

**Stellungnahme zum  
Deutschen Diabeteszentrum,  
Leibniz Zentrum für Diabetes-Forschung  
an der Heinrich-Heine-Universität Düsseldorf (DDZ)**

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## Vorbemerkung

Die Einrichtungen der Forschung und der wissenschaftlichen Infrastruktur, die sich in der Leibniz-Gemeinschaft zusammengeschlossen haben, werden von Bund und Ländern wegen ihrer überregionalen Bedeutung und eines gesamtstaatlichen wissenschaftspolitischen Interesses gemeinsam gefördert. Turnusmäßig, spätestens alle sieben Jahre, überprüfen Bund und Länder, ob die Voraussetzungen für die gemeinsame Förderung einer Leibniz-Einrichtung noch erfüllt sind.<sup>1</sup>

Die wesentliche Grundlage für die Überprüfung in der Gemeinsamen Wissenschaftskonferenz ist regelmäßig eine unabhängige Evaluierung durch den Senat der Leibniz-Gemeinschaft. Die Stellungnahmen des Senats bereitet der Senatsausschuss Evaluierung vor.

Für die Bewertung einer Einrichtung setzt der Ausschuss Bewertungsgruppen mit unabhängigen, fachlich einschlägigen Sachverständigen ein. Ihr stand eine vom DDZ erstellte Evaluierungsunterlage zur Verfügung. Die wesentlichen Aussagen dieser Unterlage sind in der Darstellung (Anlage A dieser Stellungnahme) zusammengefasst.

Wegen der Corona-Pandemie musste der für den 7. und 8. Dezember 2020 vorgesehene Evaluierungsbesuch am DDZ in Düsseldorf entfallen. Die Bewertung erfolgte im Rahmen eines Ersatzverfahrens, das der Senatsausschuss Evaluierung (SAE) in Umsetzung eines Grundsatzbeschlusses des Senats der Leibniz-Gemeinschaft vom 31. März 2020 eingerichtet hat. Der Senat hält in diesem Grundsatzbeschluss fest, dass das Ersatzverfahren ein Notbehelf ist und ausschließlich auf Einrichtungen angewendet wird, die im Regelturmus von sieben Jahren evaluiert werden. Die Bewertungen, auf deren Grundlage der Senat Stellung nimmt, sind auf zentrale Kernfragen der Entwicklung und Perspektive einer Leibniz-Einrichtung fokussiert. Ausführliche Einschätzungen und Schlussvoten zu Teilbereichen und Planungen für „kleine strategische Sondertatbestände“ müssen regelmäßig entfallen.

Die Bewertungsgruppe erstellte den Bewertungsbericht (Anlage B). Das DDZ nahm dazu Stellung (Anlage C). Der Senat der Leibniz-Gemeinschaft verabschiedete am 1. Juli 2021 auf dieser Grundlage die vorliegende Stellungnahme. Der Senat dankt den Mitgliedern der Bewertungsgruppe und des Senatsausschusses Evaluierung für ihre Arbeit.

## 1. Beurteilung und Empfehlungen

Der Senat schließt sich den Beurteilungen und Empfehlungen der Bewertungsgruppe an. Das Deutsche Diabetes-Zentrum (DDZ), Leibniz Zentrum für Diabetes-Forschung an der Heinrich-Heine-Universität Düsseldorf (HHU) arbeitet sehr erfolgreich auf dem Gebiet der Prävention, Früherkennung, Diagnostik und Therapie des Diabetes mellitus sowie seinen Begleit- und Folgeerkrankungen. In sehr überzeugender Weise wird dazu molekular- und zellbiologische Grundlagenforschung mit klinischer, epidemiologischer und versorgungsbezogener Forschung kombiniert.

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<sup>1</sup> Ausführungsvereinbarung zum GWK-Abkommen über die gemeinsame Förderung der Mitgliedseinrichtungen der Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e. V.

Unter dem seit 2008 tätigen Direktor hat sich das DDZ nach zuvor schwierigen Jahren hervorragend entwickelt. Der bereits bei der **letzten Evaluierung** weit vorangeschrittene Reformprozess wurde abgeschlossen. Mit neuen Gruppen deckt das DDZ jetzt das gesamte Spektrum der Diabetesforschung ab. Insbesondere durch seine klinischen Studien ist es mittlerweile international weithin sichtbar.

Mit seinen **Arbeitsergebnissen** trägt das DDZ zur Reduzierung der individuellen und gesellschaftlichen Belastung durch den Diabetes mellitus bei. Die Forschungsergebnisse sind von hoher Qualität und werden in beeindruckender Anzahl in sehr hochrangigen Zeitschriften veröffentlicht. Das DDZ ist an verschiedenen äußerst wertvollen epidemiologischen Kohortenstudien beteiligt. Hervorzuheben ist die vom DDZ geleitete Deutsche Diabetes-Studie, die bundesweit an acht Standorten im Rahmen des Deutschen Zentrums für Diabetesforschung (DZD) durchgeführt wird. Zudem betreibt das DDZ gemeinsam mit dem Leibniz-Institut für Umweltmedizinische Forschung (IUF) das NAKO Studienzentrum in Düsseldorf. Das DDZ bereitet Informationen zum Diabetes und zur Prävention der Erkrankung sowohl für medizinische und pflegende Fachkräfte als auch für eine breite Öffentlichkeit auf. Es wird begrüßt, dass dazu das Nationale Diabetes-Informationszentrum des DDZ wie bei der letzten Evaluierung empfohlen gestärkt wurde. Das DDZ verfügt über sehr gute Strukturen für eine Translation von Forschungsergebnissen in die klinische Praxis. In seinem Klinischen Studienzentrum kooperiert es dazu eng mit dem Universitätsklinikum Düsseldorf (UKD). Zudem hat das DDZ die präklinische Medikamentenentwicklung ausgebaut. Das Wertschöpfungspotenzial in der Zusammenarbeit mit Unternehmen sollte im Anschluss daran noch besser ausgeschöpft werden.

Die Leistungen des DDZ werden in fünf Teilinstituten erbracht, die in Forschungsprogrammen zusammenarbeiten. Das DDZ wird seine Arbeiten zukünftig an dem übergreifenden Thema „Präzisionsdiabetologie“ orientieren und hat dafür ein geeignetes Konzept entwickelt. Die Teilinstitute sollten sich jedoch noch eindeutiger auf dieses **Gesamtkonzept** hin ausrichten. Das DDZ plant außerdem, mit zusätzlichen Mitteln der Bund-Länder-Förderung („kleiner strategischer Sondertatbestand“) eine neue unabhängige Forschungsgruppe „Computergestützte Diabetologie“ und eine zentrale Biobank einzurichten. Ziel ist es, bestehende und neue Daten, auch aus funktionellen Studien („fluxomics“) zu Menschen und Modellorganismen, zu bündeln und auszuwerten. Die Planungen des DDZ sind schlüssig und sollten unter Einbeziehung der Hinweise im Bewertungsbericht weiterverfolgt werden.

Die institutionelle **Förderung** des DDZ stieg seit der letzten Evaluierung von ca. 11 Mio. € (2012) auf 14 Mio. € (2019). Auch die Drittmiteinnahmen wurden in dieser Zeit von 5 Mio. € (31 % des Gesamtbudgets) auf 7,8 Mio. € (36 %) gesteigert. Davon gehen 6,5 Mio. € auf Bundesmittel für Aufgaben im DZD und für die NAKO Gesundheitsstudie zurück. Das Institut sollte sein Drittmittelportfolio weiter diversifizieren, dabei die Erträge aus Förderungen der DFG erhöhen und insbesondere das Potenzial zur Einwerbung von EU-Mitteln besser ausschöpfen.

Das DDZ ist national und international sehr gut vernetzt. Ausgesprochen eng ist das Institut mit Universität und Universitätsklinikum Düsseldorf (UKD) verbunden. Es wird begrüßt, dass die **Zusammenarbeit** in der Stoffwechsel-, Diabetes- und kardiovaskulären

Forschung weiter vertieft wird. Dazu wurden gemeinsam umfangreiche Mittel für einen neuen Forschungsbau eingeworben (CARDDIAB, ca. 73 Mio. Euro).

Der **wissenschaftliche Direktor** des DDZ leistet hervorragende Arbeit. Er ist im Hauptamt Direktor einer Klinik am UKD. Das DDZ leitet er im Nebenamt und führt dort außerdem das mit inzwischen 70 Stellen größte Teilinstitut, in dem auch das klinische Studienzentrum angesiedelt ist. Angesichts der mittlerweile erreichten Größe des Instituts sollte geprüft werden, wie eine Entlastung erreicht werden kann. Der Senat empfiehlt außerdem, für die in einigen Jahren anstehende ruhestandsbedingte Neubesetzung die Leitung des DDZ im Hauptamt vorzusehen.

Das DDZ hat den Anteil von **Wissenschaftlerinnen** in Leitungspositionen seit der vergangenen Evaluierung erhöht, sollte aber Neubesetzungen für eine weitere Verbesserung nutzen. Zum 31. Dezember 2019 war unter den fünf Institutsleitungen nur eine Wissenschaftlerin (20 %), unter den 14 Gruppenleitungen waren es sechs (43 %). Insgesamt sind 60 % des wissenschaftlichen Personals am DDZ Frauen.

Es wird begrüßt, dass in der **Satzung** die Funktionstrennung zwischen Kuratorium und Wissenschaftlichem Beirat wie empfohlen klar geregelt wurde. Die Amtszeit der Beiratsmitglieder ist auf im Regelfall vier Jahre begrenzt, allerdings ist eine Wiederwahl nicht nur einmal, sondern unlimitiert möglich. Diese Möglichkeit wird auch genutzt. Der Senat erwartet vom Kuratorium, dass es diese Praxis ab jetzt ändert und eine effektive Regelung zur Begrenzung der Beiratsmitgliedschaft auf maximal acht Jahre in der Satzung verankert.

Mit seinen Leistungen und Strukturen erfüllt das DDZ die Anforderungen, die an eine Einrichtung von überregionaler Bedeutung und gesamtstaatlichem wissenschaftspolitischen Interesse zu stellen sind. Die Arbeiten erfordern ein breites Fach- und Methodenspektrum. Sie führen zu Forschungs-, Infrastruktur- und Transferleistungen, die in dieser Form nicht an einer Hochschule erbracht werden können. Eine Eingliederung in eine Hochschule wird daher nicht empfohlen.

## 2. Zur Stellungnahme des DDZ

Der Senat geht davon aus, dass das DDZ die Empfehlungen und Hinweise aus dem Bewertungsbericht bei seiner weiteren Arbeit berücksichtigt.

## 3. Förderempfehlung

Der Senat der Leibniz-Gemeinschaft empfiehlt Bund und Ländern, das DDZ als Einrichtung der Forschung und der wissenschaftlichen Infrastruktur auf der Grundlage der Ausführungsvereinbarung WGL weiter zu fördern.

## **Annex A: Status report**

### **German Diabetes Center (DDZ) - Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf**

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## 1. Key data, structure and tasks

### Key data

Year established:	1964
Admission to joint funding by Federal and <i>Länder</i> Governments:	1977
Admission to the Leibniz Association:	1997
Last statement by the Leibniz Senate:	2014
Legal form:	Registered association
Responsible department at <i>Länder</i> level:	Ministry of Culture and Science of North Rhine-Westphalia (MKW NRW)
Responsible department at Federal level:	Federal Ministry of Health (BMG)

### Total budget (2019)

- € 14.1m institutional funding
- € 7.8m revenue from project grants

### Number of staff (2019)

- 109 individuals in research and scientific services
- 85 individuals in service sector
- 17 individuals in administration

### Mission and tasks

The German Diabetes Research Association (*Deutsche Diabetes-Forschungsgesellschaft e. V., DDFG e. V.*) runs the legally non-independent German Diabetes Center (DDZ).

“The **purpose of the association** is the promotion of science, research and the public health system. The association has the task of conducting and promoting research in the field of diabetes mellitus in order to record the effect of this disease on the human organism and to devise measures for the prevention and treatment of diabetes mellitus and its accompanying and secondary diseases.” (§2 (1) association’s articles)

“The association’s purpose is realised in particular through:

- a) the implementation of a translational research strategy. The research projects encompass all aspects of diabetes mellitus and its related metabolic disorders, from the basic issues to the impact on society,
- b) the maintenance and use of laboratories for research purposes, and
- c) public relations work, including the holding of events.” (§2 (2))

DDZ comprises **five subdivisions** (called **institutes**), each of whom leads one of the **research programs A – E** and contributes to **program F** (German Diabetes Study, GDS) as well as to all other programs in an inter- and transdisciplinary and coordinated manner. Each institute comprises a variable number of **research groups, junior research groups**

or **platforms**. Furthermore, the DDZ has **staff units** for preclinical models (Oskar Minowski Laboratory), the National Diabetes Information Center (NDC), press office and administration (cf. appendix 1).

## 2. Overall concept, activities and results

According to **DDZ's mission statement**, the institute aims at contributing to reducing the individual, social and societal burden of diabetes through interdisciplinary research. Its focus is to offer translational networking of molecular and cell biology research with clinical, epidemiological and care-related research. Its scientific contributions aim at improving prevention, early detection, diagnosis and treatment of diabetes and its comorbidities and complications, as well as at increasing the knowledge on the epidemiology and health economics of diabetes in Germany.

DDZ's **research portfolio** comprises **(a)** key activities (as defined by the six research programs), as well as long-term **(b)** regional (as an institute affiliated with Heinrich Heine University Düsseldorf) and **(c)** national institutional scientific cooperation (as a founding member of the German Center for Diabetes Research, DZD e. V. – cf. chapter 6).

