Leibniz-Institut für Molekulare Pharmakologie

within the Forschungsverbund Berlin e.V.
an institute of the Leibniz Association

FMP

FVB Forschungsverbund Berlin e.V.

Leibniz Leibniz-Gemeinschaft

Zertifikat seit 2013
audit berufundfamilie

Leibniz compared with other research organisations

Max Planck Society

Basic research
centered on individuals

- 83 institutes
- 22,000 employees
  incl. 13,300 scientists
- 1.8 billion Euro
- 50% Federal Gov. 50% States

Helmholtz Association

Large-scale research
centered on programs

- *18 research centers*
- *38,000 employees*
- *4.4 billion Euro*
- *90% Federal Gov. 10% States*

Leibniz Association

Strategic research
centered on topics

- 91 institutions
- 18,600 employees
  incl. 9,500 scientists
- 1.7 billion Euro
- 50% Federal Gov 50% States

Fraunhofer Society

Applied research
centered on products

- 69 institutes
- 24,500 employees
- 2.1 billion Euro
  incl. 1.9 billion Euro via contract research

Leibniz Association

91 institutions

(research institutes, museums)

„ Research relevant for the society as a whole “

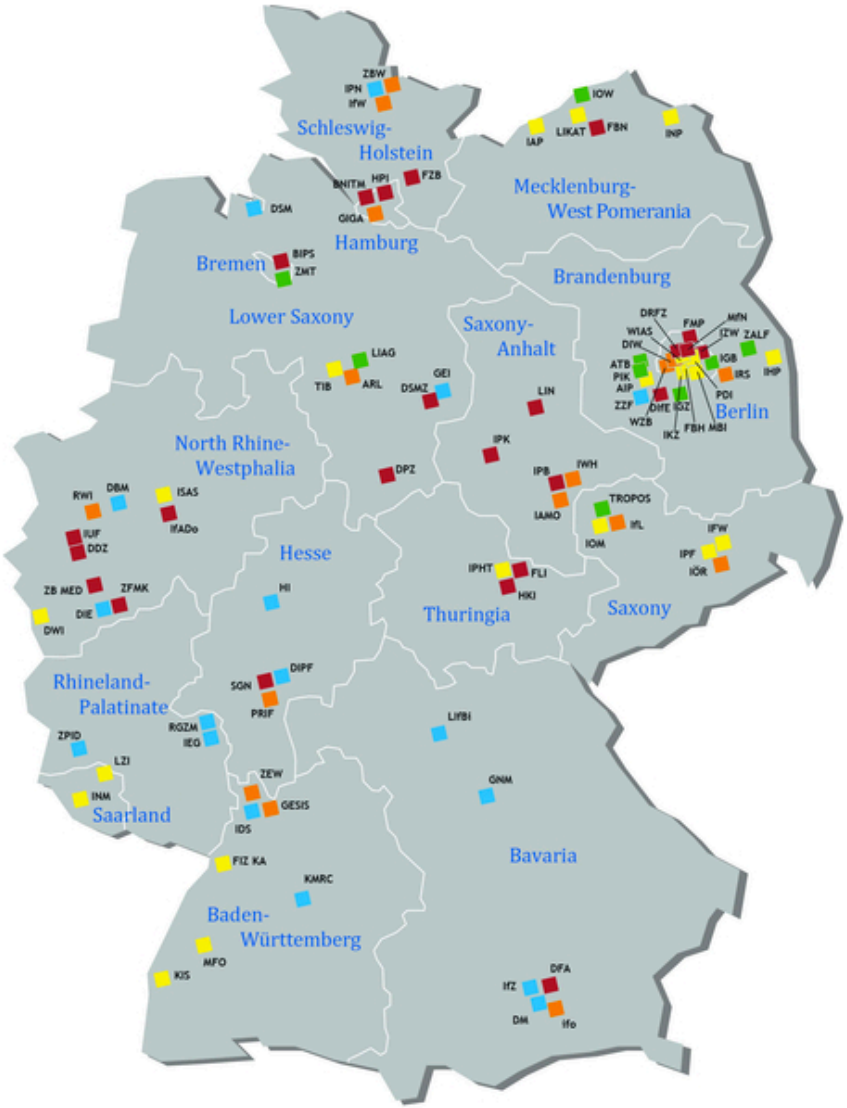
„ Theoria cum praxi“

appr. 18.600 employees,

including appr. 9.500 scientists

Budget of 1.7 billion Euro,

50% Federal Government, 50% States



Leibniz-Institutes 2016

Forschungsverbund Berlin e.V. - Eight Leibniz institutes share a common administration

