



DZD
German Center for
Diabetes Research

Translational Research

For a Future Without Diabetes



Diabetes – A Growing Threat

How Big Is the Problem?

Widespread disease –
347 million people
worldwide have diabetes

WHO projects that diabetes will be
the **7th** leading cause
of death in 2030

Every **10th** German
suffers from diabetes (7.6 million)
> **about 20%** of these patients
are **not aware** of their condition

Effects of Diabetes



- Cardiovascular disease is responsible for between 50% and 80% of deaths in people with diabetes.
- Diabetes is a leading cause of blindness, amputation and kidney failure.

The Disease Diabetes

Type 1

Onset usually in children and young adults.
Lack of insulin production caused by autoimmune disorder.
Therapy:
○ Insulin is essential.

Type 2

Mainly affects adults and elderly people.
Insulin resistance (insulin effect decreased) followed by insulin deficiency (insulin production decreased).
Prevention and therapy:
○ Lifestyle intervention (diet and exercise).
○ Later on oral drugs and insulin therapy.

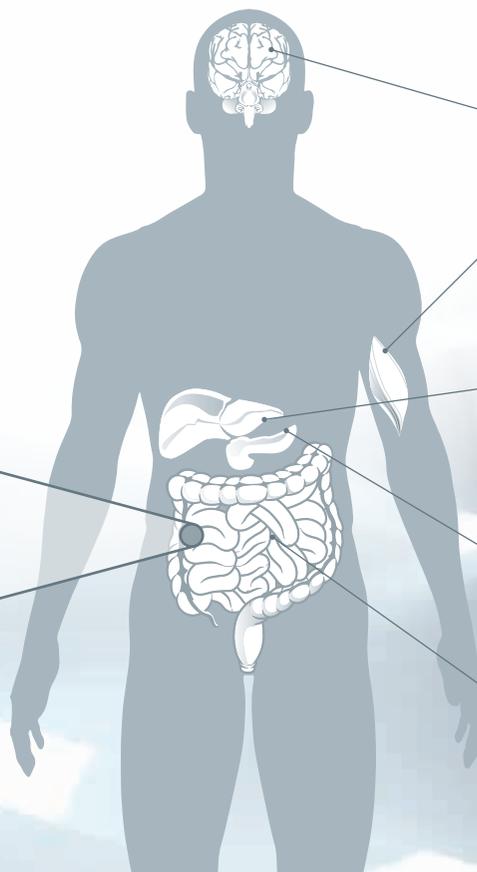
Gestational Diabetes

Pregnant women.
Raised blood sugar during pregnancy causing increased risk of type 2 diabetes in future.
Treatment by:
○ Lifestyle intervention.
○ Sometimes insulin therapy.

Systemic Disorder Type 2 Diabetes



Visceral Fat Tissue – The organ fat in the abdomen has a strong association with type 2 diabetes.



Brain – It is the mastermind in coordinating normal glucose regulation.

Muscle – Insulin resistance is characterized by reduced insulin-stimulated glucose uptake.

Liver – It stores and manufactures glucose, a malfunction may lead to type 2 diabetes.

Pancreatic Islets – They are home to the insulin-producing beta cells.

Gut/Microbiome – A poor mix of gut microbes may lead to an increased risk for type 2 diabetes.

DZD Translational Research

Taking research from bench to bedside

The DZD sets up a unique translational research concept to counteract the dramatic increase in diabetes:

- Applying next-generation thinking.
- Bridging research expertise across disciplinary borders.
- Turning exciting discoveries into action.