**Research Program A:** Diabetes-related signalling in pancreatic islets and liver (lead: Institute for Vascular and Islet Cell Biology) including

- Pathophysiology of the beta cell
- Development of novel approaches for diabetes treatment
- Endothelial cells and hepatic cells in diabetes

**Research Program B:** Pathogenic mechanisms and molecular targets for diabetes (lead: Institute for Clinical Biochemistry and Pathobiochemistry) including

- Experimental genetics and molecular mechanisms of insulin resistance and type 2 diabetes
- Genetics and environmental interactions
- Regulation of cellular energy metabolism and organ communication

**Research Program C:** Origin, development and consequences of diabetes (lead: Institute for Clinical Diabetology) including

- Dysregulation of energy metabolism and inflammatory pathways as mechanisms of the development of diabetes, its complications and comorbidities
- Early detection, prevention and treatment of diabetes, its complications and comorbidities
- New methods of comprehensive clinical phenotyping

**Research Program D:** Epidemiology and therapy assessment of diabetes (lead: Institute for Biometrics and Epidemiology) including

- Epidemiology, risk factors and early detection for diabetes and its complications
- Efficacy and safety of pharmacotherapy of diabetes
- Statistical methods for design and analysis of experimental, clinical and epidemiological studies in diabetes research

- Systematic reviews and (network) meta-analyses of lifestyle factors and diabetes
- German National Cohort (GNC, *NAKO Gesundheitsstudie*)

**Research Program E:** Patient-centred research and health economics evaluation in diabetes (lead: Institute for Health Service Research and Health Economics) including

- Patient-relevant outcomes in diabetes care
- Diabetes-related complex interventions and health economic evaluation
- Patients' needs and preferences in diabetes

**Research Program F:** German Diabetes Study (GDS, *Deutsche Diabetes Studie*; jointly run by all five institutes of DDZ) including

- Characterisation of the progression and comorbidities of diabetes in adulthood

## Research

Since the last evaluation, DDZ institutes worked together for **(a)** deconstructing classical diabetes types into subgroups (clusters, subtypes) and specific comorbidities and complications, **(b)** reconstructing diabetes by investigating underlying mechanisms, **(c)** identifying and testing targets for the tailored treatment and diabetes management and **(d)** analysing epidemiological and health economic trends.

Between 2017 and 2019 DDZ researchers contributed to 585 **publications**, including 564 articles in peer-review journals (cf. appendix 2). The scientific results generated in the five institutes are described in more detail in chapter 7.

## Research infrastructures

During the last years, DDZ has expanded the existing infrastructure and invested in novel hardware to broaden the spectrum of its cohorts, enlarged its clinical research center (CRC), improved comprehensive phenotyping with specialised platforms, laboratories and biobanks, accelerated translational studies using complementary approaches in (pre)clinical models, broadened the access to big data, and facilitated drug development.

DDZ oversees/contributes to the following **cohorts** and **registries**:

German Diabetes Study ( <b>GDS</b> <i>Deutsche Diabetes Studie</i> )	Recent-onset type 2 (T2D) or type 1 diabetes (T1D)	Baseline: 978 T2D, 454 T1D, 197 controls 5-years follow up: 502 (ongoing) 79 % by DDZ, 21 % by other centres
The effect of bariatric surgery on insulin sensitivity and energy metabolism ( <b>BARIA-DDZ</b> )	Grade III obesity +/- non-alcoholic fatty liver disease (NAFLD) +/- T2D/ T1D	Baseline: 197 Follow up (3 m - 5 years): 143 (ongoing)
Mechanisms of diabetic cardiomyopathy ( <b>DICARDI</b> )	Heart failure +/- diabetes and +/- heart transplantation with indication for myocardial biopsy	Baseline: 238 (409 myocardial biopsies)
Metabolic phenotyping and follow up in people with diabetes and ST-elevation myocardial infarction ( <b>DISTEMI</b> )	Sub-population of the ST-elevation myocardial infarction (STEMI) cohort +/- T2D/T1D at Heinrich Heine University Düsseldorf	Baseline: 53 cases, 54 controls Follow up: 32 cases, 44 controls
DDZ Diabetes Incidence Register	Children and young adults (<35 years) + T2D/T1D	>11.000 newly diagnosed T1D and T2D in children and young adults since 1989



Probing the role of sodium channels in painful neuropathies study ( <b>PROPANE</b> )	Painless or painful diabetic neuropathy	Baseline: 386 5-years follow up: ongoing
German National Cohort ( <b>GNC NAKO Gesundheitsstudie</b> )	Representative sample of the adult population in the Düsseldorf area	Baseline: 9.100 Follow up: ongoing (planned 6.000)
German gestational diabetes study ( <b>PREG</b> )	Females with and without gestational diabetes	Baseline: 51 Postnatal follow up: ongoing
<i>Kooperative Gesundheitsforschung in der Region Augsburg</i> ( <b>KORA</b> )	Representative sample of the adult population in a Southern German region	Baseline: 4.261 14-year follow up: 2.279

For DDZ's specific infrastructures cf. chapter 4.

## Transfer

Transfer at DDZ is directed towards use of (pre)clinical research results in the scientific community and application in clinical practice, focusing on maintaining health, managing diabetes and data transfer for large data bases. DDZ also consults for decision makers on (inter)national levels, communicates information and actively interacts with people with (pre)diabetes and the general public.

Application of new knowledge: Findings on novel drug targets, biomarkers, diagnostic scores, clinical trials and efficacy of therapies are translated directly by DDZ researchers as members of (inter)national guideline committees (e. g. American Diabetes Association, ADA; European Association for the Studies of Diabetes, EASD; *Deutsche Diabetes Gesellschaft*, DDG; *Nationale Versorgungsleitlinie*). Also, research data are made available to (inter)national consortia and registers (Meta-Analysis of Glucose, MAGIC; Diabetes genetics, DIAGRAM; EURODIAB). Scientific know-how is transferred via academic education/training as well as hands-on courses for students, research technicians and nurses, medical and clinician scientists (EASD training course, Rainbow workshop, and DZD clamp courses).

Patents: DDZ researchers submitted patents related to diagnostic biomarkers such as metabolite signatures of type 2 diabetes or TBC1 domain family member 1 for obesity and to morphinan compounds for treating diabetes and related disorders (cf. appendix 2).

DDZ seminars and lecture program: DDZ organises scientific meetings, plenary lectures and seminars by inviting (inter)national researchers to present their recent findings. For this, DDZ has developed specific formats such as the Düsseldorf Diabetes Lecture (8 lectures 2017–2019) and DDZ Seminars (22 lectures 2017–2019). Further, the Von Mering Gold Medal is bestowed annually upon one scientist to recognise long-standing contributions to German diabetes research.

Consultancy: DDZ scientists advise its funding bodies and professional scientific associations. They are members of advisory bodies to the government, research institutions and universities and have leading positions in (inter)national professional research organisations, e. g. the Committee Medicine of the German Science Council, the Forum Health Science, the National Diabetes-Surveillance, the National Diabetes Information Strategy as well as the International Life Sciences Institute, Brussels, Medical University Vienna, *l'Agence Nationale de la Recherche*, ANR, EU-funded ePredice, the global DISCOVER study,

and the GNC Epidemiological Steering Committee. Between 2017–2019 DDZ has produced 125 expert reviews (cf. appendix 2).

Communication: DDZ connects to the public and via its **National Diabetes Information Center** (NDC), which coordinates the reach out to affected and healthy citizens, health care professionals and the scientific community. Starting in 2018, NDC relaunched its information platform ( $\approx 215.000$  visitors in 2019) with interactive modules on epidemiology and risk assessment and a barrier-free homepage. Also, DDZ started the nationwide campaign *Diabetes – Not just a Question of Type* with 16 short films in German, English, Turkish and Arabic language as well as print material. DDZ provides information via internet ([diabetesinformationsdienst.de](http://diabetesinformationsdienst.de); [diabinfo.de](http://diabinfo.de)) and social media. Furthermore, NDC operates a regional innovation network of stakeholders (RIN Diabetes/*Regionales Innovationsnetzwerk Diabetes*), supported by the state government, organises special events and helps to implement prevention programs in the Düsseldorf region.

### 3. Changes and planning

#### Development since the previous evaluation

Since 2013, DDZ has increased its original four to now **six programs** to further sharpen its transdisciplinary approach by connecting basic and patient-oriented clinical research, epidemiology, and health services research, as postulated by its new mission statement and by its claim "Understanding diabetes – helping people" (*Diabetes erforschen – Menschen helfen*). According to DDZ, the overarching strategy to initiate **Precision Diabetology** led to intensified translational research on mechanisms underlying the different diabetes subtypes and diabetes-related comorbidities as well as to strengthened research activities in patient-centred health care. This, as DDZ points out, now allows to explore common and novel therapeutic approaches through the **complete translational research chain**, i.e. preclinical (Program A, B), clinical (Program C, D, E), and epidemiological (Program D, E), followed by the transfer into routine care, considering the perspective of people with diabetes (Program E, F).

The previous program on preclinical research was developed into the **new Programs A and B**, primarily investigating the basic mechanisms of diabetes-relevant organ systems and molecular targets in preclinical models and clinical samples. While the new program A addresses diabetes-related signalling in pancreatic islets as well as in the cardiovascular system and liver, the new program B targets more molecular mechanisms involved in the development and progression of insulin resistance and type 2 diabetes.

The main projects of **Program C** have remained to address energy metabolism and inflammatory pathways in humans, but now also focussing on the better understanding of subgroups of non-autoimmune diabetes and on broadening its portfolio regarding diabetes-related complications such as non-alcoholic fatty liver diseases (NAFLD).

Based on the recommendations from 2013, the original Program C was extended to the **new Programs D and E**, examining population-based approaches for diabetes prevention and care with Program D focusing on epidemiology and diabetes treatment and Program E focusing on patient-relevant and health economic aspects.

The prospective, multicentre cohort GDS (*Deutsche Diabetes Studie*) has been continued as the joint **Program F** of all DDZ units. The GDS steering committee decided to extend the cohort size from n=1.000 to n=2.000 and the follow up period from 5 to 20 years. While certain modules have been replaced DDZ also initiated new cohorts such as DESTEMI and DICARDI.

On its own account, DDZ introduced several coordinated activities in order to optimise the interdisciplinary research concept, to restructure less competitive research groups and to increase recruitment of excellent female junior researchers internationally.

### **Strategic work planning for the coming years**

In the coming years DDZ aims at developing **Precision Diabetology** from classical translational research for stratified diagnosis and treatment. According to DDZ, the advantages for this research strategy are given by recent phenomic validation of diabetes subgroups and by the epidemiological findings in groups with specific diabetes risk, biomarkers and comorbidities. The growing multidimensional data sets can feed into the preclinical studies to develop biomarkers and therapeutic targets in models established at DDZ. Integrated analysis of these findings will allow both for constructing data-based algorithms for stratified diagnosis, and for designing and conducting novel clinical trials. Assessment of patient-reported measures will integrate the patient perspective. Developing and evaluating patient-centred complex interventions will allow the translation of treatment tools into routine care.

Also, DDZ aims at further involving people living with diabetes for tailoring the prioritisation of research topics, at intensifying active patient involvement in research activities and at continuing to deliver unbiased information for healthcare professional, authorities and the public.

### **Planning for additional funds deriving from institutional funding**

According to DDZ, the future planning of its research strategy also requires an optimised integration of the rapidly growing size of multidimensional data sets for joint DDZ projects, but even more to meet the current challenges arising from the need to provide data for (inter)national collaborative research and to guarantee Open Access availability of big data. In order to advance research by aggregating and exploiting both existing and new data sources DDZ aims to establish the following units on the basis of additional funds totalling € 3.4m (including own funds totalling € 0.94m; minor extraordinary item of expenditure/*Sondertatbestand*):

**A new Paul Langerhans Group Computational Diabetology** to conduct research projects with focus on machine learning and the application of explainable Artificial Intelligence, as well as to provide interconnected large data sets from (pre)clinical studies to other research groups at DDZ. This group also works on the design and development of computational algorithms, methods and tools to support the understanding of diabetes based on the concept of integrative transformation and multi-dimensional connection of existing and future data sets. This unit shall be supported by a new central biobank, which

will systematically collect, store and provide high-quality samples in a standardised and quality-controlled manner and provide data and possibly samples to validate results.

- € 1m personnel for the new Paul Langerhans Group [4 postdoctoral researchers (PhD, E14/13), 4 doctoral candidates (65% E13) and 2 IT experts (E9 a/b); of these, six positions are to be filled in the first year, four more positions in the second year] and
- € 434k personnel for the biobank [1 MD/PhD (E14) and 3 technicians (E9b); of these, 2.5 positions are to be filled in the first year, another 1.5 positions in the second year],
- € 2.37m investments [IT, equipment for cryo conservation for biobanking infrastructure, pipetting robot for biobanking infrastructure, motorised sample extraction for biobanking infrastructure, hardware and licenses for Paul Langerhans Group],
- € 420k consumables.

„Extraordinary item of expenditure“: summary of funds planning

	2025	2026	Permanently
<b>Own funds + additional funds = „extraordinary item of expenditure“</b>	€ 2.253m	€ 1.167m	€ 1.167m
<b>Own funds</b> from existing funding by institution (at least 3 % of core budget)	€ 0.471m	€ 0.471m	€ 0.471m
<b>Additional funds</b> of institutional funding	€ 1.782m	€ 0.696m	€ 0.696m

## 4. Controlling and quality management

### Facilities, equipment and funding

#### *Funding*

In 2019, DDZ's **revenues** totalled € 21.9m. They were made up of € 14.1m (64%) institutional funding by federal and *Länder* governments according to AV-WGL and € 7.8m (36%) revenues from project grants (cf. appendix 3). One main source of **third-party funding** originated from the participation of DDZ in projects of the German Center for Diabetes Research (DZD e. V.; 60%). Further important third-party funding providers were federal and *Länder* governments (14%), the EU (9%), foundations (5%), and the DFG (4%). As the institute points out, researchers with an affiliation at Heinrich Heine University Düsseldorf acquired additional DFG grants (in 2019: 575k€) which are not included in the DDZ budget and are spent particularly at their university institutes or departments. DDZ has a **third-party funding strategy**, according to which DDZ does not aim at increasing the third-party funding over 40–45% of total funding.