FBH Ferdinand-Braun-Institut, Leibniz-Institut für Höchstfrequenztechnik

FMP Leibniz-Institut für Molekulare Pharmakologie

IGB Leibniz-Institut für Gewässer-ökologie und Binnenfischerei

IKZ Institut für Kristallzüchtung

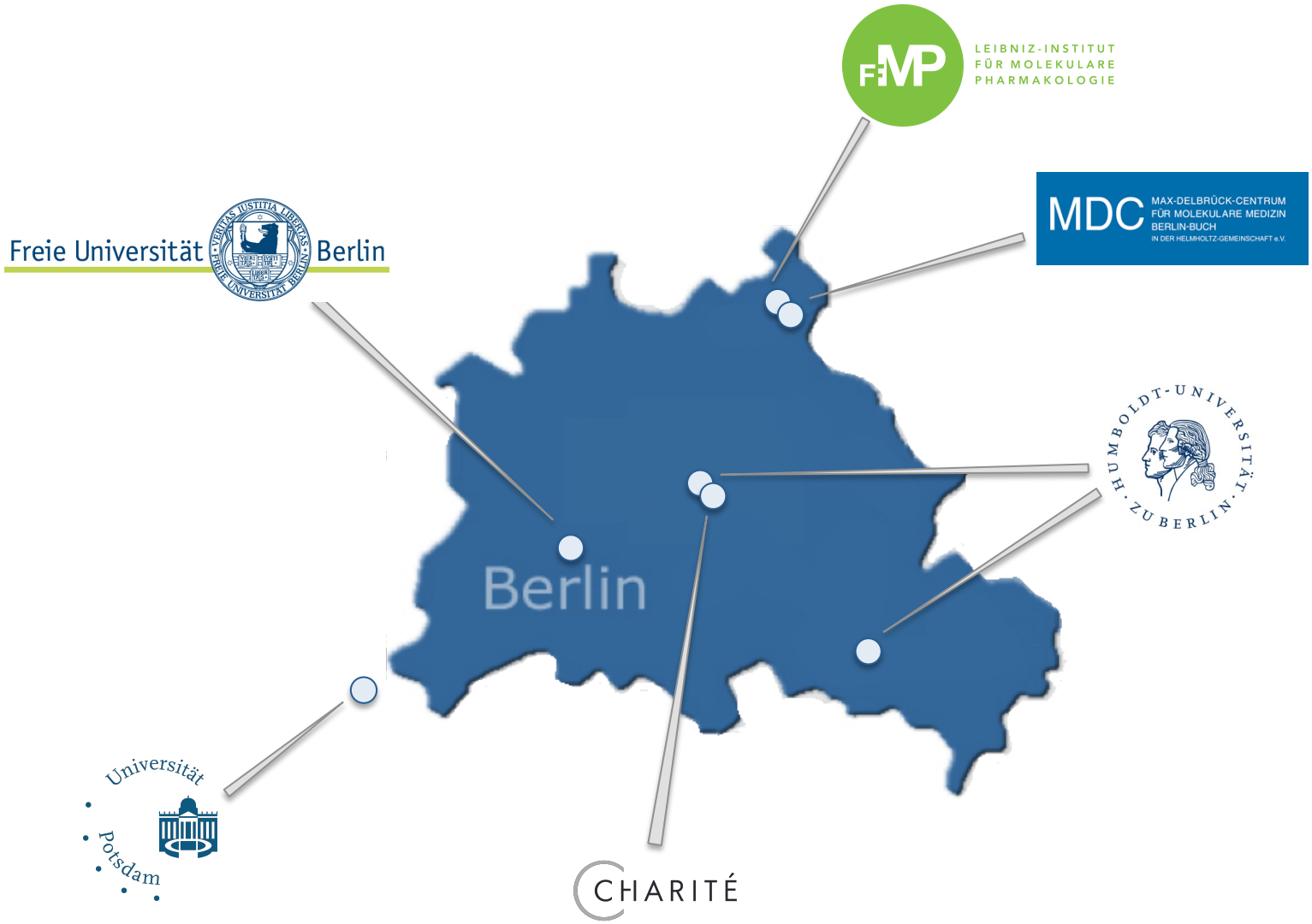
IZW Leibniz-Institut für Zoo- und Wildtierforschung

MBI Max-Born-Institut für Nichtlineare Optik und Kurzzeitspektroskopie

PDI Paul-Drude-Institut für Festkörperelektronik

WIAS Weierstraß-Institut für Angewandte Analysis und Stochastik, Leibniz-Institut im Forschungsverbund Berlin e. V.