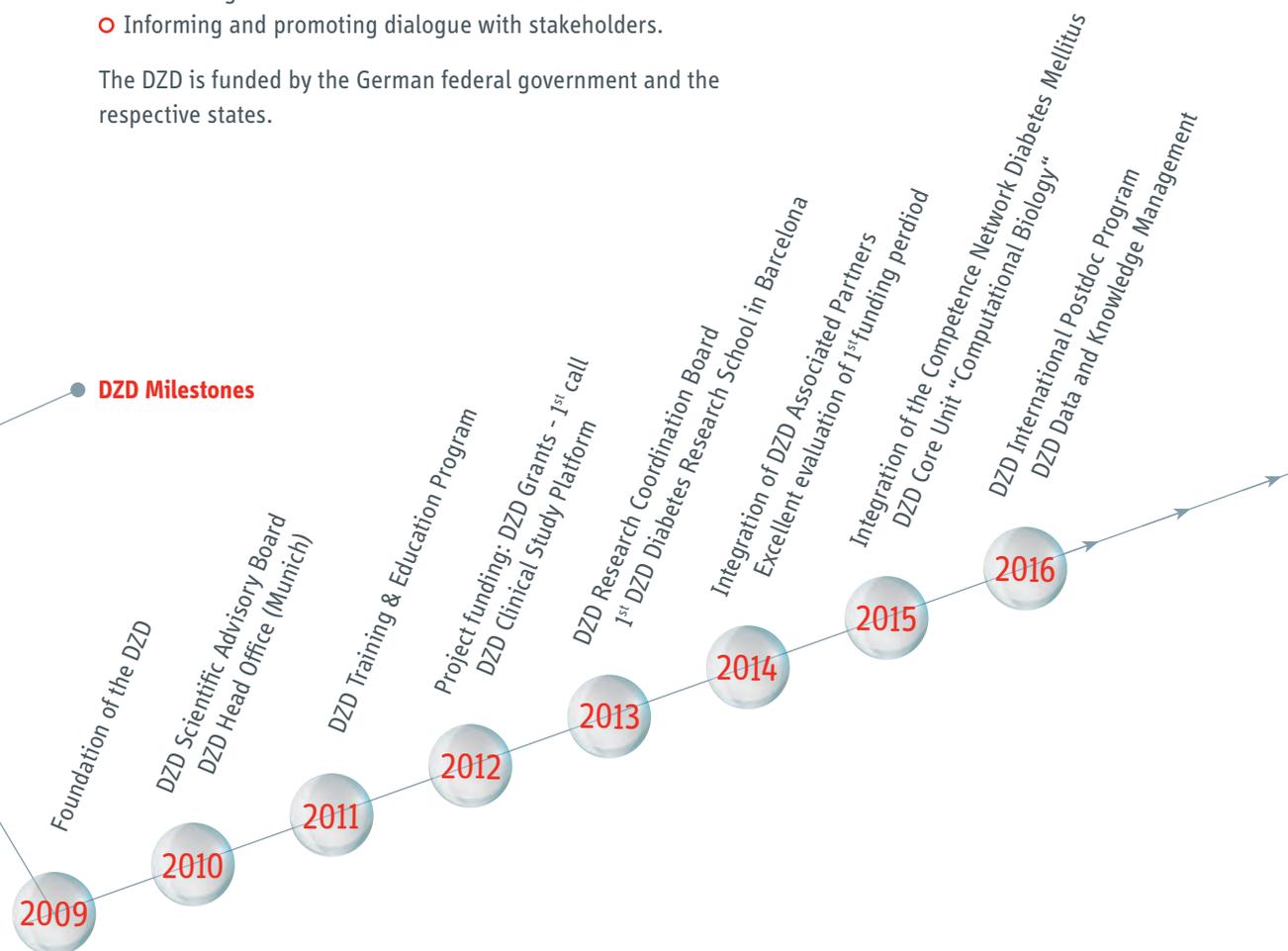
The DZD keeps an eye on the relevance to the real-life human situation and developing effective therapies.

German Center for Diabetes Research

The German Center for Diabetes Research (DZD) is a national association for translational research. It combines the efforts of leading German research institutions and universities in the field of metabolism and diabetes. More than 300 DZD scientists pursue a collaborative, integrative approach in the six DZD Research Areas. All efforts are focused on:

- Transferring knowledge generated in excellent science into medical benefits.
- Facilitating education tailored for translational research.
- Informing and promoting dialogue with stakeholders.

The DZD is funded by the German federal government and the respective states.