Since 2013, DDZ has received **additional funding** (minor extraordinary items of expenditure/*Sondertatbestand*) to purchase a high-field veterinary MRT scanner (2016; € 2.2m) and to broaden research on specific comorbidities/complications of diabetes (2018; € 0.8m).

### *Facilities*

DDZ has continued to invest in renewal and improvement of its facilities: next to the acquisition of the MRT scanner DDZ updated the MRI system for study participants in 2019. In 2017, an electrospray ionisation mass spectrometry system was purchased. Furthermore it updated the clinical study rooms in 2018 and exercise training hall in 2019, including new state-of-the-art resistance and endurance exercise devices. DDZ has enlarged its lecture hall and installed up-to-date media equipment in 2015.

### *Research infrastructure*

DDZ has the following **specific infrastructure** available:

- Clinical Research Center (CRC) orchestrating most clinical observational and interventional studies of DDZ, using state-of-the-art techniques, e. g. clamp tests, indirect calorimetry, spiroergometry, muscle/adipose tissue biopsies and phenotyping of comorbidities.
- Oskar Minkowski Laboratory – a core facility used for keeping primarily mouse models of type 1 and type 2 diabetes and the metabolic syndrome. The unit is also part of the German Diabetes Mouse Clinic, a multicentre platform of the German Center for Diabetes Research (DZD e. V.), jointly run by DDZ, the German Institute for Human Nutrition (DIfE Potsdam) and the German Research Center for Environmental Health (Helmholtz Zentrum München).
- In vivo imaging facilities – including a whole-body 3-T MR scanner for imaging and multinuclear spectroscopy in humans, an experimental MR-elastography system for assessing organ fibrosis, a 11.7-T MR scanner for translational rodent studies, and a 3D body scanner.

The following **platforms** are established at DDZ:

- Biomedical Laboratory offering metabolomic analyses as well as running methods for routine clinical chemistry and endocrine/metabolomic parameters on different standard laboratory systems.
- Proteome Analysis providing access to proteome analysis of various tissues.
- Cellular Morphology combining equipment for processing and analysing biological specimen using a fluorescence microscope and a transmission electron.
- Further supporting units are the Mito Laboratory, as an Oroboros® reference laboratory for high-resolution respirometry and the Neuropathy Laboratory.

In line with respective regulations, all data at DDZ are saved in a highly redundant central **data storage** system with backups. Data protection impact assessments are carried out in accordance with the German Data Protection Act (*Datenschutzgrundverordnung, DSGVO*). Heads of research groups are required to set up project directories, in which documentation, standard operating procedures and primary data are stored. After successful publication, directories are kept for at least ten years.

In the course of setting up the **IT environment** for the German National Cohort (*NAKO Gesundheitsstudie*), DDZ's IT was certified with regard to data access, use, security and

backup. For clinical studies following the German Drug Registration and Administration Act (*Arzneimittelgesetz, AMG*), DDZ has a long-standing collaboration with the Coordination Center for Clinical Trials at Heinrich Heine University and University Clinics Düsseldorf. Supported by an external IT service provider, a state-of-the-art network infrastructure with an integrated management of users and laboratory instruments is operated.

### **Organisational and operational structure**

The **General Assembly** of the German Diabetes Research Foundation (*Deutsche Diabetes-Forschungsgesellschaft DDFG e. V.*) oversees and approves all activities of DDZ. In cooperation with the General Assembly, the **Board of Trustees** supervises all activities and organisational changes based on the proposals by the **Executive Board** of DDZ, the submitted programme budget and the annual reports of DDZ's Scientific Advisory Board.

The Executive Board coordinates the **five institutes**, which in turn are directed by the respective directors and hold joint responsibility for **staff units** (Oskar Minkowski Laboratory, National Diabetes Information Center (NDC), press office and administration). Each institute comprises different **organisational subunits**, i.e. research groups, junior research groups and platforms. Platforms may also perform service for other institutes, but their personnel and supplies are under the responsibility of one institute. Administration comprises positions for general administration, financial management, human resources and utility management. The officer for equal opportunities, Work Council (*Betriebsrat*), ombudspersons and quality management complete the organisational structure.

Since 2013, the **Board of Directors**, comprising Executive Board, institutes' directors and head of the National Diabetes Information Center, meets biweekly to exchange information, to monitor the program and to address innovation and (infra-)structural issues. In addition, the **Board of Research Scientists** (*Forschungsrat*), representing all DDZ researchers except for the directors, meets regularly to discuss the current program and to offer suggestions to the Executive Board. Last but not least, all directors (or their deputies) of the institutes and heads of research groups and platforms meet weekly to discuss joint activities.

### **Quality Management**

DDZ has implemented guidelines for safeguarding **Good Scientific Practice** as well as for **Good Clinical Practice** in units involved in clinical trials. There are four **ombudspersons** with annual rotation of chairmanship and four-year term of office. From 2013 to 2019, no conflicts were reported.

All clinical-experimental and epidemiological studies are carried out according to rules of Good Clinical Practice/Good Epidemiological Practice upon approval by the Ethics Committee of the Medical Faculty and are registered if appropriate. All DDZ units related to clinical studies have been certified according to DIN ISO 9001 in 2019. To ensure standardised performance of laboratory and clinical procedures and data quality DDZ's research groups and platforms follow specific **Standard Operating Procedure** (SOP) lists.

The head of the Oskar Minkowski Laboratory provides (together with in-house **animal welfare** officers) consulting, guidance and supervision for adherence to the animal protection laws and quality management. All animal experimentation follows the 3R principle (Replacement, Reduction and Refinement) and is performed upon review/approval by the responsible federal state board. Animal breeding, strain maintenance, handling and documentation is conducted with support of a state-certified fraud-resistant electronic database system.

According to its **publication strategy** DDZ's top priority is to publish original articles in high (if possible top-)-ranking peer-reviewed international journals in the field of diabetes/endocrinology or related areas. Also, the centre aims at publication of narrative reviews on authoritative views, cumulative research findings and/or methodologies. Summaries of DDZ research results are spread by social media and websites. In line with recommendations of Leibniz Association, DDZ supports an **open online and barrier-free access** to quality-assured research findings. DDZ encourages to publish in open access media and – whenever legally possible – to make data accessible via repositories.

At DDZ, **technology transfer** occurs either at the level of sharing established techniques and methods based upon contracts with external individual/institutional collaborators or via patentable innovations. The DDZ patent officer coordinates the **transfer strategy**. DDZ collaborates with an external patent-marketing agency.

Quality management of **research infrastructures** is ensured by the use of Standard Operating Procedures as well as regular maintenance, calibration and servicing of analysis equipment. In addition, annual comparative analyses with external laboratories are performed. According to DDZ, the broad spectrum of different types of research data requires individual responsibility of each DDZ institute for its own **research data management**. To this end, DDZ has implemented the Current Research Information System (CRIS) PURE (Elsevier), which provides relevant data, management and evaluation as well as development of research activities of each individual scientist, research group and institute.

DDZ has implemented **performance based funding allocation** across its institutes in 2015, including a LOM system, training and feasibility grants (€ 15–50k annually), Dr-Eickelberg Foundation project grants (€ 5k annually) and a Top Paper Initiative (two projects in the amount of € 251k funded since 2015).

### **Quality management by advisory and supervisory board**

The **Scientific Advisory Board** (SAB) consists of at least seven international members of proven standing in the field of research regarding diabetes mellitus, its effect on the human organism, as well as the prevention and treatment of diabetes mellitus and its accompanying and secondary diseases. Currently, the SAB is composed of twelve members. Amongst others, its main tasks are to intensively and critically advise and support DDZ in all scientific matters, particularly in research and development planning as well as (inter-)national collaborations, to comment on the draft programme budget, and to assess the research, service and advisory performance of the individual working units of DDZ. In accordance with guidelines of Leibniz Association, the SAB performed an audit in November 2017.

The **Board of trustees** consists of eight members and takes decisions on all fundamental issues of the association. It lays down the guidelines for the activity of DDZ and oversees the executive board.

## 5. Human Resources

On 31 December 2019, DDZ employed 212 people (including one trainee, without student assistants). This corresponds to 177.1 full-time equivalents (FTE), 87.8 of which were assigned to research and scientific services, 72.8 to service positions and 15.4 to administration (cf. appendix 4 for details).

### Leading scientific positions

The German Diabetes Research Foundation (DDFG e. V.) and Heinrich Heine University Düsseldorf (HHU) have jointly agreed on a structured procedure for recruiting new institute directors at DDZ, who are at the same time full (W3) professors at HHU. Appointment procedures follow the standards stipulated by Leibniz Association as well as the respective standards by HHU. Institute directors are appointed by the Board of Trustees for a five-year term with an option of renewal. Currently, there are five **joint appointments**, four of which are financed by HHU, including the position of the director of DDZ. At present, three of the five professors also serve as director or (deputy) heads of HHU institutes.

Five senior members of staff hold adjunct professorships at HHU, one further member of staff holds a Level E professorship at a university abroad.

### Postdoctoral staff

DDZ works on three steps of **structured qualification planning**: research, management/leadership and teaching. Postdocs can achieve leadership positions within DDZ, from principal investigators of in-house funded projects to heads of junior research groups and further to heads of research groups or platforms. In addition, institutes have the option to propose high potential young investigators as heads of new **junior research groups**. Since 2013, DDZ has established six junior research groups (which are generally set up for a duration of up to five years), of which one was terminated after a two-year period and one was transferred into a research group.

Since 2013, four researchers have received six **calls for professorships**, three of them women. Furthermore, three researchers assumed acting (*Vertretungsprofessur*) or guest professorships. Eleven researchers took up leading positions in industry or clinic.

DDZ offers the option to establish a **Paul Langerhans Group**, which is independent from a particular institute and allows for gaining experience in leading a smaller research unit and for developing a specific research topic. In parallel, DDZ supports exchange visits at collaborating institutions as well as fellowships, providing teaching opportunities and postdoctoral lecture qualification (*Habilitation*). DDZ also promotes alternative career options, e.g. in medicine, clinics or industry. In 2017, a local branch of the **Leibniz Postdoc Network** was founded.



## Doctoral Candidates

DDZ adheres to the Career Guidelines of Leibniz Association, offering training for MD (Dr. med.), PH (Dr. Public Health) and PhD (Dr. rer. med.).

Formal framework of doctoral training is provided by the cooperation with Heinrich Heine University Düsseldorf, which requires involving all candidates in **structured programmes** – such as the Medical Research School Düsseldorf (MedRSD) or the Interdisciplinary Graduate Research School Düsseldorf (iGRAD). The PhD training programme requires doctoral researchers to participate in regular meetings with their Thesis Advisory Board, consisting of PhD supervisor, mentor and optionally postdocs. Also, there are formal training and supervision agreements. In addition, HHU provides programmes for special or double degrees as well as clinical training for MD candidates. DDZ also provides an **internal programme** of courses and lectures (*Doktorandenseminare*) specifically on diabetes, but also various other topics.

In 2019, DDZ had enrolled 34 doctoral researchers (with contracts at DDZ). From 2017-2019, 31 degrees qualifying candidates to study for a doctorate, 42 MD/PhD theses and three habilitations have been completed successfully.

Researchers of DDZ are currently involved in one Research Training Group (GRK2576 vivid; *Graduiertenkolleg*), Graduate Research Programmes within two Collaborative Research Centres (SFBs), as well as the Master programme Molecular Biomedicine. With 'vivid' starting in 2020, the programme will provide training for 18 doctoral researchers in basic sciences (PhD) and 24 doctoral students in medicine (MD) in the field of translational research on the pathogenesis of type 2 diabetes. Of these, ten doctoral (PHD) and >50% of MD doctoral students will be working at DDZ.

## Non-scientific staff

Since 2016 DDZ offers traineeships for a clerk for office management as well as for a laboratory assistant. Three traineeships have been completed successfully in the past years with two apprentices being employed at DDZ afterwards. Both training positions have been filled again in 2020.

DDZ offers educational programmes to support training and development of employees such as courses for IT software training, languages or special administrative skills.

## Equal opportunities and work-life balance

At DDZ, the **equality plan** is the instrument for implementing the "Research-oriented standards on gender equality" in all processes. In order to implement and maintain gender equality DDZ focuses on the following aspects: (a) equal treatment of and opportunities for women and men, (b) supporting employees in all aspects of child and elderly care, (c) promoting career development, and (d) leading positions in part-time employment.

DDZ has adopted a company agreement on equal chances and all issues relevant to equality. Since 2006, a gender equality officer and its deputy are elected having speaking rights

at all committees. DDZ supports the attendance at mentoring programmes for junior female scientists: Between 2017 and 2019 seven DDZ postdoctoral researchers participated in Selma Meyer and Leibniz mentoring programmes.

On the reporting date 31 December 2019, 23 out of 34 doctoral students were women (67%), 35 out of 56 at the level of scientific staff in non-executive positions (63%) and 6 out of 14 at the group leader level (43%, including three junior research groups of which two were led by women). At executive level, one of the five DDZ institutes was headed by a woman (20%). In relation to all jointly appointed/adjunct professorships at DDZ, two were filled with women (18%). The director's post was held by a man (cf. appendix 4). Amongst the entire institute staff, 64 % were women.

