

Rolle des Biobanking und GBN/GBA aus der Perspektive eines Dekans

Matthias Frosch

Dekan der Medizinischen Fakultät der Universität Würzburg

Nutzen

I. Drittmittelförderung durch das BMBF

BMBF-Förderprogramm *National Centralized Biobanks* (2011-16)

Deutschland bündelt Biobanken an fünf Standorten

Erstmals vernetzen Forscher an fünf Standorten die vorhandenen lokalen Biobanken. Ziel der mit 17 Mio. Euro vom Bund geförderten Nationalen Biobank-Initiative: eine kritische Masse hochqualitativer, einheitlich charakterisierter Proben für die Biomarkerforschung bereitzustellen.



Tanks zur Kryolagerung von Biomaterialien bei -140 °C.

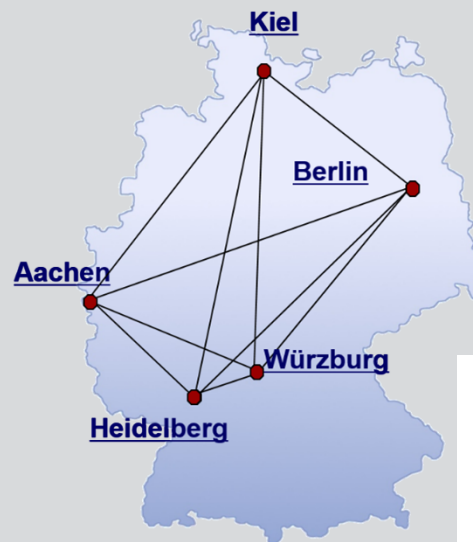
Mit einer einzigartigen Initiative besetzt die Bundesregierung einen entscheidenden Engpass der biomedizinischen Forschung, um

Die neu entstehenden, vernetzten Biobanken können sich als wahre Schatzkammern erweisen – nicht nur für die akademische Biomarker-

effektivität und damit die Patentlaufzeit. Das kommerzielle Risiko ist kleiner und der Vorteil für den Patienten – so hoffen wir – signifikant größer.“

Treibstoff für die Biomedizin

Das BMBF mit den für die Leuchtturmprojekte aus 29 Bewerbungen ausgewählten Biobank-Modellstandorten Aachen, Berlin, Heidelberg, Kiel und Würzburg Großes vorhat, wurde auf dem Expertentreffen in den Räumen der TMF – Technologie- und Methodenplattform für die vernetzte medizinische Forschung e.V. deutlich. Nach den Plänen des Ministeriums ist die Initiative nur der Auftakt, um die bisher verstreuten Proben- und Datenressourcen für die patientenorientierte Forschung nutzbar zu machen und später in die geplante europäische Biobankstruktur BBMRI [log. Biobankpt](#) einzubinden. Bis zum Sommer 2012 wird der TMF, der künftig als Kommunikations- und Vernetzungsplattform für die Biobankfor-

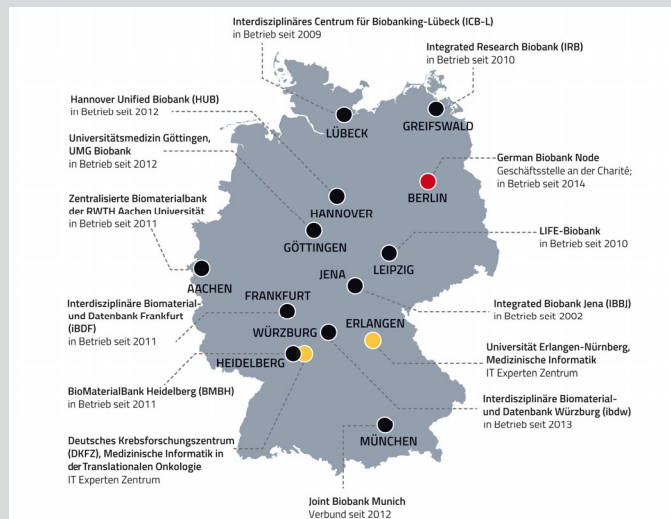


7.354 T € für Würzburg
davon 3.794 T € Investitionen
(davon ca. 3.000 T € für Freezer)

Nutzen

I. Drittmittelförderung durch das BMBF

BMBF-Förderprogramm *German Biobank Allianz* (2017 – 2020)