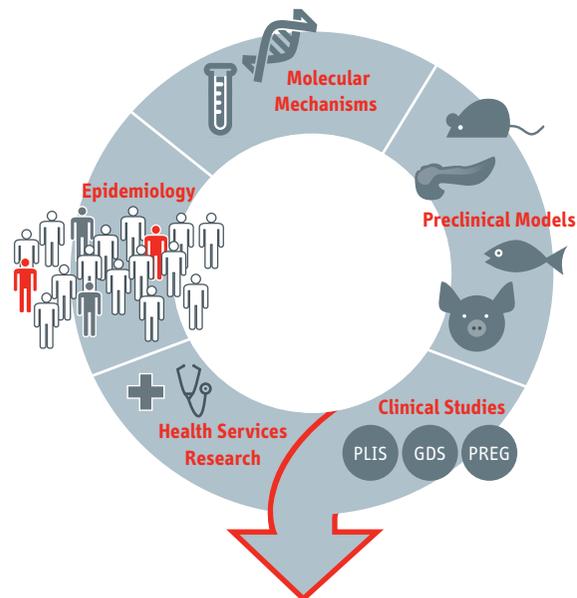
DZD Research Strategy

The future well-being of people and patients facing the threat of diabetes and its complications is the core mission of the DZD scientists' ambitious research.

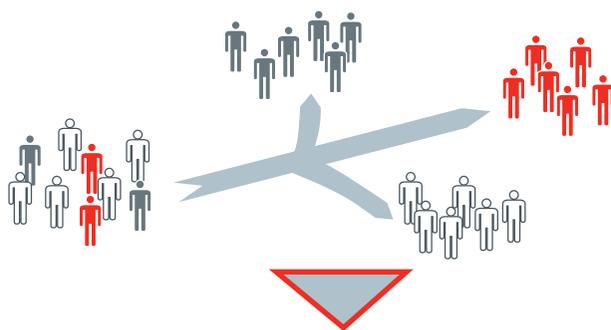
Common DZD research objectives:

- To elucidate the molecular mechanisms causing diabetes.
- To enable personalized diabetes prevention.
- To identify novel entry points for therapeutic interventions.
- To develop individualized therapies for diabetes and its complications.

The DZD research strategy takes into account all links in the value chain of translational biomedical research, integrating all types of discoveries from basic research to epidemiological and clinical studies.



**Diabetes Subphenotypes:
Stratification of Diabetes Patients & People at Risk**



**Prevent
Diabetes**

**Treat
Diabetes**

**Stop
Related
Disorders**

DZD Multicenter Clinical Studies

PLIS Prediabetes Lifestyle Intervention Study
Investigation of 1100 prediabetic individuals will result in tailored type 2 diabetes prevention strategies.

GPC German Prediabetes Cohort
8106 phenotyped individuals at risk for diabetes.

GDS German Diabetes Study
Metabolic, immunological, and lifestyle effects on the progression of diabetes and its complications in 2000 patients.

PREG Gestational Diabetes Study
Elucidation of the transgenerational regulation of metabolism in 800 women suffering from gestational diabetes and their offspring.



DZD Research Spotlights

Prevent Diabetes

LIFESTYLE is hereditary. Diet-induced obesity and diabetes can be inherited by the offspring through an **EPIGENETIC** effect. An epigenetic modification promotes obesity and precedes **FATTY LIVER** disease, both linked to type 2 diabetes.

Nature Genetics 2016 | Human Molecular Genetics 2016

"Epigenetic modifications can be inherited. Parents thus have a great responsibility for their offspring in diabetes prevention."

Martin Hrabě de Angelis (HMGU), DZD Board Member



Prediction of type 2 diabetes in adults:

GERMAN DIABETES RISK SCORE (GDRS) was updated with information about family history.

Risk score online: www.dzd-ev.de

RCP 2014

"The analyses of data of almost 34,000 people in the cohorts of the EPIC-Potsdam and the MONICA/KORA studies were the basis for updating and validating the GDRS."

Matthias Schulze (DifE), Head of the DZD Research Area "Epidemiology"



Non-alcoholic **FATTY LIVER** disease-mediated release of the **HEPATOKINE FETUIN-A** and **INSULIN RESISTANCE** increase the risk for type 2 diabetes. In cooperation with Hoffmann-La Roche, a compound has been successfully tested in humans that reduces liver fat content.