Partners in a Regional Network



Staff and Budget

Staff

280 employees, including

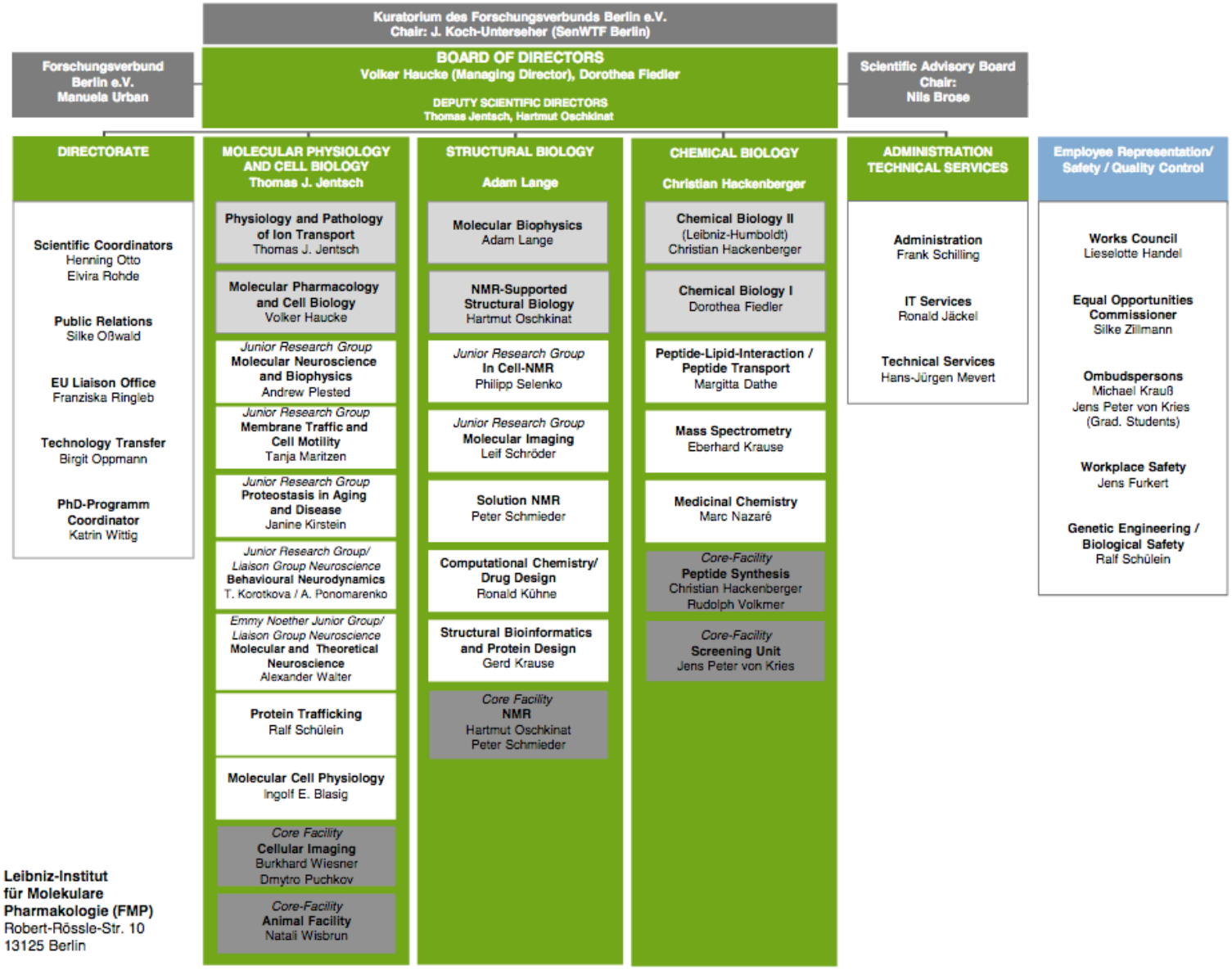
- 110 senior scientists and postdocs
- 80 graduate students
- 60 technicians

Budget

- 16 Mio € Basic Funding (50% Federal Government, 50% Länder)
- 6 Mio € Third Party Funding (DFG, BMBF, EU, others)

(all figures are approximate numbers)

Research at the FMP takes place in 6 departments, 15 research groups and 5 core facilities.

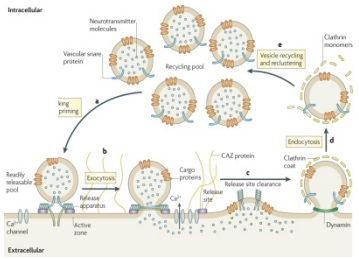


Leibniz-Institut für Molekulare Pharmakologie (FMP)
Robert-Rössle-Str. 10
13125 Berlin

Three Sections structure research at the FMP

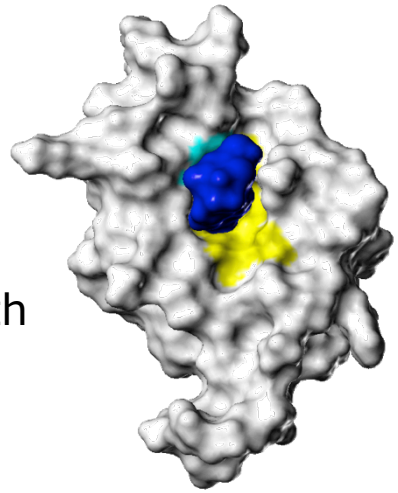
Molecular Physiology and Cell Biology
(Thomas Jentsch)