1.174 T € für Würzburg

Nutzen

II. Qualitätssicherung „weg von den Gefrierschränken“



Konzept einer zentralisierten interdisziplinären Biobank

1. Erfassung bestehender Biomaterial-Sammlungen
2. Probeneinlagerung auf Basis eines „**Broad Consent**“.
National wegweisende Pilotimplementierung am UKW bereits in 2014!
3. Festlegen der Zugangsregeln für Biomaterialien (intern/extern: MTA/DTA).
4. Implementierung eines interdisziplinären Biobank-Management-(IT)-Systems mit Integration in IT-Strukturen des Universitätsklinikums
5. Festlegung von Workflow Biomaterial-Sammlung i.R. der Routine
 - Differenzierung feste (Gewebe) und flüssige Biomaterialien (Blut)
 - Abstimmung der Logistik (interdisziplinär, fakultätsweit), und
 - einheitliche Regeln (SOP) für QM, Labelling und Storage

Nutzen

III. Strukturbildung

1. Neue Professur

Berufung von Prof. Dr. Roland Jahns
als Direktor der ibdw in 2013

2. Neues Gebäude zur Unterbringung der Freezer (2 x 515.000 Proben)

3. ibdw Governance und Probenzugang



Governance und Probenzugang

Universitätsklinikum Würzburg
ibdw

Nutzungsantrag auf Proben (Broad Consent)

Anforderungen bitte vollständig am PC ausfüllen und an die Geschäftsstelle der ibdw per E-Mail senden:

Interdisziplinäre Biomaterial- und Datenbank Würzburg (ibdw)
Geschäftsstelle
Steuerstraße 26, Haus 45
97078 Würzburg
Tel: +49 (0)931 231 47001
Fax: +49 (0)931 231 467000
Email: ibdw@ukw.de

Antragsteller*in / Kontakt

| Nachname | Vorname | E-Mail |
|----------|---------|--------|
| | | |
| | | |
| | | |

Nachweise zum Antrag

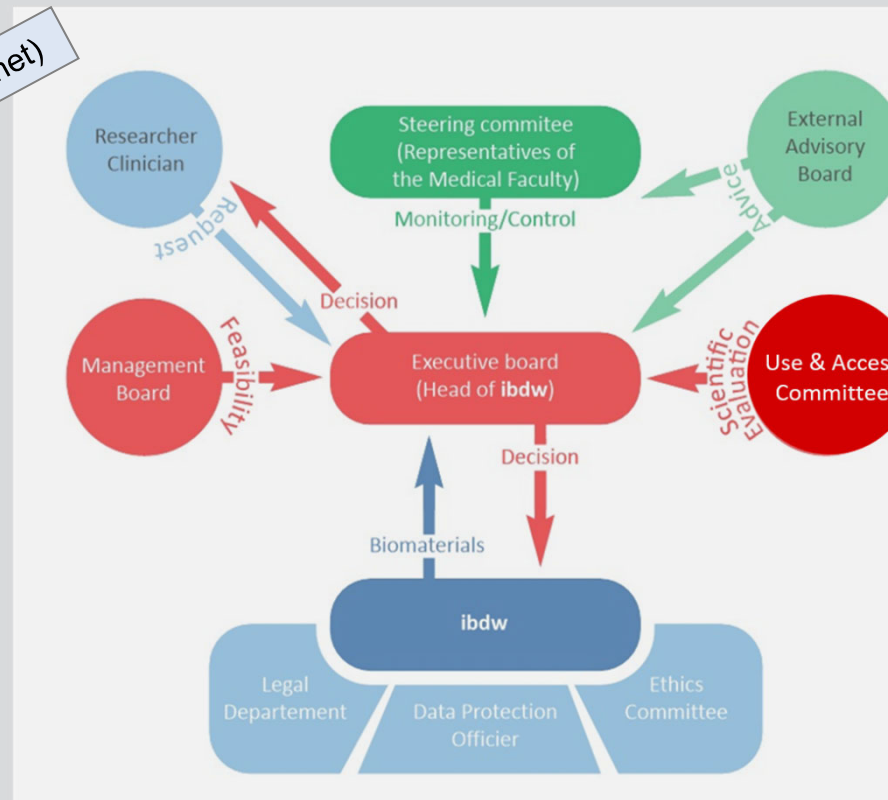
Projektbeschreibung

Studienprotokoll internal (gemäß Ethikkommission oder
Kardbeschreibung Projekt - ibdw (bei Nutzung anonymisierter Proben) → dem Antrag bitte beiliegen

