**Short Description of the IFB Research Projects**

The Integrated Research- and Treatment Center (IFB) Adiposity Diseases has diverse studies in six large research fields: hormones (adipokines), genetics, child adiposity, obesity / bariatric surgery, molecular and neuro-imaging and psychosocial aspects of obesity. The research projects are being supported by four core units. (up-dated 4/2015).

**AD2-5E82**

**Project head:** Dr. med. Wiebke Fenske  
**Project title:** Reset gut-dopamine axis as a cause of restored brain reward processing and sustained weight reduction following Roux-en-Y gastric bypass (RYGB) surgery  
**Duration:** 01.05.2015 – 31.10.2018

In this research project eating behaviors and neuronal transmitters are being examined before and after bariatric surgery (gastric bypass RYGB). Obesity or bariatric surgery reduces the amount of food that can be eaten and digested due to a size reduction of the stomach and small intestine. These operations also seem to influence the perception of reward due to eating. The perception of reward is associated with the neurotransmitter dopamine. In obese patients often a hedonistic eating behavior can be observed - food is perceived more rewarding than in normal weight individuals. By neuro-imaging via positron-emission- and magnetic-resonance-tomography the function of dopamine in the brain, eating behavior and the perception of reward in bariatric patients before and after surgery is being additionally examined. This research can help to predict which patients will benefit from bariatric surgery.

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AD2-5E83
Project head: Dr. rer. nat. Annette Horstmann
Project title: Neurobiology of conditioning to primary reinforcers and its role in obesity
Duration: 01.05.2015 – 31.10.2018

This study should clarify the influence of habitual (conditioned, automatic) behavior on decision making in obesity. Obese people mostly react automatically with increased food intake to the mere view, the smell and the taste of food, regardless of their hunger and energy needs (their homeostatic status). Using functional magnetic resonance imaging (fMRT) the response to these stimuli in obese and normal weight subjects and their impact on eating habits should be verified. Understanding these factors is important in order to improve weight reduction treatments and to recognize and dismantle for example behavioral barriers.

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AD2-5F84
Project head: Dr. rer. nat. Annette Horstmann
Project title: Retraining Automatic Action Tendencies in Obesity
Duration: 01.05.2015 – 31.10.2018

In obese people paradoxical behaviors comparable to those in drug addicts are often observed. These behaviors are unfavorable and unhealthy, they occur although the people affected know the negative consequences. Using functional magnetic resonance imaging (fMRI) the role of the brain in such mostly automatic behaviors is being investigated. In addition, the inversion of these behaviors is attempted by the patients’ unlearning through behavioral training. This and the accompanying plastic changes in the brain are also examined by fMRI. The results of these examinations will allow a better understanding of the complex interaction of unconscious automatic processes, reward expectations; conscious behavioral intentions and their neurobiological basis will be possible for behavior control in obesity. The findings from this study can be incorporated into behavioral treatment approaches.

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AD2-5G85
Project head: Dr. rer. med. Claudia Sikorski
Project title: Behavioral correlates and discrimination in weight bias – an experimental approach
Duration: 01.05.2015 – 30.04.2019

People with obesity are confronted with negative opinions and rejection (stigmatization). Scientists assume that stigmatization leads to discrimination e.g. in work life. Yet, so far there is too few scientific data on this phenomenon. This study investigates the causes and mechanisms of discrimination. In a specific experiment the reactions of study participants towards obese persons within social interaction will be scrutinized. Furthermore, judgments and reactions referring to health care issues of obese patients are being tested via questionnaires and notional portrayals of individuals. Also trial lessons in a fitness center of normal- and overweight persons will be analyzed. Moreover, the income differences of these groups in work life are being examined.