To facilitate **reconciliation of work and family life**, DDZ supports employees in all aspects of child- or home and elderly care. Amongst others, DDZ started to cooperate with an external family service provider. Also, it offers switching from full- to part-time positions (and back) or leaves of absence with gradual reintegration in special situations. In 2017, DDZ has implemented the concept of flexibility of working hours and location and laid this down in a company agreement. Since 2011, DDZ was continuously certified for work-life-balance by an external audit (*berufundfamilie*).

## 6. Cooperation and environment

### *National collaborations*

DDZ has a long-standing relationship with **Heinrich Heine University Düsseldorf** (HHU) and **University Clinics Düsseldorf** (UKD). This collaboration is regulated by a formal agreement covering (a) joint appointments of professors, (b) coordination of research, (c) coordination at all levels of academic graduate and post-graduate teaching, (d) joint scientific events and projects, (e) provision of support for young scientists through the exchange of personnel and (f) collaboration in the area of clinical studies. Furthermore, various clinical researchers of DDZ provide regular clinical service at UKD, thereby providing immediate access to patient cohorts at UKD for clinical research projects at DDZ.

Members of staff contribute to **curricular teaching** (courses and seminars) and **supervision** of bachelor, master, MD and PhD theses. A long-term cooperation of the Institute for Clinical Diabetology with the Division of Endocrinology and Diabetology at UKD offers rotational clinical training in Internal Medicine and/or Endocrinology and Diabetology (*Facharztausbildung*) to currently four postdoctoral researchers. Members of staff are also involved in the development of future focus areas of **HHU's strategic research plan**, such as 'Life Nature Society, Health and Society' and 'Diabetes and Metabolic Research'. Also, DDZ scientists lead or contribute to the increasing cooperation of diabetes and cardiovascular research at HHU culminating in a successful joint application for funding the research building 'CARDiovascular research in DIABetis' (CARDDIAB).

DDZ researchers are principal investigators or coordinators of the following **DFG-funded programmes at HHU**:

- SFB 1116/1 (2015–2018) and SFB 1116/2 (2019–2022): Master switches in cardiac ischemia
- SFB 974: Communication and systemic relevance in liver damage and regeneration
- International Research Training Group (IRTG) 1902: Intra- and interorgan communication of the cardio-vascular system
- Research Training Group (GRK 2576; 2020–2024): vivid – *in vivo* investigations towards the early development of type 2 diabetes

DDZ is one of five founding members and an executive partner within the **German Center for Diabetes Research** (DZD e. V.), which is funded by the Federal Ministry of Education and Research (BMBF) and the federal states. DDZ provides one of its five speakers and six research coordination board members. DDZ scientists lead or co-lead and/or contribute to the research areas. Also, they coordinate the clinical panel, responsible for all observational and interventional studies, chair one of the programmes of DZD (NEXT), and organise young scientists' training courses. The German Diabetes Study (GDS; *Deutsche Diabetes Studie*) is also the core prospective study on adult people with type 1 and type 2 diabetes of DZD e. V.

Since 2014 (until 2020), DDZ has been a partner of the **Leibniz Research Alliance** (*Leibniz-Forschungsverbund*) Healthy Aging; a proposal for a follow-up is currently underway. Also, together with the Leibniz Research Institute for Environmental Medicine (IUF) and two faculties of HHU, DDZ applied for a “Leibniz Campus for Metabolism and Environment” in 2019, which, however, was not recommended for funding. In cooperation with IUF, DDZ operates a study centre of the **German National Cohort** (GNC, *NAKO Gesundheitsstudie*), localised at DDZ, in which it is currently involved in a follow-up investigation for conducting oral glucose tolerance tests in all volunteers. Researchers of DDZ also collaborated with several Leibniz institutes to build a new **Leibniz Network** in 2020 addressing the role of cross-disciplinary aspects of nutrition for health. In addition, DDZ contributed to joint activities of Leibniz Association, e.g. a memorandum of understanding with the German university medicine associations.

On a regional level, the framework of the **Center of Competence for Innovative Diabetes Therapy** (KomIT) provides a cooperation for translational research to improve diabetes treatment bringing together various academic as well as industry partners. DDZ is also a member of the Association for the Promotion of the Knowledge Region Düsseldorf and the Forum Health Economy Düsseldorf.

#### *International collaborations*

DDZ collaborates with the Center for Disease Control and Prevention (CDC) in Atlanta/ USA in the context of cost-effectiveness of interventions of DDZ and DZD studies as well as the description of diabetes dynamics in terms of incidence and prevalence. Also, DDZ has established formal collaborations with Monash University (Melbourne) as well as it exhibits long-term collaborations with the Universities of Maastricht and Athens. DDZ researchers serve as guest professors and contribute to curricular and post-graduate teaching at universities such as Columbia, Ghent, Rotterdam and Potsdam and jointly supervise

MD, PhD and master students of various universities, *e.g.* Medical University Vienna, University of Zurich, Paracelsus Medical University Salzburg and RWTH Aachen.

### **Institution's status in the specialist environment**

DDZ mentions the following four most important institutions in the centre's environment:

- Helmholtz Diabetes Center (HDC) at the Helmholtz Zentrum München
- Steno Diabetes Center Copenhagen (SDCC)
- Novo Nordisk Foundation Center for Basic Metabolic Research (CBMR)
- Joslin Diabetes Center (JDC)

Other international institutions with similar trans-disciplinary research programs as DDZ comprise the Institute of Metabolic Science Cambridge, the Oxford Diabetes Center and the Banting and Best Diabetes Center Toronto. Also, the Baker IDI Heart and Diabetes Institute (Melbourne) has a strong expertise in diabetic complications and cooperation with the Diabetes Department at Monash University. According to DDZ, several medical schools have dedicated centres, mostly addressing specific aspects of diabetes, *e.g.* the University of Texas at San Antonio, Yale Diabetes Center, Mayo Clinic, Columbia University Diabetes Center, the Naomi Berrie Diabetes Center or the Barbara Davis Center for Diabetes.

## **7. Subdivisions of DDZ**

### **Institute for Biometrics and Epidemiology (IBE)**

[32.5 FTE, thereof 13.5 FTE Research and scientific services, 2.6 FTE Doctoral candidates, and 16.4 FTE Service staff]

The Institute for Biometrics and Epidemiology consists of two research groups and a junior research group:

- Research group "Biometrics"
- Research group "Epidemiology"
- Junior research group "Systematic Reviews"

IBE is responsible for program D (epidemiology and therapy assessment of diabetes mellitus) and investigates population-based aspects of diabetes, with a focus on disease dynamics, underlying risk factors, diabetes treatment, and the prevention of diabetes complications and comorbidities. To achieve these aims, IBE collects original data, cooperates with external partners like population-based cohorts or providers of routine data, as well as summarises and generates evidence from existing studies in systematic reviews. IBE contributes statistical planning and analyses to program F and advises all research groups of DDZ on methodical issues, offers statistical training of junior researchers and develops new statistical methods for diabetes research. Finally, IBE runs a study centre of the German National Cohort (*NAKO Gesundheitsstudie*).

As most important results IBE refers, amongst others, to the following:

- Estimation of diabetes prevalence and incidence for all participants of the German statutory Health insurance

- Analysis of treatment intensification in people with type 2 diabetes of the German Diabetes Study/GDS
- Analysis of absolute excess death counts associated with diabetes from nationwide routine data from 65 million people in the German Statutory Health system
- Meta-analysis on optimal thresholds for population-based diabetes screening for HbA<sub>1c</sub> and fasting plasma glucose levels
- Population-based cohort study of 30.579 children and adolescents with type 1 diabetes in 446 diabetes centres

2017–2019 IBE published 267 articles in peer reviewed journals, three individual contributions to edited volumes, and one monograph. 75 publications were compiled in cooperation with other institutes of DDZ. In the same period, IBE had approx. € 3.3m in institutional funding. Also, it received third-party funds amounting to almost € 4.5m. Of these € 2.9m were obtained from federal and *Länder* governments (thereof € 2.7m German National Cohort), € 1.3m from other sponsors (thereof € 1m DZD e. V.) and € 0.16m from the DFG. IBE compiled 25 expert reviews and had three patents granted/applied. Five academic degrees, four doctoral degrees and two habilitations were supervised successfully.

In the coming years IBE plans to continue its methodical work on disease dynamics of diabetes and on meta-analysis. New emphasis will be given to recent developments of causal inference in medical research, which will also follow developments in the field of artificial intelligence, machine learning, and data science. IBE aims to provide insights into pharmacogenetic/pharmacoepidemiological aspects of glucose-lowering treatments. The junior research group Systematic Reviews shall be promoted to a regular research group and generate evidence on risk factors, focussing on lifestyle behaviour and interventions, on diabetes prevention, diabetes-related complications and patient-relevant outcomes, including health-related quality of life.

### **Institute for Clinical Biochemistry and Pathobiochemistry (ICB)**

[28.4 FTE, thereof 11.5 FTE Research and scientific services, 4.7 FTE Doctoral candidates, and 12.2 FTE Service staff]

The Institute for Clinical Biochemistry and Pathobiochemistry consists of two research groups and is responsible for three platforms:

- Research group “Pathobiochemistry”
- Research group “Genomics”
- Platforms “Proteomics”, “Cell Morphology” and “Genomics”

ICB is responsible for program B (pathogenetic mechanisms and molecular targets for diabetes mellitus) and investigates the molecular basis of the onset and progression of metabolic diseases. Its focus is the identification and molecular analysis of novel risk genes for obesity and type 2 diabetes, the overall genetic susceptibility as well as the interaction of lifestyle factors, particularly exercise in the prevention and progression of metabolic diseases. To this end, both mouse models reflecting aspects of the human disease and human primary cells are utilised to investigate molecular mechanisms including experimental genetics, gene/environment interactions and tissue communication. The overall goal is to contribute to improving prediction, prevention and treatment of diabetes. ICB

contributes its expertise on biochemical methods and primary cell culture to program F. ICB is partner in the German Diabetes Mouse Clinic of DDZ e. V.

As most important results ICB refers, amongst others, to the following:

- Identification of a novel adipokine from visceral adipose tissue associated with insulin resistance and NAFLD
- Characterisation of TBC1D1 as critical regulatory protein for insulin and contraction-mediated muscle glucose transport
- Identification of two risk genes, *Pop4* and *Atp4a*, for beta cell failure from a systematic linkage study of mouse strains
- Characterisation of a pro-inflammatory adipokine from visceral adipose tissue and detection of increased levels of human obesity
- Identification of a novel function of TBC1D1 in beta cells

2017–2019 ICB published 83 articles in peer reviewed journals of which 20 were compiled in cooperation with other institutes of DDZ. In the same period, it had approx. € 7.1m in institutional funding. Also, it received third-party funds amounting to almost € 3.8m. Of these € 3.4m were obtained from other sponsors (thereof € 3.3m DDZ e. V.), 0.34 from the DFG and € 0.11m from foundations. ICB had three patents granted/applied. 15 academic degrees as well as 8 doctoral degrees were supervised successfully.

ICB plans to expand research on the development of insulin resistance and type 2 diabetes by utilising recent technology, to elucidate mechanisms involved in disease onset and progression at the molecular level. New tailored *in vivo* and *in vitro* systems are being developed that allow in-depth analysis of the molecular basis of insulin resistance, in particular in skeletal muscle, and the mechanisms and requirements for successful interventions through environmental/lifestyle factors. To this end, existing mouse models and interventions, e. g. endurance exercise through interval training, together with recent analytical methods will be further developed.

### **Institute for Clinical Diabetology (ICD)**

[67.9 FTE, thereof 26.4 FTE Research and scientific services, 7.5 FTE Doctoral candidates, and 34 FTE Service staff]

The Institute for Clinical Diabetology consists of six research groups and is responsible for one platform:

- Research group “Energy Metabolism”
- Research group “Inflammation”
- Research group “Neuropathy”
- Research group “Metabolic Imaging”
- Research group “Clinical Research Center”
- Research group “Nephropathy”
- Platform “Biomedical Laboratory”

ICD is responsible for program C (origin, development and consequences of diabetes) and drives the clinical-translational research of DDZ by emphasising studies in humans. Its six research groups address key roles of energy metabolism and inflammatory pathways in

the pathogenesis of diabetes and its comorbidities, the early detection and management of diabetes and its complications and the development of methods of clinical phenotyping. Major achievements in the past years include contributions to the validation of new diabetes subgroups and the better understanding of NAFLD and diabetic neuropathy. ICD initiated program F and leads all clinical-experimental modules and analyses. It performs scientific services for all DDZ institutes and in (inter)national cooperation. ICD is leading the clinical programs and NAFLD research of DZD e. V.

As most important results ICD refers, amongst others, to the following:

- Validation of cluster analysis identifying five diabetes subgroups
- Monitoring of the time course of metabolic and epigenetic changes upon surgical weight loss in insulin resistant humans
- Investigator-initiated multicentre randomised controlled trial on the effect of the SGLT-2 inhibitor, empagliflozin, on liver fat content in recent onset type 2 diabetes
- Simultaneous assessment of lipotoxins in blood and multiple tissues of obese humans as biomarkers of NAFLD
- Assessment of early impairment of cardiac autonomic function in recent onset type 2 and type 1 diabetes of the German Diabetes Study/GDS

2017–2019 ICD published 237 articles in peer reviewed journals as well as ten individual contributions to edited volumes. 168 publications were compiled in cooperation with other institutes of DDZ. In the same period, ICD had approx. € 10.4m in institutional funding. Also, it received third-party funds amounting to almost € 9.5m. Of these € 7.1m were obtained from DZD e. V., € 1.3m from industry, € 0.4m from the DFG, and € 0.31 from foundations. ICD had five patents as well as three other industrial property rights granted/applied. Two academic degrees, 22 doctoral degrees and one habilitation were supervised successfully.