Ethische Freigabe

gültige Ethik-votum (siehe Bedenken/Einwände) oder
Unbedenklichkeitsklärung der Ethikkommission (bei Nutzung anonymisierter Proben) → dem Antrag bitte beiliegen

Online-application (PDF intranet)



M. Kiehntopf, Jena
F. Betsou, Paris
H. Domdey, München
W. Hoffmann, Greifswald
M. Hummel, Berlin

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Proben)
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4. Erfolgreiche Drittmittelinwerbung / Beteiligung an Netzwerken



Nutzen

Beteiligung der ibdw an:

- Klinischen Studien und Register
 - *DZHI: STAAB; STAAB-Covid - Populationskohorte; AHF (Acute Heart Failure)-Registry*
 - *ZESE: „1000 klinische Genome“, u.a.)*
- Koordinierte DFG-Programme
 - SFB-TR 240; SFB 1525; KFO 5001*
- Nationale und bayerische Förderprogramme
 - Medizin Informatik Initiative/ABIDE-MI; NUM/NAPKON; NCT-WERA; CCC-MF, Bayerisches Zentrum für Krebsforschung, The Bavarian-Czech Biobank Landscape*

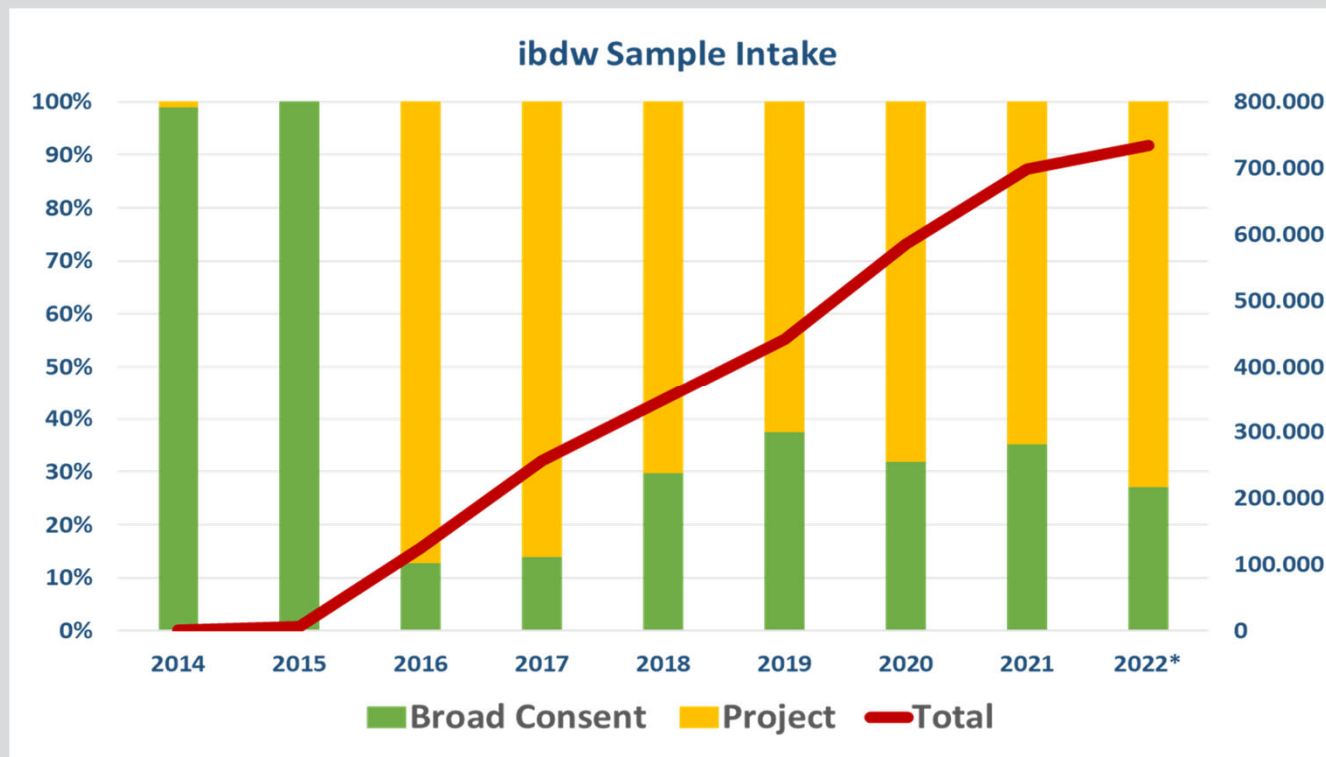
Deutsches Zentrum für
Herzinsuffizienz (DZHI)