Nature Medicine 2013 | Lancet Diabetes & Endocrinology 2014

"Increased liver fat content is an important risk factor not only for obese but also for lean people. With the PLIS multicenter study we aim to design individualized prevention strategies."

Norbert Stefan (IDM), DZD Research Coordination Board Member



Respiratory infections in early life increase **RISK FOR TYPE 1 DIABETES**. An orally administered **INSULIN VACCINE** may prevent islet autoimmunity. In a preclinical model **INSULIN MIMETOPES** exceed the immunogenic effect of the natural epitopes.

JAMA 2016 | JAMA 2015 | Nature Communications 2016

"Our preventive vaccine gives the body a little help if the immune system doesn't learn how to protect from type 1 diabetes by itself."

Anette-Gabriele Ziegler (HMGU), Head of the DZD Research Area "T1D"



Treat Diabetes



Improving the quality of life for people with type 1 diabetes: **TRANSPLANTATION** of human islets into the chamber system for auto-regulated insulin secretion. No need for immunosuppression. **REPLENISHMENT OF BETA CELLS:** The protein Flattop is a marker to distinguish between mature beta cells and their precursors in the pancreas.

PNAS 2013 | Nature 2016

"We regard the beta-cell chamber system as a milestone on the way to an insulin-independent life for patients with type 1 diabetes."

Barbara Ludwig (PLID), DZD Group Leader



HORMONE TRIPLET molecule unifying the action profiles of three gastrointestinal hormones (GLP-1, GIP and glucagon) reduces blood sugar level and body fat considerably better than existing drugs in humans.

Nature Medicine 2015

"Our 3-in-1-molecule seems to break the vicious circle of the bodies' signals inducing weight gain. Such single-molecule polytherapies are emerging as potentially transformative therapeutics for obesity and diabetes."

Matthias Tschöp (HMGU), Head of the DZD Research Area "Novel Therapeutic Approaches"



Therapy target **BETA CELLS:** Aged **INSULIN SECRETORY GRANULES** display reduced competence for glucose-stimulated transport. New finding for a well-known cough suppressant: It improves insulin secretion – important for type 2 diabetes – and **PROTECTS PANCREATIC ISLETS** from cell death – interesting for type 1 diabetes.

PNAS 2015 | Nature Medicine 2015

"The Human Islet Biobank is a very special and unique DZD infrastructure as it constitutes a precious tool for new therapeutic approaches in beta cells."

Michele Solimena (PLID), DZD Board Member

Stop Related Disorders



Hepatic mitochondrial flexibility is lost in **STEATOHEPATITIS** – this discovery could serve as future target for prevention and treatment.

Cell Metabolism 2015

"All partners of the DZD cooperating in the German Diabetes Study aim to achieve an improved understanding of diabetes pathophysiology and to develop individualized therapeutic strategies."

Julia Szendrödi (DDZ), DZD Group Leader



Every third diabetes patient suffers from neuropathic pain or the diabetic foot syndrome. Early detection methods of **NERVE DAMAGE** such as corneal confocal microscopy are a prerequisite for the prevention of late complications.

Diabetes 2014

"So far we are missing examination tools for a reliable early diagnosis of diabetic nerve damages. Our findings are an important step towards novel preventive strategies."

Dan Ziegler (DDZ), DZD Group Leader

DZD Research Infrastructures

Access to state-of-the-art infrastructures is central to the success of the DZD's translational research strategy. From the beginning, the DZD has aimed at building and expanding sustainable world-class facilities in the key technologies for metabolic research:



Preclinical Models

Understanding the biological system on the cellular and the organism level is a prerequisite for the identification of novel therapeutic targets.

German Diabetes Mouse Clinic | Large Animal Model | Zebrafish | Human Islet Biobank | Imaging Platform



Translational Research

The development of new diagnostic or therapeutic strategies requires specific key infrastructures.

Clinical Study Platform | GMP Laboratory | High-Throughput Facilities



Pheno- and Genotyping

'Omics' technologies reveal details about the molecular signatures of diabetes and associated changes during the progression of the disease.