In the future, ICD will focus on Precision Diabetology as its common field of interest with regard to tailored diagnosis, monitoring of progression and treatment of diabetes. To this end it plans to adapt its clinical phenomics methods and cohorts to facilitate joining international cohorts and cross-validation of DDZ-generated data, thereby generating multidimensional data sets for developing diagnostic and prognostic algorithms for stratified diabetes detection and treatment. In parallel, it aims to examine hypotheses on the pathogenesis addressing tissue cross-talk involving adipose tissue, energy metabolism as well as peripheral/autonomic nerve function. Furthermore, ICD wants to pursue its strategy to examine the preventive and therapeutic interventions with one focus on different efficiency in diabetes subgroups and factors determining individual response.

### **Institute for Health Services Research and Health Economics** (ISE)

[11.5 FTE, thereof 7.75 FTE Research and scientific services, 1.75 FTE Doctoral candidates, and 2 FTE Service staff]

The Institute for Health Services Research and Health Economics was established in 2017 after developing from a research group of the Institute for Biometrics and Epidemiology (IBE) to an independent Paul Langerhans Group in 2016. It consists of two research groups and a junior research group:

- Research group “Patient-relevant Outcomes”
- Research group “Complex Interventions and Economic Evaluation”
- Junior research group “Patients’ Needs and Preferences”

ISE is responsible for program E (patient-centred research and health economic evaluation in diabetes) and aims to contribute to improving effectiveness and efficiency of diabetes care considering real-life conditions, patients’ perspectives, and social relevance. It performs coordinated research on patient-relevant outcomes of diabetes-related complications in clinical cohorts or population-based data bases, patient-reported needs and preferences, and develops complex interventions with health economic evaluation. Major achievements include knowledge about the population risk of diabetes-associated amputation, myocardial infarction and stroke, and insights into information needs, time needed for health-related activities and health care preferences. ISE contributes to program F by analysing the patients’ perspective and also interacts with all other institutes. In DZD e. V., ISE is responsible for health services research and health economics.

As most important results ISE refers, amongst others, to the following:

- Analysis of drug costs in four glucose tolerance categories (diagnosed, undetected diabetes, prediabetes, glucose tolerance) in the Cooperative Health Research in the Augsburg Region (KORA) survey
- Development and validation of a questionnaire for assessing time spent on diabetes self-care
- Analysis of self-reported and health-insurance data on physician visits comparing different recall lengths
- Analysis of major lower-extremity amputations for individuals with diabetes across Belgium
- Provision of time trends regarding surveillance for blindness using big data in a German population

2017–2019 ISE published 46 articles in peer reviewed journals of which 13 were compiled in cooperation with other institutes of DDZ. In the same period, it had approx. € 1.2m in institutional funding. Also, it received third-party funds amounting to almost € 1.1m. Of these € 0.68 m were obtained from DZD e. V. and € 0.38m from federal and *Länder* governments. ISE compiled 24 expert reviews. Three academic degrees and six doctoral degrees were supervised successfully.

In the coming years ISE plans to strengthen efforts to elucidate clinical and cost-effectiveness of diabetes prevention and care in daily practice considering patients’ individual needs and preferences. Furthermore, it aims to deepen the analysis of patient-relevant outcomes and patient-reported measures using and combining different data sources, develop and evaluate interventions to strengthen patient-centred research approaches. Also, patient involvement will be further intensified. In this context, ISE will advance the implementation of its new Citizen Advisory Board (CAB) into its research process. To evaluate patient-relevant outcomes in more detail, the course of diabetes-related complications and the trend of the risk of its end-stages will be analysed in different age-sex groups and stratified for socioeconomic position. Using the platform of the *European Association for the Study of Diabetes* Study Group, international comparisons will be performed. Beyond



that ISE aims to apply methods of artificial intelligence to big data as to data from statutory health insurances to identify currently unknown patterns of health care use and comorbidities.

### **Institute for Vascular and Islet Cell Biology (IVI)**

[11 FTE, thereof 4.1 FTE Research and scientific services, 3.15 FTE Doctoral candidates, and 3.75 FTE Service staff]

The Institute for Vascular and Islet Cell Biology consists of two research groups and a junior research group:

- Research group “Beta Cell Defects”
- Research group “Islet Cell Research”
- Junior research group “Preclinical Drug Development”

IVI is responsible for program A (diabetes-related signalling in pancreatic islets and liver) and works on pancreatic islets as well as blood and lymphatic vasculature to better understand development, survival, and function of these tissues and identify drug targets for treatment of diabetes and its complications. It uses and provides to DDZ state-of-the-art genetic manipulation of cells, mice and human tissues to gain mechanistic insights into signalling pathways and uncover drug targets and small molecules. IVI designs and tests new compounds targeting the islets as to delay development and progression of diabetes. Key findings include the identification of angiocrine signals for liver health and small molecules to increase islet cell survival. IVI contributes to program F by addressing beta cell function, interacts with the other institutes by leading drug development at the Center of Competence for Innovative Diabetes Therapy (KomIT) and contributes to the islet cell program of DZD e. V.

As most important results IVI refers, amongst others, to the following:

- Identification of specific binding sites (NMDA receptors) on pancreatic beta cells regulating insulin secretion
- Characterisation of the biomechanics of beta cells
- Identification of the blood glucose-lowering properties of dextrorotary, but not levorotary morphinans
- Demonstration of additive blood glucose lowering action by dextromethorphan and sitagliptin in type 2 diabetes
- Characterisation of hepatic blood flow and its mechanical forces in liver regeneration

2017–2019 IVI published 12 articles in peer reviewed journals as well as two individual contributions to edited volumes. Two publications were compiled in cooperation with other institutes of DDZ. In the same period, IVI had approx. € 1.7m in institutional funding. Also, it received third-party funds amounting to almost € 2.2m. Of these € 1.1m were obtained from the EU, € 0.89m from DZD e. V. and € 0.2m from foundations. IVI compiled 125 expert reviews and had one patent granted. Six academic degrees and two doctoral degrees were supervised successfully.

In the coming years IVI aims to develop novel anti-diabetic Dextromethorphan (DXM)-derived compounds for phase I/II randomised controlled trails. To this end, long-term toxicology studies of leading compounds will commence during 2020 and 2021 and cardiovascular effects of these compounds be investigated in mouse models. IVI will further investigate Ceramide Synthase (CerS) to generate specific inhibitors for this enzyme class. Moreover, CerS will also be studied in endothelial cells. Since further drug development requires substantial investments, IVI patents shall be used to set up a Start-up company with funding from venture capital. Future work will also use *in vivo* knockout and overexpression approaches to define efficacy of angiocrine signals in mice and human primary cells to promote hepatic survival and growth. To this end, IVI will use a state-of-the-art methodological portfolio to better understand liver physiology.

## 8. Handling of recommendations from the previous evaluation

DDZ responded as follows to the **nine recommendations** of the last external evaluation (see also statement of the Senate of the Leibniz Association issued on 17 July 2014, pages B-2/B-4):

- 1) *“Overall, DDZ has developed remarkably and extremely positively in the last few years. The **processes of change** that have been initiated now provide the foundations for continuing the successful development of the Diabetes Center, where topics are addressed using an overarching, interdisciplinary approach. DDZ’s leadership must continue its commitment to driving these processes which have not yet all been completed due to the fact that the leadership positions were only filled in the recent past.”*

According to DDZ, the institute has initiated a series of changes: All leaders, who had been appointed just before the last evaluation, have consolidated their positions since then and recruited (junior) research groups for their institutes with this also improving the trans-/interdisciplinary research concept of DDZ. Following a step-wise strategy, DDZ developed a research group over a Paul Langerhans Group to a fifth institute thereby strengthening patient-oriented research. Moreover, DDZ started six junior research groups, of which two were funded by additional funding (*Sondertatbestand*) to intensify and broaden research on specific comorbidities/complications of diabetes.

- 2) *“DDZ’s past performance has generated substantial and necessary progress which it should now use to enhance its **scientific visibility** yet further. To achieve this, the working units that produced fewer publications in the past or were less successful in acquiring competitive funding, must also play a more active role in the future.”*

DDZ points out, that it has implemented several means to stimulate research activities (publications, third-party funding and patents) such as performance-related resource allocation as well as bottom-up programmes for young researchers. This stimulated young researchers for inter-/transdisciplinary projects and formed the basis for new junior research groups. Nevertheless, some research groups were reorganised or abandoned to improve the efficiency of DDZ.

- 3) *“DDZ should remember that it is still in the throes of transition. The personnel restructuring of the institutes has, admittedly, largely been completed and, once the work*

*focus had been successfully realigned, scientific productivity increased in subsequent years and collaboration not only within the centre but also with external partners was improved further. The consolidation in personnel and structures must, however, be perpetuated in content terms as well. This will enable DDZ to reinforce its **position as a national reference centre for clinical diabetes research** tasked with providing information and advice to the general public and to become more visible both in Germany and internationally.”*

DDZ states that it has further expanded its leadership role in clinical diabetology and diabetes information on the national level since 2013. Furthermore, its international visibility has been demonstrated by more than 160 invited lectures and more than 90 accepted oral communications at the key international congresses (2017–2019). Along these lines, as DDZ points out, it has further boosted its already increased scientific productivity. Also, senior researchers have been appointed to lead posts in relevant (inter)national boards in the field sciences or politics.

- 4) *“It is recommended to continue diversifying the portfolio of **third-party funding** and, in particular, to increase the amount of funding acquired from the EU and the DFG.”*

Following DDZ, it has increased third-party funding from different sources, including EU and DFG (cf. chapter 4).

- 5) *“The Review Board endorses DDZ’s plans to purchase a **high-field veterinary MRT scanner**. This purchase is necessary, for example, in order to conduct in vivo measurements of glycogen and ATP synthesis rates in mouse models and compare them with clinical studies on humans.”*

The MRT scanner was purchased in 2016 with additional funds from institutional funding (*Sondertatbestand*) and installed in 2017-2018.

- 6) *“The Review Board considers the **National Diabetes Information Center** to be an exceptionally important component of DDZ that is of strategic significance for its position as a non-university national reference centre for diabetes research. Information provision is also very important because it helps to prevent the disease. However, the provision of staff and resources as well as the scope of the centre are not yet in accordance with its strategic significance. It is therefore recommended to strengthen the National Diabetes Information Center sustainably by research activities in the social science and health education sectors and to increase its visibility significantly amongst academics, doctors and patients. In order to achieve these goals, the information centre’s financial provisions must be enhanced also by DDZ’s own funding, strategic research collaborations must be organised and web-based social networks must be utilised to a greater extent than has been the case so far.”*

According to DDZ, funding of the National Diabetes Information Center (NDC) has been substantially increased, as is also demonstrated by a more than 3-fold rise in staff. To further support NDC activities, DDZ employed a press officer in 2015, who is responsible for web-based social media, too. Beyond this, DDZ applied for competitive funding of a Regional Innovation Network (RIN) Diabetes by the state ministry NRW. RIN Diabetes was also awarded the label ‘Place of Progress’ in 2016. As DDZ points out, there

are cooperative projects of NDC and the newly founded Institute for Health Services Research and Health Economics. Furthermore, DDZ's director initiated a collaboration network between NDC, the German Research Center for Environmental Health (*HelmholtzZentrum Munich*) and the German Center for Diabetes Research (DZD e. V.) to build a national information network ([diabinfo.de](http://diabinfo.de)), which has been launched in 2020.

- 7) *"In the past, DDZ has tried to increase the proportion of women researchers who also hold positions of responsibility. However, the current **proportion of women amongst the leading scientific personnel** is clearly too low. DDZ is expected to implement the agreed target quotas contained in the binding cascade model. For this purpose, it is necessary to keep intensifying, amongst others, efforts to recruit excellent, female (junior) researchers internationally."*

DDZ states, that it is obliged to the cascade model and follows the aim to recruit outstanding female scientists for leadership positions. Since 2013, it has been able to recruit five women to head one institute, two research groups, a junior research group, and a platform.