Nutzen

IV. Einlagerung und Ausgabe

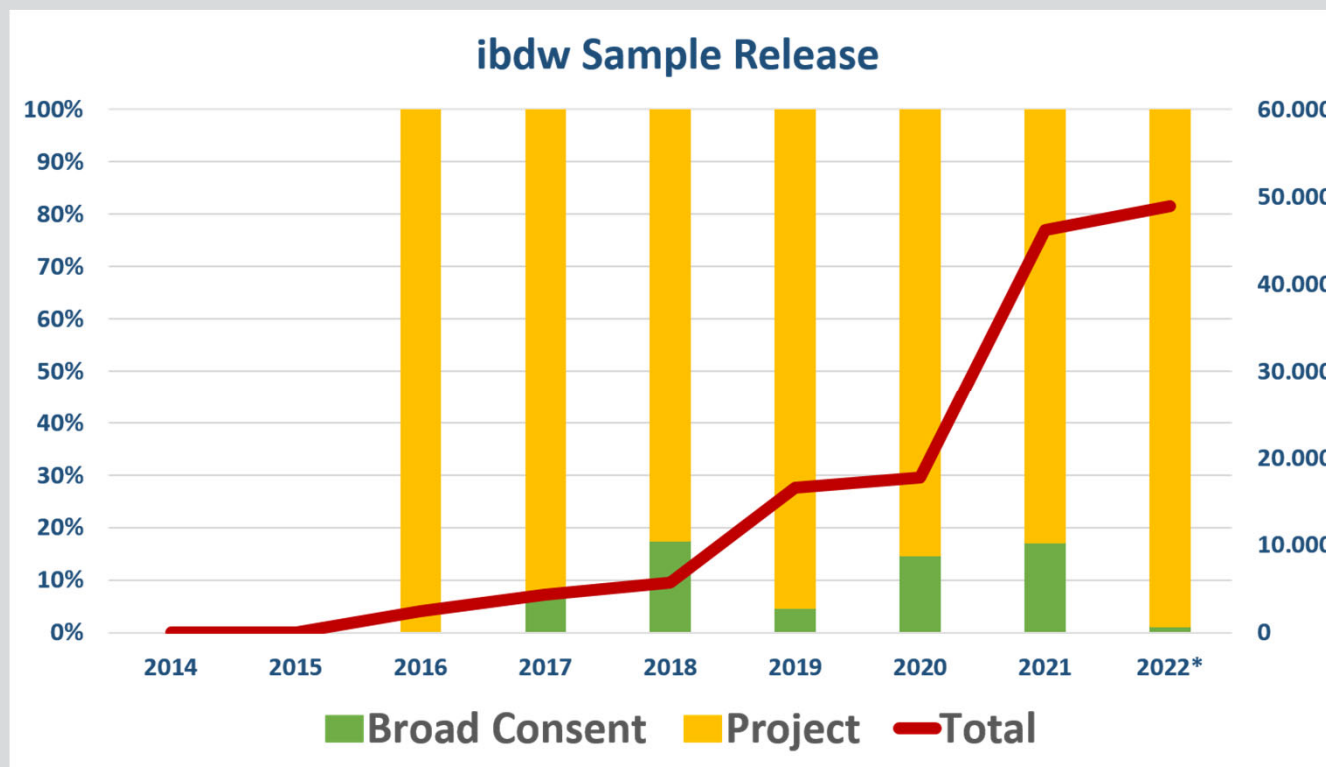
ibdW Einlagerung: Probenstatistik 2014-2022* - broad versus project-specific



Nutzen

IV. Einlagerung und Ausgabe

ibdW Auslagerung: Probenstatistik 2014-2022* - **broad** versus **project-specific**