Genomics | Proteomics | Metabolomics | Computational Biology

DZD Training & Education

With its unique focus on all aspects of translational research the DZD is dedicated to educating a new generation of internationally competitive scientists and clinicians in the diabetes field. The DZD Training & Education Program provides a high-level qualification in translational diabetes research and promotes a close network of these clinical and basic junior scientists. Equal opportunity – regardless of gender or social and cultural background – is a hallmark of the DZD.

An annual highlight is the “DZD Diabetes Research School” where renowned scientists discuss the most important current questions in the field of diabetes in a relaxed atmosphere with an international group of students and young scientists.



DZD Organization and Partners

DDZ | German Diabetes Center in Düsseldorf

Leibniz Center for Diabetes Research
Auf'm Hennekamp 65, 40225 Düsseldorf
Speaker: Prof. Dr. Dr. h.c. Michael Roden

DIfE | German Institute of Human Nutrition Potsdam-Rehbrücke

Member of the Leibniz Association
Arthur-Scheunert-Allee 114-116, 14558 Nuthetal
Speaker: Prof. Dr. Annette Schürmann

HMGU | Helmholtz Zentrum München

German Research Center for Environmental Health
Ingolstädter Landstrasse 1, 85764 Neuherberg
Speaker: Prof. Dr. Dr. h.c. Martin Hrabě de Angelis

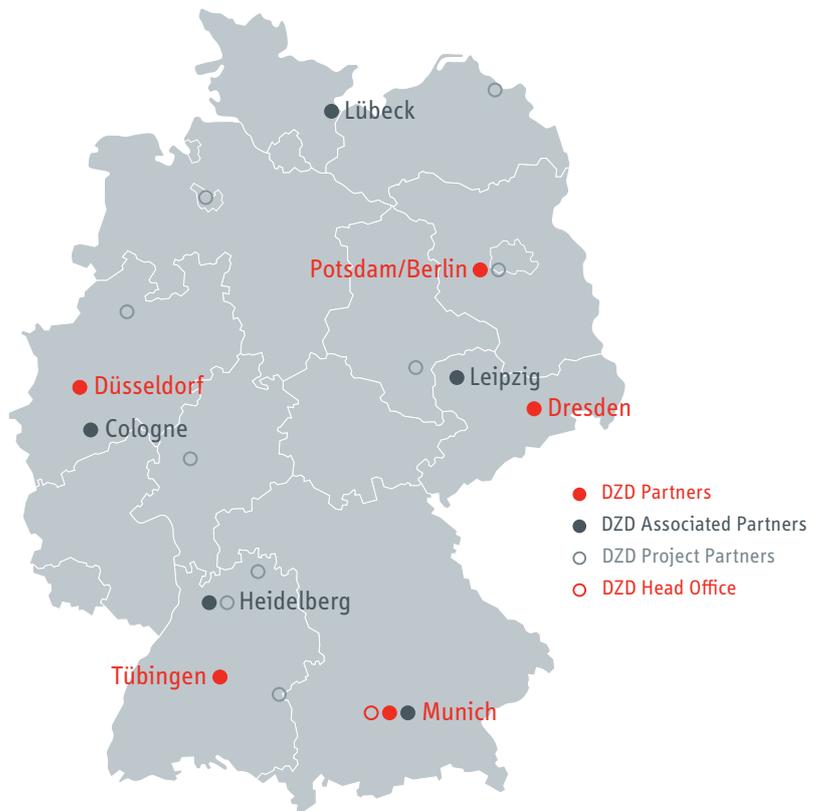
IDM | Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Zentrum München at the Eberhard Karls University of Tuebingen

Geschwister-Scholl-Platz, 72074 Tübingen
Speaker: Prof. Dr. Dr. h.c. Hans-Ulrich Häring

PLID | DZD-Paul Langerhans Institute of the Helmholtz Zentrum München at the University Hospital and Faculty of Medicine Carl Gustav Carus of TU Dresden

Fetscherstrasse 74, 01307 Dresden
Speaker: Prof. Dr. Dr. Michele Solimena

Associated partners at the universities in Heidelberg, Munich, Lübeck, Leipzig and Cologne.



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