- 8) *"According to the statutes, the **Chair of DDZ's Scientific Advisory Board** is a voting member of the Supervisory Board. In order to make a clear distinction between the functions of supervision and scientific advice, this regulation must be changed. As is usually the case at Leibniz institutions, the Chair of the Scientific Advisory Board should be a non-voting member of the Supervisory Board in a purely advisory capacity."*

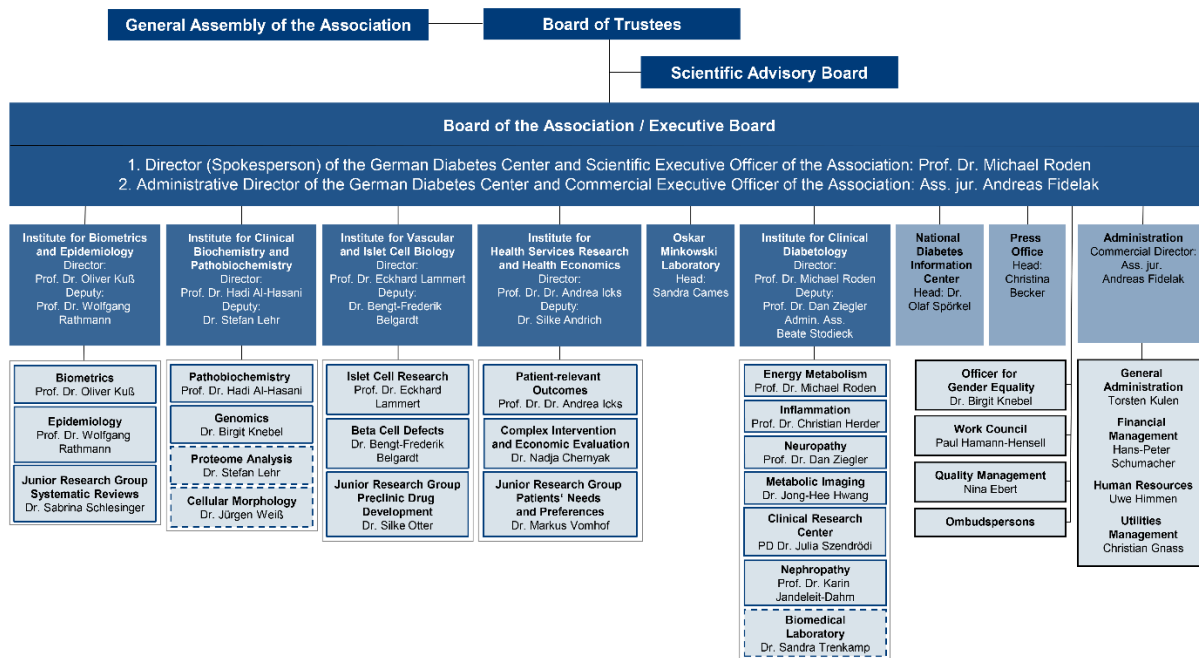
The bylaws of the German Diabetes Research Foundation (*Deutsche Diabetes-Forschungsgesellschaft*) have been modified accordingly.

- 9) *"Attention is drawn to the fact that the **management principles** (Bewirtschaftungsgrundsätze) currently in place at DDZ do not conform to the valid resolutions on the implementation of the *Ausführungsvereinbarung WGL*. They must be adjusted as soon as possible."*

As DDZ points out, new management principles were developed to conform the *Ausführungsvereinbarung WGL* and have been approved by the State of North Rhine-Westphalia. They are effective for all respective activities of DDZ since 2017.

Appendix 1

Organisational Chart (31.12.2019)



Cooperation of institutes within the research programs

Institutes	Research program					
	A: Diabetes-related signalling in pancreatic islets and liver	B: Pathogenetic mechanisms and molecular targets for diabetes	C: Origin, development and consequences of diabetes	D: Epidemiology and therapy assessment of diabetes	E: Patient-centered research and health economic evaluation in diabetes	F: German Diabetes Study
IBE	+	+	++	+++	++	++
ICB	++	+++	+	+	+	++
ICD	+	++	+++	++	++	+++
ISE	+	+	++	++	+++	+
IVI	+++	++	+	+	+	+

The institute is responsible for the respective program as “+++”: leader, “++”: main co-operator or “+”: associated co-operator.

## Appendix 2

### Publications, patents, and expert reviews

	Period		
	2017	2018	2019
<b>Total number of publications</b>	<b>177</b>	<b>213</b>	<b>195</b>
Monographs	1	1	–
Individual contributions to edited volumes	6	3	3
Articles in peer-reviewed journals	168	205	191
Editorship of edited volumes	2	4	1

<b>Industrial property rights</b> <sup>1)</sup>	<b>2017</b>	<b>2018</b>	<b>2019</b>
Patents (granted/applied)	3 <sup>2)</sup>	4	4
Other industrial property rights (granted/applied)	1/1	1/1	1/1
Exploitation rights/licences (number)	–	–	–

	<b>2017</b>	<b>2018</b>	<b>2019</b>
Number of expert reviews	30	51	44

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<sup>1</sup> Concerning financial expenditures for revenues from patents, other industrial property rights and licences see Appendix 3.

<sup>2</sup> One patent transferred to German Diabetes Research Association (DDFG e. V.) in 2017.

### Appendix 3 Revenue and Expenditure

Revenue		2017			2018			2019		
		k€	%	%	k€	%	%	k€	%	%
<b>Total revenue (sum of I, II, and III; excluding DFG fees)</b>		21,164			22,290			22,237		
<b>I.</b>	<b>Revenue (sum of I.1., I.2. and I.3)</b>	<b>20,881</b>	<b>100 %</b>		<b>22,027</b>	<b>100 %</b>		<b>21,936</b>	<b>100 %</b>	
1.	<u>INSTITUTIONAL FUNDING (EXCLUDING CONSTRUCTION PROJECTS AND ACQUISITION OF PROPERTY)</u>	12,963	62 %		13,949	63 %		14,105	64 %	
1.1	Institutional funding (excluding construction projects and acquisition of property) by Federal and <i>Länder</i> governments according to AV-WGL	12,963			13,949			14,105		
1.2	Institutional funding (excluding construction projects and acquisition of property) not received in accordance with AV-WGL	–			–			–		
2.	<u>REVENUE FROM PROJECT GRANTS</u>	7,918	38 %	100 %	8,078	37 %	100 %	7,831	36 %	100 %
2.1	DFG	309		3.9 %	294		3.6 %	287		3.7 %
2.2	Leibniz Association (competitive procedure)	–		–	–		–	–		–
2.3	Federal, <i>Länder</i> governments thereof: GNC ( <i>NAKO Gesundheitsstudie</i> )	1,705 910		21.5 % 11.5 %	1,757 1,091		21.8 % 13.5 %	1,109 685		14.2 % 8.7 %
2.4	EU	38		0.5 %	522		6.5 %	670		8.6 %
2.5	Industry	417		5.3 %	794		9.8 %	388		5.0 %
2.6	Foundations	75		0.9 %	190		2.4 %	431		5.5 %
2.7	other sponsors thereof: German Center for Diabetes Research (DZD e. V.)	5,374 5,118		67.9 % 64.6 %	4,521 4,343		56.0 % 53.8 %	4,946 4,665		63.0 % 59.6 %
3.	<u>REVENUE FROM SERVICES</u>	–	–		–	–		–	–	
3.1	Revenue from commissioned work	–			–			–		
3.2	Revenue from publications	–			–			–		
3.3	Revenue from exploitation of intellectual property for which the institution holds industrial property rights (patents, utility models etc.)	–			–			–		
3.4	Revenue from exploitation of intellectual property without industrial property rights	–			–			–		
<b>II.</b>	<b>Miscellaneous revenue</b> (e.g. membership fees, donations, rental income, funds drawn from reserves)	283			263			301		
<b>III.</b>	<b>Revenue for construction projects</b> (institutional funding by Federal and <i>Länder</i> governments, EU structural funds, etc.)	–			–			–		
<b>Expenditures</b>		<b>k€</b>			<b>k€</b>			<b>k€</b>		
<b>Expenditures (excluding DFG fees)</b>		21,444			21,358			22,092		
1.	Personnel	10,342			10,884			11,607		
2.	Material expenses	8,565			8,495			8,247		
2.1	<i>Proportion of these expenditures used for registering industrial property rights (patents, utility models etc.)</i>	24			21			5		
3.	Equipment investments	2,513			1,958			2,233		
4.	Construction projects, acquisition of property	–			–			–		
5.	Other operating expenses	–			–			–		
DFG fees (if paid for the institution – 2.5% of revenue from institutional funding)		313			339			342		

## Appendix 4

## Staff

(Basic financing and third-party funding / proportion of women (as of: 31.12.2019))

	Full time equivalents		Employees		Female employees		foreigners
	Total	on third-party funding	Total	on temporary contracts	Total	on temporary contracts	Total
	Number	Percent	Number	Percent	Number	Percent	Number
<b>Research and scientific services</b>	<b>87.8</b>	<b>42.9 %</b>	<b>109</b>	<b>78.9 %</b>	65	89.2	<b>23</b>
1 <sup>st</sup> level (scientific director)	1.0 <sup>1</sup>	–	1	–	–	–	1
2 <sup>nd</sup> level (heads of DDZ institutes)	4.0 <sup>2</sup>	–	4	–	1	–	–
3 <sup>rd</sup> level (group leaders or equivalent)	10.8	18.5 %	11	18.2 %	4	25.0 %	3
Junior research group leaders	2.5	40.0 %	3	100.0 %	2	100.0 %	–
Scientists in non-executive positions (A13, A14, E13, E14 or equivalent)	48.9	46.7 %	56	83.9 %	35	94.3 %	15
Doctoral candidates (A13, E13, E13/2 or equivalent)	20.6	57.5 %	34	100.0 %	23	100.0 %	4
<b>Service positions</b>	<b>72.8</b>	<b>29.6 %</b>	<b>85</b>				
Laboratory (E9 to E12, upper-mid-level service)	26.7	15.0 %	32				
Laboratory (E5 to E8, mid-level service)	27.2	48.1 %	33				
Animal care (E5 to E8, mid-level service)	6.6	–	7				
Workshops (E5 to E8, mid-level service)	8.3	54.2 %	9				
Information technology - IT (E9 to E12, upper-mid-level service)	1.0	–	1				
Technical (large equipment, service) (E5 to E8, mid-level service)	3.0	–	3				
<b>Administration</b>	<b>15.4</b>	<b>–</b>	<b>17</b>				
Head of the administration	1.0	–	1				
Staff positions (from E13, senior service)	1.0	–	1				
Staff positions (E9 to E12, upper-mid-level service)	3.0	–	3				
Internal administration (financial administration, personell etc.) (E9 to E12, upper-mid-level service)	9.4	–	11				
Building service (E1 to E4)	1.0	–	1				
<b>Student assistants</b>	<b>7.9</b>	<b>48.4 %</b>	<b>27</b>				
<b>Trainees</b>	<b>1.0</b>	<b>–</b>	<b>1</b>				
<b>Scholarship recipients at the institution</b>	<b>–</b>	<b>–</b>	<b>–</b>		–		–
Doctoral candidates	–	–	–		–		–
Post-doctoral researchers	–	–	–		–		–

<sup>1</sup> financed by Heinrich Heine University Düsseldorf (HHU)<sup>2</sup> three of four positions financed by HHU



## **Annex B: Evaluation Report**

### **German Diabetes Center (DDZ) - Leibniz Institute for Diabetes Research at Heinrich Heine University Düsseldorf**

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Appendix:

Members of review board

## 1. Summary and main recommendations

The DDZ works on the prevention, early detection, diagnosis, and therapy of diabetes mellitus, its comorbidities and complications. To this end, the DDZ combines molecular and cell biological fundamental research with clinical and epidemiological health care-related research. Through its research results, the DDZ helps reduce the burden of diabetes mellitus on individuals and society. The DDZ has very successfully completed its period of transition that started in 2008. Now, the institute covers major aspects of diabetes-related research at the highest level and is highly visible internationally, especially in the field of clinical studies.

The DDZ's overall concept, which covers the full range from basic to translational research, is coherent. The DDZ's research activities are organised into five 'institutes', of which the Institute for Clinical Diabetology (ICD), led by the DDZ's director, is by far the largest. The institutes are complemented by a unit for preclinical models (the Oskar Minkowski Laboratory) and a unit that organises knowledge transfer concerning diabetes (the National Diabetes Information Center). The institutes work together in an inter- and transdisciplinary manner within six research programmes. This cooperation, which is evident in a number of joint publications, should, however, be further intensified (see below).

The DDZ's scientific output is of a very high quality and is documented in an impressive number of publications in high-ranking journals. The DDZ's cohorts are immensely valuable for research. The German Diabetes Study (GDS) deserves a particular mention. It is led by the DDZ and carried out across Germany at eight sites within the framework of the German Centre for Diabetes Research (DZD). The DDZ is engaged in translating its research results into clinical applications, especially through close collaboration with the University Hospital of Düsseldorf (UKD). Through its information platforms, the DDZ provides quality-assured information on diabetes prevention for people with diabetes and medical staff. It is good to see that the National Diabetes Information Centre has been strengthened considerably following a recommendation in the last evaluation.

The DDZ is closely connected to Heinrich Heine University Düsseldorf (HHU) and the UKD, where the five senior scientists hold W3 professorships. The close connection facilitates the dovetailing of fundamental research and clinical applications. The cooperation will be further strengthened by the joint plans for a translational science building for cardiovascular research in diabetes (CARDDIAB), which will be erected on the university campus.

Special consideration should be given to the following main recommendations in the evaluation report (highlighted in **bold face** in the text):

### Overall concept, activities and results (chapter 2)

1. The DDZ has expanded its preclinical drug development since the last evaluation, for instance by setting up a junior research group. Since 2019, it has also been developing a virtual **Centre of Competence for Innovative Diabetes Therapy (KomIT)** using around €3.5m from the European Regional Development Fund (ERDF). KomIT is coordinated by the DDZ and involves seven other partners from academia and small to medium-sized enterprises. KomIT holds great potential for further valorisation of research results. How-

ever, a structured process should be established to help decide which steps in the translational chain can usefully be carried out by the DDZ itself and at which point they should be handed over to partners in industry.

### Changes and planning (chapter 3)

2. Based on its highly regarded work on differentiating type 1 and type 2 diabetes (T1D and T2D) into five subgroups and on diabetes-related comorbidities, the DDZ has developed a **Precision Diabetology concept** that forms an appropriate overall framework for the future work of the institutes. However, at present, alignment with the overall concept appears to vary considerably between the five institutes. The DDZ should keep an eye on this.

Furthermore, in its future work, the DDZ must prove the utility of the subgroup concept compared with the previous TD1 and TD2 classification.

