickman JN, Garrett WS.	2013 July
	Various mice strains were used for brain imaging. For this animals were anesthetized and the brain was imaged under the influence of various drugs.	Stress-related disorders in mice.	Neuroimage	~5.9	Functional MRI to assess alterations of functional networks in response to pharmacological or genetic manipulations of the serotonergic system in mice.	Razoux F, Baltés C, Mueggler T, Seuwen A, Russig H, Mansuy I, Rudin M.	2013 July
	Groups of mice were fed a high-fat diet for 8 weeks. At an age of 12–14 weeks, animals were fasted (12 h) and adipose tissue was dissected.	Obesity in mice.	BBA – Molecular and Cell Biology of Lipids	~5.3	Malfunctioning of adipocytes in obesity is linked to quantitative surfaceome changes.	Moest H, Frei AP, Bhattacharya I, Geiger M, Wollscheid B, Wolfrum C.	2013 July
	Various mice strains were infected with a virus at doses that led to a chronic infection. 10-12 days after infection the virus titer was estimated and organs analyzed.	Virus infection in mice.	European Journal of Immunology	~5.1	Non-neutralizing antibodies protect from chronic LCMV infection independently of activating FcγR or complement.	Richter K, Oxenius A.	2013 July
3	Stainless steel pins were inserted in the fifth and seventh caudal vertebrae of mice. Due to swollen tissue around the pins, several mice had to be excluded from the experiment. This was the first caudal-vertebrae-loading study where loading was applied for more than 4 weeks. Mice were lost throughout the study due to inflammation around the pins. Three weeks after insertion of the pins the scanning and loading regime was started. For mechanical loading, pins were fixed in a previously developed caudal vertebral axial compression device. The proximal pin was clamped tightly, while the distal pin was connected to a load cell which applied sinusoidally varying forces at a peak load of 8 N at 10 Hz for 3000 cycles (5 min). This load protocol was applied three times per week for 14 weeks.	Long-term effect of mechanical loading on bone microstructure in mice.	Bone	~4.5	Trabecular bone adapts to long-term cyclic loading by increasing stiffness and normalization of dynamic morphometric rates.	Lambers FM, Koch K, Kuhn G, Ruffoni D, Weigt C, Schulte FA, Müller R.	2013 August
	They fed mice an atherogenic diet for 3 months followed by giving mice cromolyn for additional 3 months.	Atherosclerosis in mice.	Atherosclerosis	~4.0	Pharmaceutical stabilization of mast cells attenuates experimental atherogenesis in low-density lipoprotein receptor-deficient mice	Jing Wang, Sara Sjöberg, Viviane Tia, Blandine Secco, Han Chen, Min Yang, Galina K. Sukhova, Guo-Ping Shi	2013 August