Nutzen

V. Die Ibw ist beteiligt an high impact Publikationen

RESEARCH

IMMUNOLOGY

Microbiota-derived peptide mimics drive lethal inflammatory cardiomyopathy

Christin Gil-Cruz¹, Christian Probst-Schubert¹, Angelina De Martin¹, Francesca Bianchi¹, Kathrin von der Grön¹, Henning Heideker¹, Lukas Ojeda¹, Heidegger Unger¹, Marie Weisner¹, Veronika Neuf¹, Gudrun Ramm^{1,2}, Markus Arnold^{1,3}, Emma M.C. Smith⁴, Valérie Beutin-Jahn^{1,5}, Roland Lenzel^{1,6}, Maximilian Hugel¹, Catherine Heideker¹, Jan H. Langerhans¹, Mirko J. Gessner¹, Hans Reichel¹, Lukas Flatz¹, Urs Eisenacher^{1,7}, Markus B. Gessler⁸, Kathy B. McCoy⁹, Bernhard Lutjeharms⁹

Myocarditis can develop as an inflammatory cardiomyopathy through chronic stimulation of agonist T helper 1 (Th1) and Th17 cells. However, mechanisms governing the cardiotoxicity of progressing of heart specific T cells have remained elusive. Using a mouse model of spontaneous autoimmune myocarditis, we show that progression of myocarditis to lethal heart disease depends on cardiac myosin-specific CD4⁺ T cells represented as the main type by conventional immunosuppressive agents. Both the successful prevention of lethal disease in mice by antibody therapy and the significantly elevated bacteriophage-coded CD4⁺ T cell and cell responses observed in human myocarditis patients suggest that mimic peptides that control bacteria can prevent inflammatory cardiomyopathy in genetically susceptible individuals. The ability to restrain cardiac-specific T cells through manipulation of the microbiome thereby transforms inflammatory cardiomyopathy into a targetable disease.

Myocarditis is an inflammatory heart disease that can develop into lethal cardiomyopathy (1). An autoimmune activation of heart-specific T cells is associated with the generation of autoimmune response against major heart proteins (2,3). However, the exact mechanism of disease progression to lethal heart disease remains unclear. We show that progression of heart-specific T cells to lethal heart disease depends on cardiac myosin-specific CD4⁺ T cells and that these cells are represented as the main type by conventional immunosuppressive agents. Both the successful prevention of lethal disease in mice by antibody therapy and the significantly elevated bacteriophage-coded CD4⁺ T cell and cell responses observed in human myocarditis patients suggest that mimic peptides that control bacteria can prevent inflammatory cardiomyopathy in genetically susceptible individuals. The ability to restrain cardiac-specific T cells through manipulation of the microbiome thereby transforms inflammatory cardiomyopathy into a targetable disease.

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Original scientific paper

European Journal of Preventive Cardiology

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Pages 1488-1497

Characteristics and Course of Heart Failure Stages A–B and Determinants of Progression – design and rationale of the STAAB cohort study

Martin Wagner^{1,2}, Theresa Tiffel^{1,2}, Caroline Mörbach^{2,3}, Götz Gelbrich^{1,2}, Stefan Störk^{1,2} and Peter U Heuschmann^{1,2,4,5} on behalf of the STAAB Consortium

Abstract
Background: Data from the general population on the natural course of heart failure is lacking. The objectives of the STAAB cohort study are to determine the prevalence of heart failure stages A–B in a representative sample of the general population and to prospectively investigate the progression from asymptomatic cardiac dysfunction into symptomatic heart failure. Here we present study design, participation rates and baseline characteristics of the first 1488 enrolled subjects.

Methods: A random sample of inhabitants from the city of Würzburg stratified by age (50–79 years) and gender was drawn from the local registration office. Subjects receive invitation letters, while send-out batches are continuously adapted to response rates by age and gender. At baseline examination, data on echocardiographic cardiac function, comorbidities and preclinical cardiovascular phenotypes are collected. After 3–5 years, changes in cardiac function and occurrence of clinical events will be assessed in a follow-up visit.