3. The DDZ aims to advance research by aggregating and exploiting both existing and new data sources, including from functional studies ('fluxomics') in humans and model organisms, by establishing a **new independent Computational Diabetology research group**, with a related central biobank. The new group is to have a focus on machine learning and artificial intelligence. It will also provide interconnected large datasets from (pre)clinical studies to other research groups at the DDZ. These ideas are meaningful and should be pursued further. For this purpose, the DDZ intends to apply for additional institutional funding from the federal and *Länder* governments (minor extraordinary item of expenditure, *Sondertatbestand*). The application should describe the designated group's work in more detail. In addition, the DDZ should investigate in more detail how the group is to be integrated in the existing work of the DDZ and, in particular, how the necessary close dovetailing with the two epidemiological institutes is to be achieved.

### Controlling and quality management (chapter 4)

4. The DDZ should increase its revenue from **DFG and EU grants** and offer higher incentives for these. It is important for early-career scientists in particular to establish their credentials by acquiring these kinds of research grants. The DDZ's potential to receive European-level funding for research projects, and particularly for collaborative work with partner institutions, should be exploited more intensively.
5. It is welcomed that the DDZ's statutes were changed according to recommendations in the last evaluation. Among other things, the **term of office for advisory board members** was restricted to two terms of four years, as is usual for Leibniz institutions. In order to ensure scientific objectivity, this new regulation must now be put into practice. Currently, five of the 12 members have already been in post for more than eight years.

### Human resources (chapter 5)

6. As of 31 December 2019, the **proportion of women** among staff in research and scientific services was pleasingly high, at 60%. Six of the 14 (junior) group leaders (43%) and one of the five heads of DDZ institutes (20%) were women. The DDZ should ensure greater involvement of female scientists at the senior management levels.

## 2. Overall concept, activities and results

The DDZ works on the prevention, early detection, diagnosis, and therapy of diabetes mellitus, its comorbidities and complications. To this end, the DDZ combines molecular and cell biological fundamental research with clinical and epidemiological health care-related research. Through its research results, the DDZ helps reduce the burden of diabetes mellitus on individuals and society.

The DDZ's overall concept, which covers the full range from basic to translational research, is coherent. The DDZ's research activities are organised into five 'institutes' (see chapter 7), of which the Institute for Clinical Diabetology (ICD), led by the DDZ's director, is by far the largest. The institutes are complemented by a unit for preclinical models (the Oskar Minkowski Laboratory) and a unit that organises knowledge transfer concerning diabetes (the National Diabetes Information Center, see below).

The institutes work together in an inter- and transdisciplinary manner within six research programmes that cover the spectrum from basic and patient-oriented clinical research to epidemiology and health services research. Each institute leads one programme, and all the institutes contribute to the sixth programme, which includes the German Diabetes Study (GDS). This is carried out across Germany at eight sites, within the framework of the German Centre for Diabetes Research (DZD) and is led by the DDZ (see below). Cooperation between the institutes within the research programmes, which is evident in a number of joint publications, should be further intensified (see chapter 3).

### Research

The DDZ's scientific output is of a very high quality and is documented in an impressive number of publications in high-ranking journals. The publication output has also been increased considerably in terms of quantity since the last evaluation. The constant increase in productivity has led to a significant increase in international visibility. There are still significant differences in the publication output of the individual institutes. However, those institutes that publish less are producing work of extremely high quality that enjoys a particularly high reputation in the scientific community.

In recent years, the DDZ institutes have successfully worked together on deconstructing the classic diabetes types into subgroups (clusters, subtypes) and on specific comorbidities and complications. Other important research included cytological studies, e.g. to identify an N-methyl-D-aspartate (NMDA) receptor and its effect on liver fat levels, and a large multicentre trial to test the findings, which resulted in a patent application.

### Cohorts

The DDZ has successfully developed its cohorts, which are immensely valuable for research. They allow phenotyping, and with new methods, such as machine learning and artificial intelligence, more opportunities will arise. Some DDZ-cohorts are still rather small and may grow; the German Diabetes Study (GDS) is excellently positioned. Through the GDS, scientists have discovered a broad variation and substantial overlap of the features of diabetes between the classic T1D and T2D shortly after diagnosis. Another very positive development is that, since 2014, the DDZ, in collaboration with the Leibniz Institute for Environmental

Medical Research (IUF), has been operating a study centre for the German National Cohort (NAKO health study).

The DDZ is commended for its aim to integrate its cohorts to improve comparability and compatibility with other national and international cohorts and studies. For this complex task, the DDZ should define intermediate goals and check progress against them on a regular basis.

### **Translation**

The DDZ is engaged in translating its research results into clinical applications. A central element of this process is the Clinical Research Center, which is a research unit focusing on clinical experimental studies, with expertise in phenotyping methods and clinical trials.

**The DDZ has expanded its preclinical drug development since the last evaluation, for instance by setting up a junior research group. Since 2019, it has also been developing a virtual Centre of Competence for Innovative Diabetes Therapy (KomIT) using around €3.5m from the European Regional Development Fund (ERDF). KomIT is coordinated by the DDZ and involves seven other partners from academia and small to medium-sized enterprises. KomIT holds great potential for further valorisation of research results. However, a structured process should be established to help decide which steps in the translational chain can usefully be carried out by the DDZ itself and at which point they should be handed over to partners in industry.**

A research building, built with acquired funds of approx. €73m, in collaboration with the Department of Endocrinology and Diabetology, the Department of Cardiology, Pulmonology and Angiology and the Center for Health and Society at the UKD/HHU will help to further strengthen the translation work. With the translational science building for cardiovascular research in diabetes (CARDDIAB), the UKD and the DDZ aim to optimise collaboration in the fields of metabolism, diabetes and cardiovascular research. The project opens up excellent perspectives for future scientific development and the translation from preclinical and clinical trial findings into practical medical care.

### **Transfer**

The DDZ is active and successful in transferring its research findings. It provides quality-assured information on diabetes prevention for people with diabetes and medical staff. It is good to see that the National Diabetes Information Centre (NDC) has been strengthened considerably following a recommendation in the last evaluation. A successful initiative called *Diabetes – Nicht nur eine Typ-Frage!* (Diabetes – not just a question of type!) presents short, explanatory videos about diabetes on the website and on social media.

In 2020, the diabinfo information platform (with information in German and Turkish) went live as part of the national communication strategy of the German Federal Centre for Health Education (BZgA) at the DDZ. It is run in collaboration with the DZD and Helmholtz Zentrum München. These commendable activities should be brought together on the institute's website and developed further, taking into account user and patient feedback.

### 3. Changes and planning

#### Development since the previous evaluation

The DDZ has very successfully completed its period of transition that started in 2008. Now, the institute covers major aspects of diabetes-related research at the highest level. Some research groups have been closed down since the last evaluation (e.g. in epigenetics, signal transduction and immunomodulation) and for good reason – either because the institute’s research focus has developed in other directions or because performance expectations were not met. At the same time, other groups have been set up or expanded. So, for instance, the research group on public health and health economics (until 2014 part of the Institute for Biometrics and Epidemiology) was expanded and turned into a new, independent institute: the Institute for Health Services Research and Health Economics (ISE). The Institute for Beta Cell Biology was created in a similar way from a Paul Langerhans Group (independent research group) shortly before the last evaluation. In 2019, it was renamed and is now the Institute for Vascular and Islet Cell Biology (IVI). Moreover, starting in 2018, additional funds from the federal and *Länder* governments were used to set up two new groups (Nephropathy and Patients’ needs) to complement the research concept on diabetes-related comorbidities and complications.

#### Strategic work planning for the coming years

In parallel with these structural changes, the DDZ has also achieved very good progress in terms of its research, which should now be pursued further as planned. **Based on its highly regarded work on differentiating type 1 and type 2 diabetes (T1D and T2D) into five subgroups and on diabetes-related comorbidities, the DDZ has developed a Precision Diabetology concept that forms an appropriate overall framework for the future work of the institutes. However, at present, alignment with the overall concept appears to vary considerably between the five institutes. The DDZ should keep an eye on this.**

**Furthermore, in its future work, DDZ must prove the utility of the subgroup concept compared with the previous TD1 and TD2 classification.** In doing so, it should not lose sight of the very valid indications that a remission of TD2 is possible through lifestyle interventions in the early stage of the disease.

**The DDZ aims to advance research by aggregating and exploiting both existing and new data sources, including from functional studies (‘fluxomics’) in humans and model organisms, by establishing a new independent Computational Diabetology research group (Paul Langerhans Group), with a related central biobank. The new group is to have a focus on machine learning and artificial intelligence. It will also provide interconnected large datasets from (pre)clinical studies to other research groups at the DDZ. These ideas are meaningful and should be pursued further. For this purpose, the DDZ intends to apply for additional institutional funding from the federal and *Länder* governments (minor extraordinary item of expenditure, *Sondertatbestand*). The application should describe the designated group’s work in more detail. In addition, the DDZ should investigate in more detail how the group is to be integrated in the existing work of the DDZ and, in particular, how the necessary close dovetailing with the two epidemiological institutes is to be achieved.**

## 4. Controlling and quality management

### Facilities, equipment and funding

#### *Funding*

The institutional funding provision is sufficient to cover the DDZ's current portfolio of activities. Since the last evaluation, the institute's core budget has increased from €11m in 2012 to €14m in 2019. In addition to the annual increases in the Joint Initiative for Research and Innovation, the institute has received permanent additional funding from the federal and *Länder* governments since 2018 (*Sondertatbestand*) to expand its research in the area of comorbidities/complications of diabetes.

In the same period, third-party funding increased from €5m (31% of the budget) in 2012 to €7.8m (36%) in 2019. As recommended, the DDZ has diversified its portfolio of third-party funding. Although a large proportion still comes from the federal government, especially through the DZD and, since 2013, for the NAKO health study, more funds are now being obtained from the EU (including one ERC Starting Grant), and from businesses and foundations. This trend should be continued. The DDZ's revenue from DFG grants is still low however, and comes to less than the DFG fee. In this context, it should be borne in mind that substantial further DFG resources for the DDZ's participation in e.g. Collaborative Research Centres and Research Training Groups are administered by Düsseldorf University, including a new Research Training Group that has been funded since 2020. Moreover, researchers affiliated to Heinrich Heine University Düsseldorf obtain additional DFG grants there (2019: €575,000).

**The DDZ should increase its revenue from DFG and EU grants and offer higher incentives for these. It is important for early-career scientists in particular to establish their credentials by acquiring these kinds of research grants. The DDZ's potential to receive European-level funding for research projects, and particularly for collaborative work with partner institutions, should be exploited more intensively.**

#### *Facilities and equipment*

The Clinical Research Center (CRC) is responsible for clinical observational and interventional studies at the DDZ. The Oskar Minkowski Laboratory is a core facility used for keeping mouse models of type 1 and type 2 diabetes and the metabolic syndrome.

Furthermore, DDZ has established a biomedical laboratory and platforms for proteome analysis and cellular morphology. Since the previous evaluation, the institute has expanded and upgraded its imaging facilities. Following a recommendation at that time and using additional funds from the federal and *Länder* governments (*Sondertatbestand*), it has purchased a high-field magnetic resonance imaging and spectroscopy (MRI/MRS) scanner. Keeping the institute's equipment up-to-date is important for the DDZ's competitiveness.

### Organisational and operational structure

The organisational and operational structures are appropriate and effective.

The Scientific Director of the DDZ does an outstanding job. His main role (*Hauptamt*) is as Director of the Department of Endocrinology and Diabetology at the University Hospital of Düsseldorf (UKD). His employment at the DDZ is secondary (*Nebenamt*). At the DDZ he also

heads the Institute for Clinical Diabetology (ICD), which is by far the largest institute at the DDZ, with nearly 70 full-time equivalent employees and seven sub-units (including the Clinical Research Center). In view of the central role that the Scientific Director plays at the DDZ, the Supervisory Board is called on to plan his succession in good time, for when he leaves in a few years. Following significant growth at the DDZ since the last evaluation, it should check to what extent the three substantial leadership roles (director of the UKD and DDZ and head of the ICD) can be carried out by one individual. An initial load reduction could be achieved by splitting the ICD (see chapter 7). This offers new opportunities to increase the number of female scientists in leadership positions (see chapter 5).

### **Quality management**

The institute's quality management is aligned with the established standards. Rules are in place to ensure good scientific and clinical practice. The DDZ has purchased and implemented a Current Research Information System (CRIS), and a performance-based allocation system (LOM) has been in place since 2015. Relevant LOM metrics are 3-year averages for third-party funding (only public peer-reviewed funding, not industry) and cumulative impact factors. It is welcomed that the institute has reacted to recommendations in the last evaluation by adjusting its statutes and management principles (*Bewirtschaftungsgrundsätze*) in line with Leibniz standards.

### **Quality management by advisory boards and supervisory board**

The Supervisory Board and the Scientific Advisory Board (SAB) fulfil their role in an adequate manner. In between evaluation periods, the SAB conducts an audit of the DDZ as a whole and of its individual units. **It is welcomed that the DDZ's statutes were changed according to recommendations in the last evaluation. Among other things, the term of office for advisory board members was restricted to two terms of four years, as is usual for Leibniz institutions. In order to ensure scientific objectivity, this new regulation must now be put into practice. Currently, five of the 12 members have already been in post for more than eight years.**

## **5. Human Resources**

As of 31 December 2019, the DDZ employs 212 people (177.1 FTE). This number has increased from 174 (146.0 FTE) at the time of the last evaluation.

### **Management**

Institute directors are appointed by the Board of Trustees for a five-year term with an option of renewal. Appointment procedures follow the standards stipulated by the Leibniz Association as well as the relevant HHU standards.

### **Postdoctoral staff and doctoral candidates**

The DDZ provides a stimulating environment for young researchers and follows the Career Guidelines of the Leibniz Association.