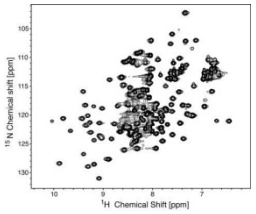
Molecular mechanisms in cell biology and physiology

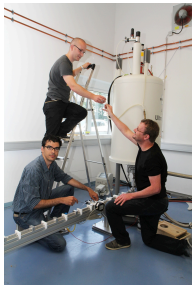


Structural Biology
(Adam Lange)

Drug-target interactions with atomic resolution

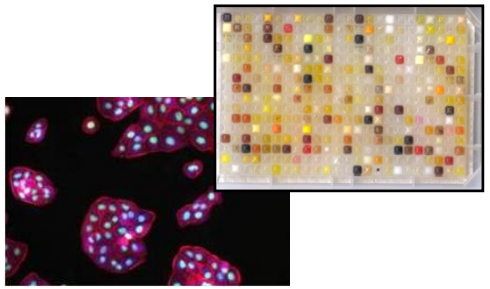






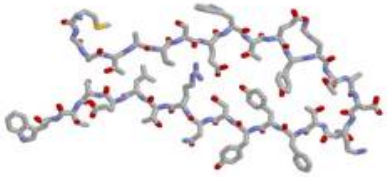
Chemical Biology
(Christian Hackenberger)

Molecular tools for probing cellular processes

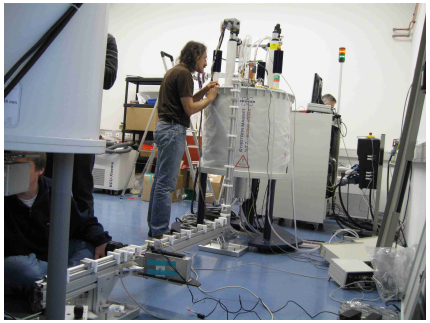


Enabling technologies at the FMP

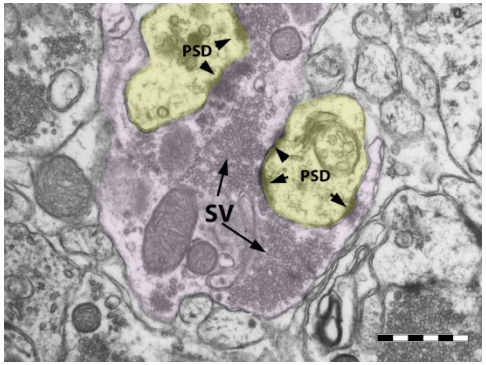
Advanced chemistry



NMR-based structural biology



Electron microscopy

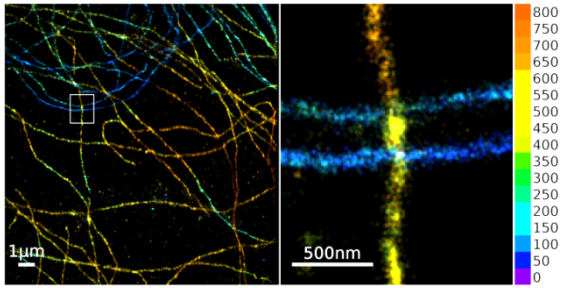


SILAC-based proteomics

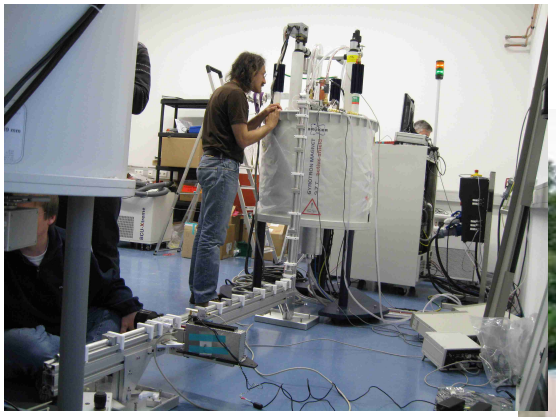
Small molecule screening

Transgenic animals

Functional imaging / Super-resolution microscopy



The FMP hosts an outstanding NMR cluster



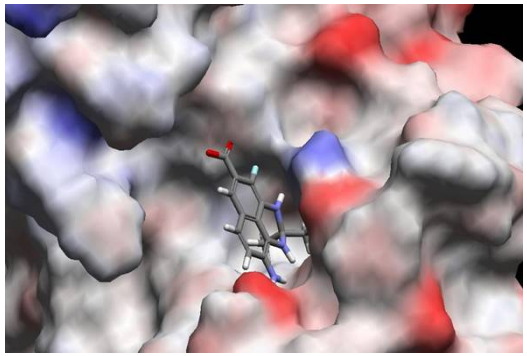
- NMR Cluster: several high-end NMR spectrometer
- Development of NMR techniques for structural biology
- Focus on Solid-state NMR
- Acquisition of newest equipment:

  → *1.1 GHz wide bore NMR spectrometer*
- Access for collaboration partners (*Bio-NMR / iNEXT*)
- Partner of INSTRUCT, the European structural biology network

instruct Integrating Biology

Our Mission – Molecular Pharmacology

Basic reseach in the field of molecular pharmacology



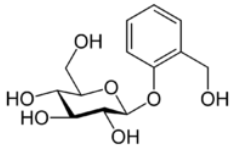
Aim: Extend the currently narrow basis for drug-based therapies in the run-up to drug research

Focus of research:

- Identification, characterisation, and manipulation of novel and / or challenging biological targets for pharmacological intervention
- Development of novel chemical tools, probes and experimental strategies to address biological function.
- Interdisciplinary research that integrates structural biology, biochemical, chemical, and bioimaging approaches
- Methods development (e.g. NMR, MRI, chemical syntheses)

(Patho-) mechanisms → Drug screening → Preclinical phase → Clinical phase → Approval / Marketing

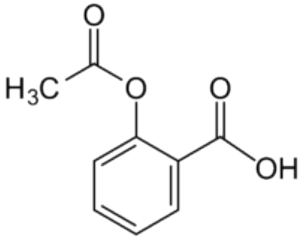
Salicylates, Drugs Througout Two Millennia



Salicin

Glucoside from willow bark

Johann Andreas Buchner
1828



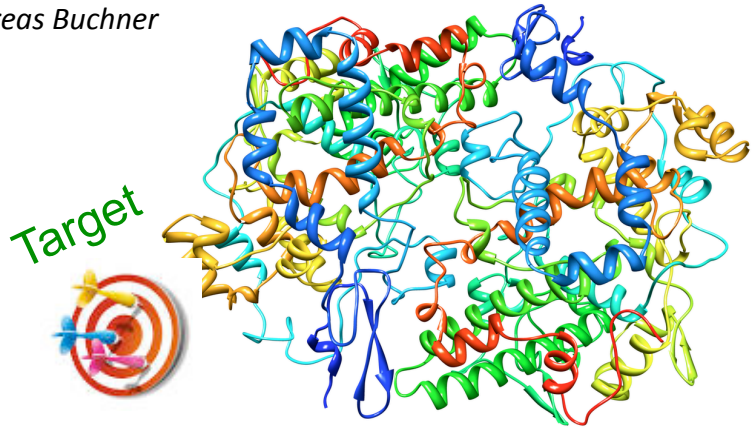
Acetylsalicylic acid

Felix Hoffmann, Bayer
1897

Willow bark extracts

- Pain relief
- Anti-pyretic

Pliny the Elder *50 AD*
Hippocrates *400 BC*



Cyclooxygenases (COX 1 / COX2)

Inhibition of prostaglandin H2 synthesis

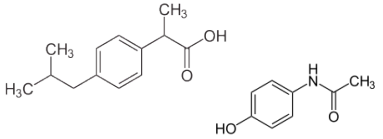
- Analgesic effects
- Antipyretic effects
- Antiinflammatory action
- Antithrombotic effects

describe appr. 1970

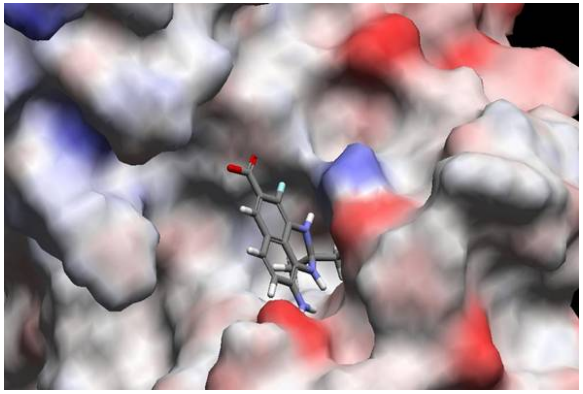
Other non-steroidal anti-inflammatory drugs

Ibuprofen, Paracetamol

developed appr. 1950



Molecular Pharmacology at the FMP



Research at the FMP aims at:

- Interaction of small molecules with cellular targets
- Effects at the cellular and organismic level

Most drug targets are proteins

- *Structure and function of proteins*
- *Modulating protein function*
- *Protein-protein interactions*
- *Protein-Ligand interactions*
- *Small molecules as chemical, diagnostic and therapeutic tools*
- *Biological macromolecules as drug targets*

Finding innovative drugs for novel targets

- Currently 40.000 drugs available
- appr. 400 protein structures as targets
- appr. 10.000 proteins considered drug targets