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AD2-5G86
Projektleitung: Dr. rer. med. Claudia Sikorski
Project title: Internalized stigma as stressor – pathophysiological and psychological consequences for intervention development
Duration: 01.08.2016 – 30.04.2019

The stigmatization and discrimination obese people are facing, have a negative stress-like impact on their health – especially if the negative external image becomes the self-image (self-stigma). Study participants (probands) with a high level and with a low level of self-stigma are interviewed, saliva- and blood samples and tested for cortisol, a hormone that is associated with stress. Based on previous research on stigma complemented by the results of this study the scientists will develop a new intervention approach in cognitive behavioral therapy, which enables the patients to better cope with stigmatization. The groups of probands treated this way will be interviewed, and saliva- and blood samples will be tested again. In the long run an intervention manual will be drafted to effectively treat stigmatized patients. This is important since especially self-stigma reduces the success of weight reduction therapies.

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AD2-6A87

Project head: Prof. Dr. med. Mathias Fasshauer
Project title: The role of the kidney in adipokine physiology
Duration: 01.05.2015 – 30.04.2020

The production and effect of various hormones of the adipose tissue (adipokines) is impaired in adiposity. This is often associated with diseases of the large blood vessels (atherosclerosis or macroangiopathy). It has not been examined yet, if the small blood vessels are also affected (microangiopathy). Among others, a microangiopathy leads to an aggravation of the kidney function – as often observed in type-2-diabetes. This study examines in animal models if the adipokine levels are increased in chronic or acute kidney weakness and if adipokines are discharged by the kidneys. Likewise, it will be determined whether adipokines contribute to kidney impairment in obesity and diabetes. A special focus is on the adipokine „adipocyte fatty acid-binding protein“ (AFABP). For the first time, the interaction of AFABP and other dysfunctional adipokines on the one hand, and kidney function on the other hand is determined.

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AD2-6B76

Project head: PD Dr. rer. nat. Jane Neumann
Project title: Instrumental learning and Pavlovian to instrumental transfer in obesity
Duration: 01.05.2015 – 31.10.2017

Instrumental learning and behavior mean adequate behaviors e. g. a healthy food choice, and the ability to react appropriately in a given situation. In obesity there may be a deficit in instrumental learning and behavior. The so called “Pavlovian-to-Instrumental Transfer” (PIT) is the influence of positive and negative stimuli from the environment onto the instrumental behavior. This project examines obesity- and gender-related alterations in instrumental learning and the influence of stimuli on instrumental behavior. The examinations will look at the behavioral and neuronal aspects. Normal- and overweight study participants do tests, in which they learn the association of special stimuli with behaviors and reward. By magnetic resonance tomography the activities in the brain will be measured. This study may contribute to clarify the obesity-specific deficits in instrumental learning and decision-making as well as the specific brain regions. This may help to develop new behavioral or pharmacological therapy approaches.

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AD2-6B98

Project head: Prof. Dr. med. Swen Hesse

Project title: Cholinergic network modulation in disinhibited eating behavior

Duration: 01.05.2015 – 30.04.2020

Overweight and obesity are partly due to a lack in regulating one’s eating behavior. This study examines the mechanisms of uncontrolled eating behavior. The neuro-transmitter acetylcholine and further transmitters as well as certain brain regions are crucial for the regulation of appetite and eating. With brain imaging via the combined positron-emission- and magnetic-resonance-tomography these brain regions and transmitters are being examined in study participants – with and without food stimuli. In addition the probands fill out questionnaires with reference to eating behavior. The results of this research could be a first step toward novel pharmaceutical or behavioral treatment approach, which can improve the regulation of eating behavior in obese patients.

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AD2-6C89

Project head: Prof. Dr. rer. nat. Anja Hilbert

Project title: Cognitive remediation therapy for adults with obesity – a randomized-controlled efficacy study (CRT)

Duration: 01.05.2015 – 31.01.2018

Obese individuals show difficulties in decision-making, planning, problem-solving, and in controlling behaviors. This is called a deficit in executive functioning. These difficulties are associated with a smaller weight loss in the conservative and surgical obesity treatment. Despite the relevance of restricted executive functioning in obesity, the research of this phenomenon has only now begun to develop therapeutic approaches to improve these functions in obese patients. Cognitive remediation therapy comprises mental trainings to improve the executive functions. The thinking about one’s own thinking is being taught (improvement of meta-cognition), and new cognitive strategies are being developed and tried out in daily life. Cognitive remediation therapy is an established treatment in diverse psychic disorders, e. g. in attention deficit and hyperactivity syndrome. There are indications that cognitive remediation therapy can improve executive functioning and weight loss in obesity. The goal of this study is to test the efficiency of this therapy, which the obese patient undergoes before weight reduction treatment.