Results: Between December 2013 and April 2015, 4499 subjects were invited, of those, 1510 (34.6%) responded positively and 1488 were examined (24.2%). Successful recruitment was on average while the participation rate was highest in subjects aged 60–69 years (98%). Hypertension (42%) and dyslipidaemia (37%) were the most commonly reported comorbidities, 7% reported on diabetes and 23% of men (ie, 17% of women) were smokers.

Conclusions: STAAB recruits a representative population-based sample suited to provide reliable estimates of the frequency of asymptomatic cardiac dysfunction and determinants of disease progress on into symptomatic heart failure. These findings will build the ground for developing preventive strategies for heart failure at different stages of the disease continuum.

Keywords: Population-based study, prevalence, heart failure, risk factors

Received 30 May 2016; accepted 2 November 2016

Introduction
Chronic heart failure is one of the major causes for mortality and morbidity in developed countries.^{1,2} There is evidence that heart failure is a progressive condition, beginning with risk factors for cardiac dysfunction, proceeding to asymptomatic structural heart disease, and resulting in symptomatic heart failure.^{3,4} Such a perspective emphasizes the importance of early detection and prevention of heart failure. Most of all, comprehending the heart failure continuum in the

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Molecular Oncology, in press

RNA polymerase I inhibition induces terminal differentiation, growth arrest and vulnerability to senolytics in colorectal cancer cells

Christoph Otto^{1*}, Carolin Kastner^{2,3*}, Stefanie Schmidt^{2,3}, Konstantin Uttinger¹, Apoorva Balasubramanian¹, Sarah Denk^{2,3}, Mathias T Rosenfeldt¹, Andreas Rosenwald¹, Florian Roehrig², Carsten P Ade¹, Christina Schuelein-Voelck¹, Markus E Diefenbacher¹, Christoph-Thomas Germer^{1,5}, Elmar Wolf⁶, Martin Eilers^{2,5} and Armin Wiegerr^{1,2,3,5}

- 1 Experimental Visceral Surgery, Department of General, Visceral, Transplantation, Vascular and Pediatric Surgery (Department of Surgery I), University Hospital Würzburg, Würzburg, Germany
- 2 University of Würzburg, Department of Biochemistry and Molecular Biology, BioCenter, Würzburg, Germany
- 3 Department of General, Visceral, Transplantation, Vascular and Pediatric Surgery (Department of Surgery I), University Hospital Würzburg, Würzburg, Germany
- 4 Institute of Pathology, Universität Würzburg, Würzburg, Germany
- 5 University of Würzburg, Comprehensive Cancer Center Mainfranken, Würzburg, Germany
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Introduction
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Julius-Maximilians-