Aims

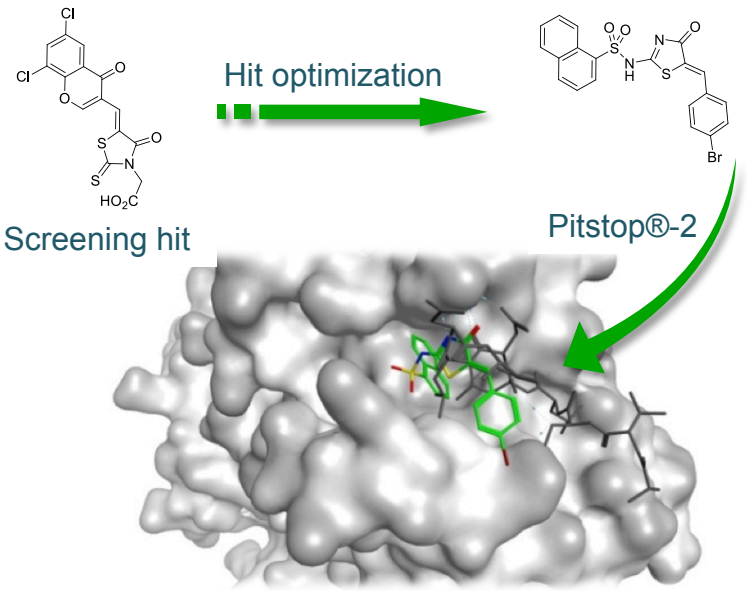
- Identification and characterization of bioactive substances
- Development into lead structures
- Characterization and validation of novel targets

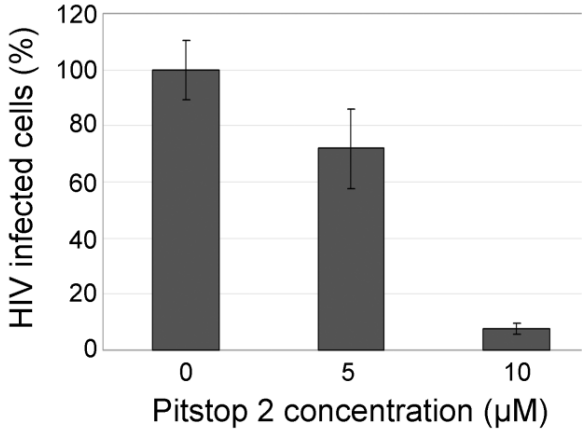
→ **Basic research in the field of molecular pharmacology**

→ **Extending the basis for drug-based therapies**

→ **Research in the run-up of pharmaceutical drug research**

Development of clathrin inhibitors as anti-viral and anti-mitotic agents

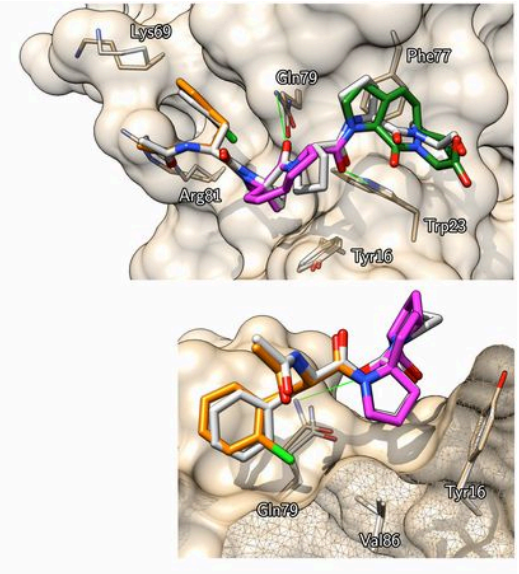




- Pitstop® compounds selectively inhibit clathrin-mediated endocytosis by interfering with clathrin function
- Anti-viral (e.g. HIV, Crimean-Congo hemorrhagic fever virus [CCHFV]) and anti-mitotic activities

von Kleist, L. *et al*. **Cell** 146, 471–484 (2011); Robertson, M. *et al* **Nature Protocols** 9, 1592-606 (2014); Stahlschmdit, W. *et al.* **J Biol Chem** 57, 131-43 (2014); Cai, Y. *et al*. **J Virol** 89, 844-56 (2015)

Selected Scientific Highlights

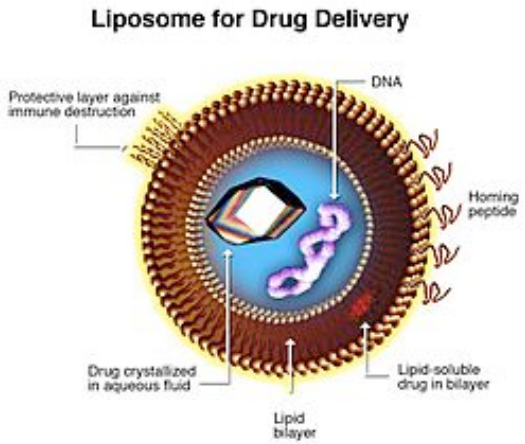


Proteomimetics (ProM), a novel class of bioactive compounds influencing protein-protein interactions, inhibit for example migration of cancer cells. (*Kühne, Oschkinat, ...*)