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AD2-6C90

Project head: Prof. Dr. rer. nat. Anja Hilbert

Project title: Longitudinal assessment of bariatric surgery: psychological aspects
(PRAC, extension of study)

Duration: 01.05.2015 – 30.04.2020

Obesity or bariatric surgery is the most effective treatment in extreme obesity to ensure long-term weight loss and an improvement of associated diseases. However, a significant proportion of patients experience poor or insufficient weight loss, as well as weight regain over time. It appears that bariatric surgery influences the eating behavior and the psycho-social adaptation. These factors are decisive for controlling the weight after surgery. In the psycho-social register of adiposity surgery (PRAC start 2012) the data of questionnaires of patients from six treatment centers in Germany are being collected. The data cover information on eating behavior, psychopathology, life quality and further psychosocial factors. This project continues the research started and extends it to a long term data collection up to eight years after bariatric surgery. The prior aim of the project is to understand the connection of psychosocial aspects with the success of bariatric treatment in the long run. Furthermore, it will detect patients who need more psychological follow-up care after bariatric surgery.

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AD2-6D91

Project head: Prof. Dr. med. Arne Dietrich

Project title: Metabolic surgery for type-2-diabetes within BMI range of 28 to 40 kg/m² (MetaSurg)

Duration: 01.05.2015 – 30.04.2017

Obese patients often suffer from type 2 diabetes. They benefit especially from bariatric surgery, because after the intervention the diabetes usually improves considerably or even recedes completely (remission). The most common obesity (bariatric) surgery is the gastric bypass (Roux-en-Y Gastric Bypass, RYGB). In the MetaSurg study the surgical results of the RYGB are compared with the results after applying an intestinal tube (Endo Barrier™) regarding weight loss, comorbidities such as diabetes, and costs. The intestinal tube is inserted with the help of an endoscope and lines a part of the duodenum and small intestine, where it prevents the digestion of food and thus leads to a long-term weight loss and thus also to an improvement of the metabolism. Study participants will be supervised over eight years. The long-term medical- and cost-effectiveness of the two interventions will be be clarified.

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AD2-6D93
Project head: Prof. Dr. med. Arne Dietrich
Project title: Improving glucose metabolism beyond the effects of bariatric surgery by standardized postoperative exercise programs (GluMBSE)
Duration: 01.05.2015 – 30.04.2019

For some patients with morbid obesity surgical interventions, like for example the gastric bypass (Roux-en-Y Gastric Bypass or RYGB), are the only chance to sustainably lose enough weight. The RYGB is the so-called gold standard. In about 70 percent of the patients the gastric bypass operation leads to an improvement of the sugar (glucose) metabolism after the surgery - independently from the weight reduction. It is yet unknown in what way exercise after the intervention supports the positive change in glucose metabolism. Therefore, this study examines the effects of a supervised sports program and whether there are different results in a strength- or in an endurance-training program compared to a control group with normal activity. The sport program is supervised by sports scientists who adapt the training plans to the individual capabilities. Besides various parameters of the glucose metabolism (oral glucose tolerance test, insulin sensitivity of body cells, etc.) the performance and basal metabolism are investigated in the study participants. Furthermore, the scientists examine the muscles, the energy balance of the cells (mitochondria), abdominal adipose tissue, liver, gut flora and bladder function of the patients.