The success of the DDZ's support can be seen in the fact that, since the last evaluation, four postdoctoral researchers have been offered professorships at universities and 11 have accepted leading positions in industry and clinical practice. The activities of the local branch of the Leibniz Postdoc Network to encourage interdisciplinary exchanges between medicine and the natural sciences are highly commendable.

The fixed-term junior research groups have proved to be a very successful instrument. They are generally set up within one of the institutes for a duration of up to five years. Since 2013, the DDZ has established six such groups, of which one was terminated after a two-year period, two were converted into a research group and three are still active.

In terms of career support, the DDZ also uses independent groups, called Paul Langerhans Groups (PLGs). They allow scientists to gain experience in leading a smaller research unit and to develop a specific research topic. In future, the PLGs should be advertised in conjunction with a specific topic, and ideally staffed with external candidates.

The DDZ offers doctoral training leading to an MD (Dr. med.), PH (Dr. Public Health) or PhD (Dr. rer. med., Dr. rer. nat.). The formal framework is provided by the partnership with Düsseldorf University, which stipulates that all candidates must be involved in structured programmes. In 2019, 34 doctoral candidates were employed at the DDZ. Only four of them (12%) were foreign nationals. This proportion should be increased. Between 2017 and 2019, 42 doctoral candidates at the DDZ successfully completed their MDs/PhDs.

### **Equal opportunities and work-life balance**

**As of 31 December 2019, the proportion of women among staff in research and scientific services was pleasingly high, at 60%. Six of the 14 (junior) group leaders (43%) and one of the five heads of DDZ institutes (20%) were women. The DDZ should ensure greater involvement of female scientists at the senior management levels.**

## **6. Cooperation and environment**

*Heinrich Heine University Düsseldorf (HHU) and the University Hospital of Düsseldorf (UKD)*

The DDZ enjoys extraordinarily close links with the HHU and UKD. The Scientific Director is at the same time Director of the Department of Endocrinology and Diabetology (see chapter 4), and two other DDZ institute heads also lead an institute at the university or university hospital. Of the five senior scientists at the DDZ, four hold W3 professorships at the Faculty of Medicine, and one holds a similar professorship at the Faculty of Mathematics and Natural Sciences. Four of these positions are financed by the HHU/UKD and one by the DDZ. The close connection facilitates the dovetailing of fundamental research and clinical applications.

A particularly high number of DDZ scientists are involved in university teaching, at undergraduate, Master's and PhD level, and in specialist medical training. A new interdisciplinary interfaculty Master's programme in molecular biomedicine deserves a particular mention in this context. The collaboration with university partners in DFG-funded Collaborative Research Centres (*Sonderforschungsbereiche*) and Research Training Groups (*Graduiertenkollegs*) is noteworthy. Finally, the newly established collaboration with the Department of

Cardiology, Pulmonology and Angiology at the UKD/HHU in the cardiovascular area will enhance future scientific development. To this end, a new joint research centre (CARDDIAB) is to be established (see chapter 2).

#### *National cooperation*

Another area of cooperation of particular relevance is the DDZ's collaboration with other German diabetes research institutions in the German Centre for Diabetes Research (DZD), namely the Helmholtz Diabetes Centre at HMGU Munich and the German Institute for Human Nutrition (DIfE, Potsdam), which generates scientific and financial added-value. For instance, the German Diabetes Study (GDS) is a joint project carried out within the framework of the DZD. The diabinfo platform is another joint project. In cooperation with the Leibniz Institute for Environmental Health (IUF, Düsseldorf), the DDZ operates a study centre for the German National Cohort (NAKO health study).

To foster the translation of research results into application, the newly established Center of Competence for Innovative Diabetes Therapy (KomIT) brings together various academic and industry partners (see chapter 2).

#### *International cooperation and visibility*

The DDZ is highly visible at the international level, especially in the field of clinical studies. It has very good international partnerships, including close connections to some of the leading institutes, e. g. the Center for Disease Control and Prevention (CDC) in Atlanta (USA) in the context of studies on the cost-effectiveness of interventions, and the description of diabetes dynamics in terms of incidence and prevalence.

In 2018, the DDZ established a formal collaboration with Monash University in Melbourne, Australia, that specifically relates to the part-time appointment of the deputy head of the Diabetes Department at Monash as head of the Nephropathy research group at the DDZ.

## **7. Subdivisions of the DDZ**

### **Institute for Biometrics and Epidemiology (IBE)**

[32.5 FTE, of whom 13.5 FTE research and scientific services staff, 2.6 FTE doctoral candidates, and 16.4 FTE service staff]

The IBE consists of two research groups and one junior research group. The institute investigates population-based aspects of diabetes, with a focus on risk factors, treatment and prevention of diabetes complications and comorbidities. It collects its own data (primary data) and uses data from the health care system (secondary data). Additionally, the IBE provides valuable statistical (methodological) support to other DDZ institutes and conducts a programme of methodological research.

Since a change of leadership shortly before the last evaluation, the IBE has developed into an institution that is well established internationally, especially regarding meta-analyses and, more generally, evidence synthesis. The institute covers an appropriately wide range of methodological research areas, collaborations and services. The recently established junior research group on Systematic Reviews provides an interesting, rather unique addition. The

institute should continue to work on its interaction with other DDZ institutes under the overarching theme of Precision Diabetology. To this end, efforts in terms of clinical study designs and clinical development programmes could be strengthened.

The IBE has an impressive publication record, with several papers in high-ranking journals. The level of third-party funding is high, consisting mainly of DZD and NAKO funding, while competitive funding by the DFG and EU could be increased. Given the size of the institute, it should employ more PhD students.

### **Institute for Clinical Biochemistry and Pathobiochemistry (ICB)**

[28.4 FTE, of whom 11.5 FTE research and scientific services staff, 4.7 FTE doctoral candidates, and 12.2 FTE service staff]

The ICB investigates the molecular basis of the onset and progression of metabolic diseases, a very relevant research topic. To this end it utilises both mouse models and human primary cells. With two research groups (Pathobiochemistry, Genomics) and three platforms (Genomics, Proteomics, Cell Morphology) the institute has a very comprehensive setup, covering a broad range of basic and mechanistic research. It provides models and methodologies accessible to other groups.

The institute is an important link between the DDZ's clinical work, especially from the cohort studies, and the evaluation of new parameters and genes in their significance on metabolism. In the future, besides the molecular biological work, the comparative studies in imaging from small animal models to reverse verification in humans will be of particular interest. It will be important, though, to stay aligned with the overarching aim of the DDZ in its development towards Precision Diabetology.

The ICB's work has been published in international journals of very good quality. The institute has increased third-party funding and recently succeeded in establishing a DFG-funded Research Training Group. It is very successful in supporting its junior researchers.

### **Institute for Clinical Diabetology (ICD)**

[67.9 FTE, of whom 26.4 FTE research and scientific services staff, 7.5 FTE doctoral candidates, and 34 FTE service staff]

The ICD studies the mechanisms involved in the onset and progression of diabetes mellitus and its complications. By far the largest institute, with six groups and one platform, the ICD's spectrum of work ranges from pathophysiology of diabetes mellitus, non-alcoholic fatty liver disease (NFLD) and steatohepatitis (NASH) to complications of diabetes and clinical trials/preclinical models. The ICD provides the essential clinical link to the university hospital, provides the imaging infrastructure for metabolic patient assessment (magnetic resonance imaging and spectroscopy) and maintains extremely valuable patient cohorts.

The institute has developed impressively well and enjoys a very high standing. It has significant output in terms of publications and presentations. The ICDs research findings, e.g. on the deleterious effects of saturated fat intake and the interaction of diabetes and liver disease, are highly relevant. The institute made an important contribution to uncovering dynamic

epigenetic and metabolic changes after weight loss, and to the development of the mitochondrial flexibility concept in the context of NAFLD progression to NASH. Further investigation of aspects of inflammation will be very important.

The ICD is very active in public outreach. Staff members hold important advisory functions on expert panels and in professional associations. Moreover, there are highly promising developments in the field of drug development (KomIT, see chapter 2), cardiovascular research (CARDIAB, see chapter 2) and the development of cohorts. The ICD is very well funded, internally and externally, with third-party funding coming mainly from the DZD, but also from foundations, industry and the DFG.

Given the size of the ICD and the wide range of topics it covers between basic research and clinical application, it could be advantageous to split it, e.g. into an institute for clinical pathophysiology of metabolic diseases and an institute for complications, including cardiovascular research.

### **Institute for Health Services Research and Health Economics (ISE)**

[11.5 FTE, of whom 7.75 FTE research and scientific services staff, 1.75 FTE doctoral candidates, and 2 FTE service staff]

The ISE was established in 2017, developing from a research group in the Institute for Biometrics and Epidemiology (IBE). The team is interdisciplinary, with members from the fields of medicine, public health, care, epidemiology and health economics. In two research groups and one junior group the institute undertakes patient-centred research and health economic evaluation of diabetes prevention and treatment. It works with cohorts and population-based health insurance databases.

The ISE covers important research topics and has a good publication output. The institute is internationally well established and connected. It collaborates closely with the institute of the same name at the University Hospital of Düsseldorf, which is led by the same person. The ISE successfully obtains third-party funds from the federal and *Länder* governments. Revenue from DFG and EU project grants should be increased.

For the future, the ISE has innovative ideas and concepts, e.g. for gestational diabetes and psychological consequences of the disease. It advocates greater involvement of patients in research, and has plans for patient reported outcome measures (PROMs), a citizen advisory board and international comparisons through a newly founded EASD study group (European Association for the Study of Diabetes). The expanded use of health insurance data is also promising. When implementing its plans, which are generally well thought through, the institute should strengthen its collaboration with the other institutes. The involvement of machine learning/artificial intelligence in the research work should be described more clearly.

### **Institute for Vascular and Islet Cell Biology (IVI)**

[11 FTE, of whom 4.1 FTE research and scientific services staff, 3.15 FTE doctoral candidates, and 3.75 FTE service staff]

The IVI (previously the Institute for Beta Cell Biology) was set up in 2013, on the basis of a Paul Langerhans Group (see chapter 3). It consists of two research groups and one junior

research group. The institute focuses on mechanistic research in islet cells and blood and lymph vessels. It also works on the development of new compounds and therapies to better treat diabetes and its cardiovascular long-term complications.

The IVI's outstanding work on factors for vascular remodelling for the regeneration of the liver received the highest international attention, which is also reflected in exceptionally high-ranking publications. The translation of these results to the pancreas will be followed with the utmost attention by the scientific community. Other landmark studies include the identification of NMDA (N-methyl-D-aspartate) receptors on beta cells that regulate insulin secretion and cell survival. This finding directly resulted in patents and a novel treatment approach that proved effective in a first clinical trial – an exemplary successful translational development.

The IVI contributes to innovative approaches in clinical practice by developing new substances for interventions for diabetic metabolism. Future plans include the development of novel morphinan compounds, which will open up novel treatment options. In view of the complete failure of drugs to date to halt the decline in beta cell function, the institute should expand these plans to the pathophysiology induced by the provision of excess fat and glucose. The development of a structure for the interaction with small businesses is very commendable (KomIT, see chapter 2). The IVI achieves high levels of third-party funding, including an ERC Starting Grant. The focus on basic research offers possibilities for obtaining more funds from the DFG.

## **8. Handling of recommendations of the last external evaluation**

The DDZ successfully addressed the recommendations made by the Leibniz Association Senate in 2014 (see status report, p. A-22f). In parts, the recommendation on third-party funding (recommendation 4) still apply.

## Appendix

### 1. Review board

#### *Chair (Member of the Leibniz Senate Evaluation Committee)*

**Ulf Müller-Ladner** Department of Rheumatology and Clinical Immunology, Justus-Liebig University Giessen, Campus Bad Nauheim

#### *Deputy Chair (Member of the Leibniz Senate Evaluation Committee)*

**Nicola Fohrer** Institute for Natural Resource Conservation, Department of Hydrology and Water Resources Management, Kiel University

#### *Reviewers*

**Tim Friede** Department of Medical Statistics, University Medical Center Göttingen, Göttingen

**Anne Jörns** Institute of Clinical Biochemistry, Hannover Medical School, Hannover

**Friedemann Kiefer** Intravital Molecular Imaging, European Institute for Molecular Imaging (EIMI), Münster

**Sabine Rohrmann** Epidemiology, Biostatistics and Prevention Institute (EBPI), University of Zurich, Zurich

**Peter Rossing** Complications Research, Steno Diabetes Center Copenhagen (SDCC), Copenhagen

**Christoph Stettler** Department for BioMedical Research, University of Bern and Division of Diabetes, Endocrinology, Nutritional Medicine & Metabolism (UDEM), University Hospital – Inselspital, Bern

**Roy Taylor** Magnetic Resonance Centre, Newcastle University, Newcastle upon Tyne

**Sarah Wild** Usher Institute, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh

#### *Representative of the federal government*

absent with apologies Federal Ministry of Education and Research, Bonn

#### *Representative of the Länder Governments (Member of the Leibniz Senate Evaluation Committee)*

**Jutta Koch-Unterseher** The Governing Mayor of Berlin, Senate Chancellery – Science and Research

15 April 2021

**Annex C: Statement of the Institution on the Evaluation Report**

**German Diabetes Center (DDZ) -  
Leibniz Institute for Diabetes Research  
at Heinrich Heine University Düsseldorf**

Das DDZ bedankt sich herzlich bei der Bewertungsgruppe sowie dem Referat Evaluierung der Leibniz-Gemeinschaft für die Evaluierung und die Übermittlung des Bewertungsberichtes.

Der Vorstand und die Abteilungsleiter des DDZ haben den Bericht gelesen, diskutiert und bedanken sich für die positive und konstruktive Bewertung des Institutes und seiner Abteilungen.