Opitz et al. (2015) A modular toolkit to inhibit proline-rich motif-mediated protein-protein interactions. Proc. Natl. Acad. Sci. U.S.A. ***112****, 5011-5016*

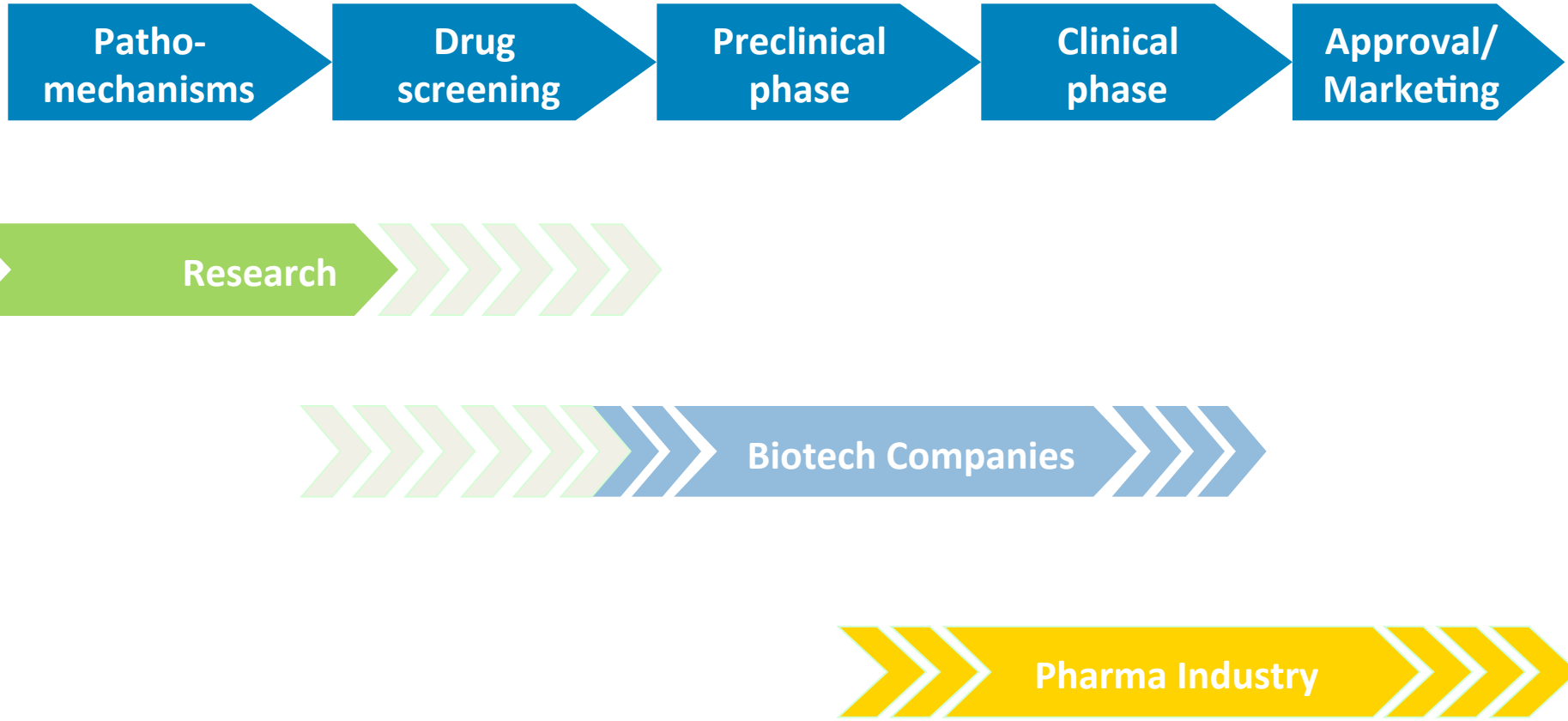
An orphan drug for treatment of ichthyosis, developed at the FMP, is receives the award Leibniz-Drug 2015 (*Dathe*)

Development of transport vesicles harboring biotechnologically generated transglutaminase 1 (TG 1) as therapeutic agent for the treatment of ichthyosis.