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AD2-6E95

Project head: Prof. Dr. Peter Kovacs

Project title: Identification and characterization of novel genes with neuronal and astrocytic influence on body weight regulation

Duration: 01.05.2015 – 30.04.2020

In the development of obesity the brain, especially the hypothalamus, plays an important role - besides the adipose tissue. In this brain region energy consumption and eating is being coordinated. Recent studies have detected new obesity risk genes in the brain which influence the emergence of obesity. The complex interaction of certain brain and neuronal cells (neurons and astrocytes) imply the influence of diverse genes in the development and degree of obesity. The study therefore investigates via DNA-analyses the different impacts of obesity risk genes on neurons and astrocytes in normal- and overweight mice. The final aim is to scrutinize the possible connection between the risk genes and eating behaviors as well as structural changes in the brain. This provides a better understanding of the brain’s role in the development of obesity especially with reference to energy metabolism (homeostasis) and eating behavior.

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AD2-6E96

Project head: Dr. rer. nat. Yvonne Böttcher

Project title: Longitudinal alterations in DNA methylation and association with obesity risk in children

Duration: 01.05.2015 – 30.04.2020

Besides the genetic hereditary impact on the obesity risk of a person, epigenetic influences are assumed to play a role. Epigenetic influences on the human genotype are natural chemical processes influencing the DNA (methylation). This DNA-methylation can be modulated by environmental influences, yet methylation does not change the components of the genes (DNA), but it influences the gene function. Methylation can turn specific genes on or off. An early genetic and epigenetic prediction of the obesity risky could be useful for appropriate prevention measures in childhood. This study examines the epigenetic influence on specific areas of the DNA and their potential association with the adiposity risk in later childhood. Moreover, the influence of age, gender and physical activity on this association will be clarified. Based on this data further research can follow whose insights will be useful for prevention and therapy programs.

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AD2-6E97
Project head: Dr. rer. nat. Yvonne Böttcher
Project title: Influence of post-bariatric exercise intervention on epigenetic profile
Duration: 01.05.2015 – 30.04.2020

The study examines the influence of a six-month exercise program (endurance and strength training) after bariatric surgery (Roux-Y-Gastric Bypass) on epigenetic processes in the skeletal muscles, blood and adipose tissue using samples that are taken before and after the exercise program. Epigenetic processes are chemical procedures (methylation) on the genomes (DNA) that can be modulated by environmental influences and which affect the gene function. Scientists assume that certain epigenetic influences correlate with adiposity and its accompanying diseases. The aim of the study is to investigate genes that are influenced differently by the different exercise programs and which affect body weight and abdominal fat (visceral adipose tissue). The generated data should help to develop recommendations for specific exercise intervention after bariatric surgery in Germany.

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AD2-6E99
Project head: Prof. Dr. rer. nat. Peter Kovacs
Project title: Bakterielle Translokation im Fettgewebe und metabolische Erkrankungen
Duration: 01.05.2015 – 31.12.2018

There is a growing number of studies indicating that the gut flora, its composition, and its functions are altered in obese persons and thus contributes to inflammation processes and metabolic diseases. Trials with animal models with high fat feeding suggest that some obesity associated diseases are due to bacterial influences. Therefore this study examines how bacteria in the adipose tissue, the degree of permeability of the guts, the inflammation of adipose tissue and the stage of obesity are interconnected. These examinations can help to better understand basic mechanisms and effects of specific bacteria in the development of obesity and metabolic diseases. The study results could be important for novel therapies, which concentrate directly on the causes of diseases.

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AD2-0773

Project head: Prof. Dr. med. Matthias Blüher
Project title: Role of environmental compounds and epigenetics in human adipose tissue dysfunction (ExpoEpiG)
Duration: 01.05.2015 – 31.10.2017

Persons with obesity often develop dysfunctions of the adipose tissue which affect health. Their adipose tissue contains enlarged fat cells, inflammation cells intrude into the fatty tissue and the visceral fat accumulates. The triggers for these dysfunctions are mostly unknown. Therefore, in this study it is being investigated, how pesticides and plasticizers in foods and in the environment get into the human adipose tissue and whether they contribute to the dysfunctions of the adipose tissue. Samples of visceral and subcutaneous adipose tissue from obese study participants and from post bariatric patients are tested for environmental or food contaminations. Finally, the substances that affect the adipose tissue most will in-depth be tested in animal models. The aim of this research is to identify environmental and food contaminants which are potentially harmful, to add them onto the list of dangerous substances, and to ban their use e. g. in convenient foods and food packages.