**UNIVERSITÄT
WÜRZBURG**



Aufwand und Kosten

Aufwand und Kosten

Kosten für Fakultät und Klinikum in der Aufbauphase

Gebäude

- Baukosten: **1.510 T €**

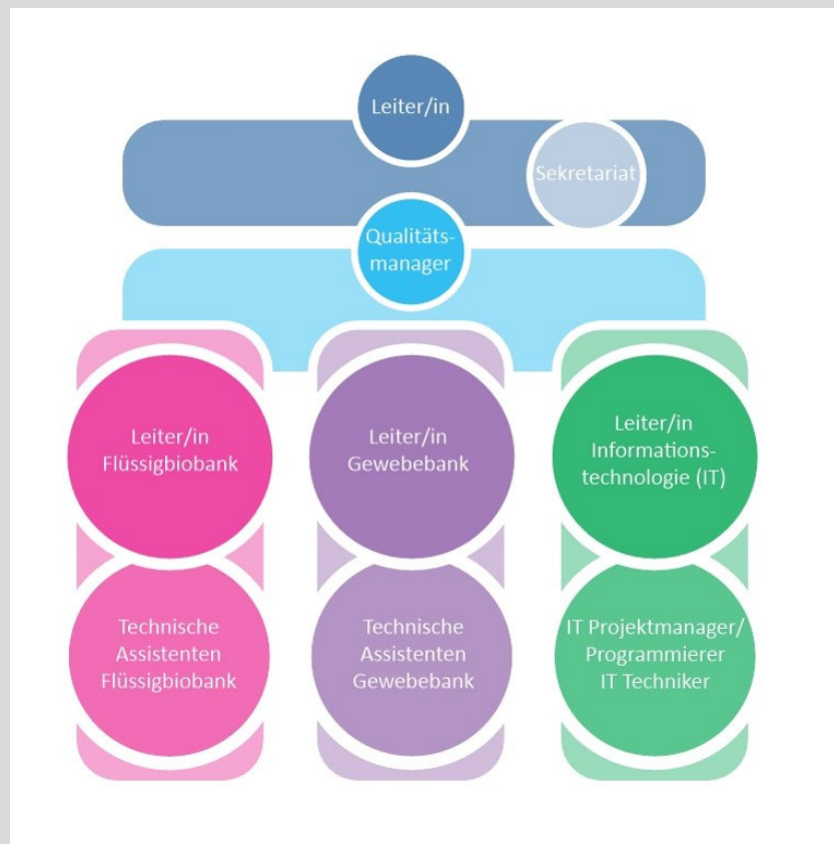
Investitionen

- Zusätzliche Investitionen aus dem Haushalt des UKW bis 2021 insgesamt: **530 T €** (davon ca. 200 T € für Software/IT-Upgrades)



Aufwand und Kosten

Organigramm und erforderliche Personalausstattung



3 Säulen-Konzept

Aufwand und Kosten

Jährliche Kosten und Finanzierung

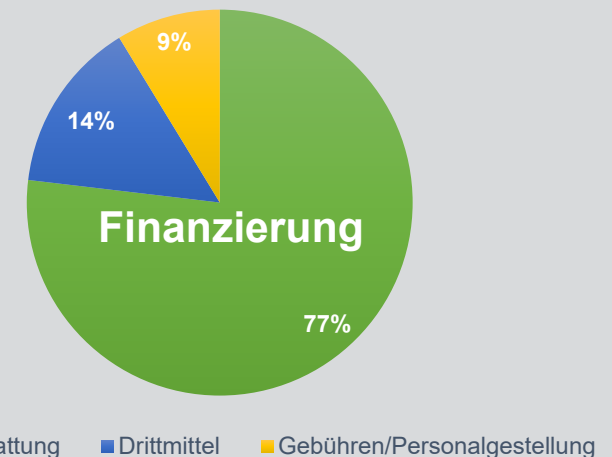
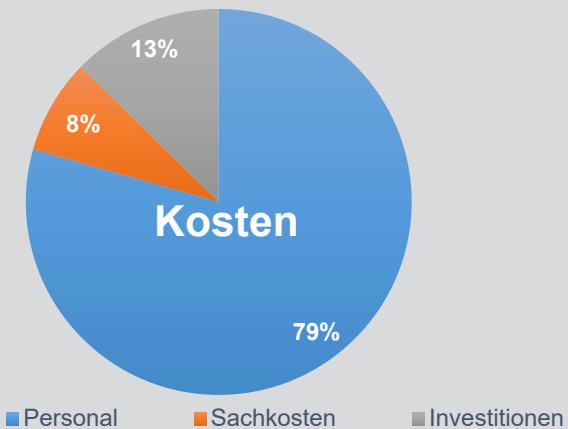
Erwartete Kosten 2022

| | |
|-------------------|------------------|
| Personalkosten | 1.002 T € |
| Sachkosten | 100 T € |
| Wartung/Unterhalt | 160 T € |
| SUMME: | 1.262 T € |

(ohne Gemeinkosten)

Finanzierungsplan 2022

| | |
|----------------------|------------------|
| Grundausstattung | 970 T € |
| Fakultät/Universität | |
| Drittmittel | 182 T € |
| Gebühren | 110 T € |
| SUMME: | 1.262 T € |



Refinanzierung der Kosten

**Kosten für Aufbereitung und Lagerung
einer Probe (in 6 Aliquots) pro Jahr 42,40 €**

Anteilige Kosten/Gebühren berechnet:

Broad consent Proben

Keine Gebühren; 100% Finanzierung durch Fakultät

PIs (intern), eigene Nutzung, ohne Drittmittel

10-15 % Eigenbeteiligung aus Haushaltsmitteln

PIs (intern), eigene Nutzung, mit Drittmitteln;

60-70% Kostendeckung aus Drittmitteln

PIs (extern)

100% der Kosten werden in Rechnung gestellt

Industrie:

Vollkostenberechnung

Fazit:

**Der Betrieb der ibdw ist teuer,
aber der Nutzen rechtfertigt die Kosten**