Source: Liposome (1999) by Kosi Gramatikoff (Wikimedia Commons)

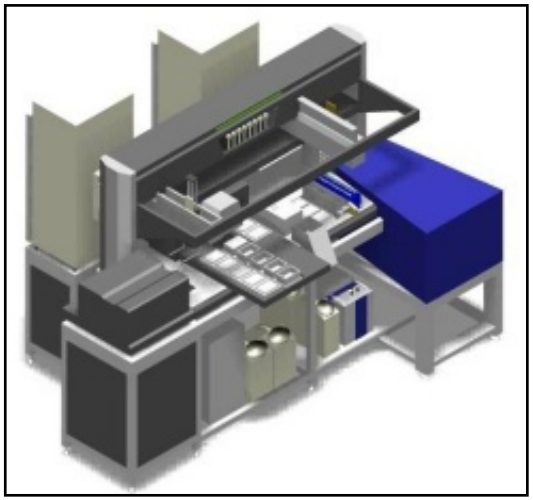
Filling a Gap in Clinical Research



FMP Chemical Biology Platform: Screening Unit, Medicinal Chemistry, and Computational Chemistry

- „Academic“ substance library (novel scaffolds)
- Projects on novel validated targets, assay development
- Chemical tools for the investigation of protein functions, diagnostic substances and drugs
- Open platform for academic partners and SME
- Hit-to-lead optimization

Screening Robot



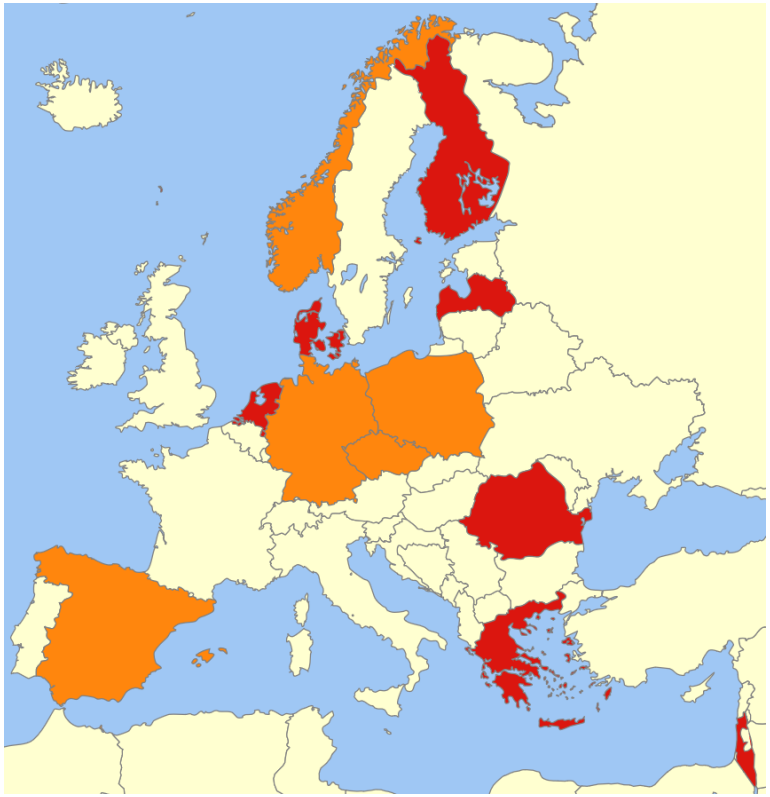
Automatic Microscope

EU-OPENSCREEN

EU-OPENSCREEN

European Infrastructure of Open Screening Platforms for Chemical Biology

- Since 2008 part of the ESFRI-*Roadmap* (*European Strategy Forum on Research Infrastructures*)
- Since 2013 part of the BMBF-Roadmap for Large Research Infrastructures
- at the moment 25 partners from 8 Ländern (Germany: FVB, MDC, HZI, BMBF, WGL, HGF)
- Status February 2017
  - Mid of 2017 implementation of the ERIC
  - Implementation of the national parts of EU-OPENSCREEN
  - FMP develops FMP Partner Site



Gründungsmitglieder 2017
Beitritt geplant für 2018

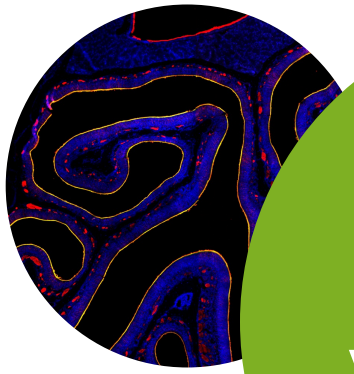
Results of FMP Activities

- Scientific Publications (approx. 100 per year)
- Structured graduate training (FMP Graduate School)
- Teaching of students
- Training of teachers
- Teaching of school children
- Information of the public, public relations
- Technology transfer

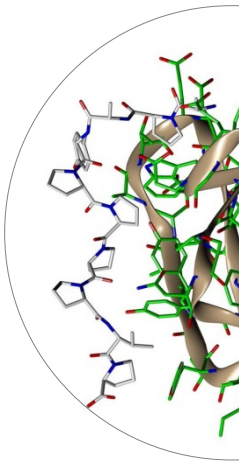
Biannual Research Report

Flyer

ChemLab
Teaching Materials



Thank you for your attention!



FMP

Leibniz Association

FVB Forschungsverbund Berlin e.V.