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AD2-0774

Project head: Prof. Dr. med. Ulf Wagner
Project title: Role of calcium-induced NLRP3 activation in obesity-induced inflammation
Duration: 01.05.2015 – 30.04.2018

This research project scientists examine how the inflammatory reactions typically occurring in obese patients are associated with calcium in the human body and with calcium receptors (G-protein coupled receptor) on macrophages (of the immune system). Therefore, the calcium concentration in the visceral and the subcutaneous adipose tissue is being measured and above all in areas of increased inflammation and cell destruction (apoptosis). The goal is to better understand the mechanisms of inflammation which are associated with calcium. Based on these findings therapy approaches could be developed to reduce the inflammation-associated diseases in obesity. The inflammation processes increase the risk of typ-2-diabetes and cardiovascular diseases in obese patients.

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AD2-0775  
**Project head:** Dr. rer. nat. Doreen Thor  
**Project title:** Specific impact of hypothalamic G-protein-signaling cascades on appetite  
**Duration:** 01.05.2015 – 31.10.2017

In order to find new ways to influence the regulation of appetite in humans, it is important to understand the underlying mechanisms. Here certain brain regions (neurons in the hypothalamus) are crucial, which regulate the energy balance (homeostasis) and the sensation of hunger. In this study special ways of neuronal signaling (signaling cascade) are being examined. The examination of this very complex brain network is possible due to especially altered receptors (DREADD). In a genetically adapted (transgenic) mouse model researchers test the influence of special neuronal receptors [G-protein-coupled receptors] on energy homeostasis and appetite regulation. Also, genetic factors are being searched that influence these receptors. A better understanding of the neuronal mechanisms of appetite control could help to develop novel pharmaceuticals and to better predict and understand side-effects of present anorexians.

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AD2-0777  
**Project head:** Prof. Dr. med. Antje Körner  
**Project title:** Early adipose tissue dysfunction with the development of obesity in children  
**Duration:** 01.05.2015 – 31.10.2017

Clinical studies have shown that obesity and the excessive accumulation of adipose tissue develops already in childhood and is associated with metabolic and cardio-vascular diseases. Therefore, this research project examines whether the alterations in the biology and functions of the adipose tissue in children are associated with the development of obesity and its associated diseases. Furthermore, the factors influencing the obesity-associated changes in biology and functions of the fatty tissue in children will be identified and characterized. Samples of children’s adipose tissue therefore are being in-depth examined and the results will be related to the clinical data of the children, for example their weight or BMI.

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**AD2-0778**  
Project head: Prof. Dr. med. Anette Kersting  
**Project title:** Bearing obesity – psychological risk factors for excessive weight gain during pregnancy  
**Duration:** 01.05.2015 – 31.10.2017  

The study examines psychological risk factors, which are closely associated with the development of obesity, and the risk factors’ impact on excessive weight gain during pregnancy. Traumatic life events, childhood neglect and maltreatment, and mental problems including eating disorders, impulsivity, and mental health problems (e.g. depression) are the examined risk factors for excessive weight gain during pregnancy. Therefore 400 women during and after pregnancy are being tested. The study’s aim is to provide insights into the excessive weight gain during pregnancy. The study’s results are prerequisite for the development of therapeutic approaches for pregnant women with a high obesity risk.

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**AD2-0779**  
Project head: Prof. Dr. med. Steffi Riedel-Heller, MPH  
**Project title:** Five A’s counseling in weight management of obese patients in primary care: A cluster-randomized controlled trail (INTERACT)  
**Duration:** 01.05.2015 – 31.10.2017  

Recent studies show that the medical attendance and counseling of obese patients by general practitioners (primary care) can be intensified. Similar to smoking cessation programs the Canadian Obesity Network developed and adapted the five As for the treatment of adiposity (Ask, Assess, Advise, Agree, Assist). The 5 As-approach aims at improving the interaction between provider / MD and patient. The goal of this study is to develop and implement a 90-minutes Internet-based online-tutorial for general practitioners. The efficiency and costs of the online-tutorial are being evaluated in a study with patients and general practitioners / primary care doctors. If the evaluation shows the efficiency of the tutorial will be made accessible and usable in medical networks free of charges.

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Project head: Prof. Dr. med. Hermann Wrigge

Project title: Strategies to preserve perioperative lung function in morbidly obese patients: postoperative continuous positive airway pressure (CPAP) following individualized protective mechanical ventilation

Duration: 01.05.2015 – 30.04.2017

Breathing and pulmonary Complications after bariatric surgery contribute significantly to the morbidity and mortality of obese patients. Studies with normal weight patients have shown that a special lung-protective mechanical ventilation during and after the surgery can reduce these complications. Therefore this study investigates whether this lung-protective ventilation during bariatric operations and a special breathing therapy postoperatively, which provides a continuous positive airway pressure, can reduce the number of pulmonary complications in obese patients.

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**CORE UNITS** support the IFB research projects

### AD2-S01

**Project head:** Prof. Dr. Markus Löffler  
**Project title:** Data Center  
**Duration:** 01.05.2015 – 30.04.2020

The core unit S1 collects the data of study participants and patients in clinical studies. Since this data is confidential, it is important to collect it centrally and safely in specialized data banks. The core unit offers support in planning, realization and evaluation of clinical studies, support and consultations in solving complex mathematical / statistical problems, as well as in modelling biological processes, and in the establishing the necessary infrastructure for a research data bank for obesity.

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### AD2-S02

**Project head:** Dr. rer. nat. Tatjana Schütz  
**Project title:** Nutrition and Clinical Phenotyping  
**Duration:** 01.05.2015 – 30.04.2020

The Core Unit "Nutrition and Clinical Phenotyping" is integrated in the central structure of the IFB. It aims to coordinate the standardized clinical assessment of various measured data in the study patients of the IFB Outpatient Clinic and in subjects of the IFB study clinic within the different treatment modules and in clinical trials. Thus, the data is collected standardized for IFB research database and thereby made available. In the context of clinical care pathways and study projects the Core Unit coordinates the nutritional therapy in study patients and carries it out. The Core Unit also regulates the methodology for data collection in subjects such as the study of nutrient intake and body composition. Thus, the Core Unit provides the quality assurance and supports the development of the IFB to a national reference center for obesity and for the care of bariatric patients.

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**AD2-S03**

Project head: Prof. Dr. Thomas Kahn  
**Project title:** Imaging Diagnostics in Adiposity  
**Duration:** 01.05.2015 – 30.04.2020

Magnetic resonance tomography and the magnetic resonance spectroscopy can assess the size and volume of visceral and subcutaneous adipose tissue, the liver fat content and the muscular fat distribution. Furthermore, the core unit helps analyzing and interpreting the data collected and supports in planning and realizing studies with extended examination methods.

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**AD2-S04**

Project head: Dr. rer. med. Nora Klöting  
**Project title:** Animal models in obesity  
**Duration:** 01.05.2015 – 30.04.2020

The causes and impacts of obesity are manifold. The genetic analysis in humans is difficult due to the clinical variety, genetic heterogeneity, and the diverse environmental influences. In animal models the genetic heterogeneity and the variety of environmental factors can be minimized by specialized breeding (congenic mice). Certain genes can be deactivated (knockout). Genes that are associated with obesity can be detected (candidate genes). The metabolism, adipose tissue and hormones, or the impact of bariatric surgery can be examined in detail, as well as the mechanisms, which protect from obesity and its associated diseases.

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