NATIONALES CENTRUM FÜR TUMORERKRANKUNGEN

Christof von Kalle

Smart Data in Oncology

Hasso Plattner Institut Potsdam

1st June 2017

dkfz.
50 Jahre – Forschen für ein Leben ohne Krebs

NCT

UniversitätsKlinikum Heidelberg

Oncology – A Leading Topic in Heidelberg

EXCELLENCE in

- Clinical Translation and Basic Research
- Clinical and Translational Cancer Programs
- Interdisciplinary Patient Care

NCT 1.0 – Principles & Practice

UniversitätsKlinikum Heidelberg

NCT

dkfz.

All
Clinical Departments with Oncological Activities

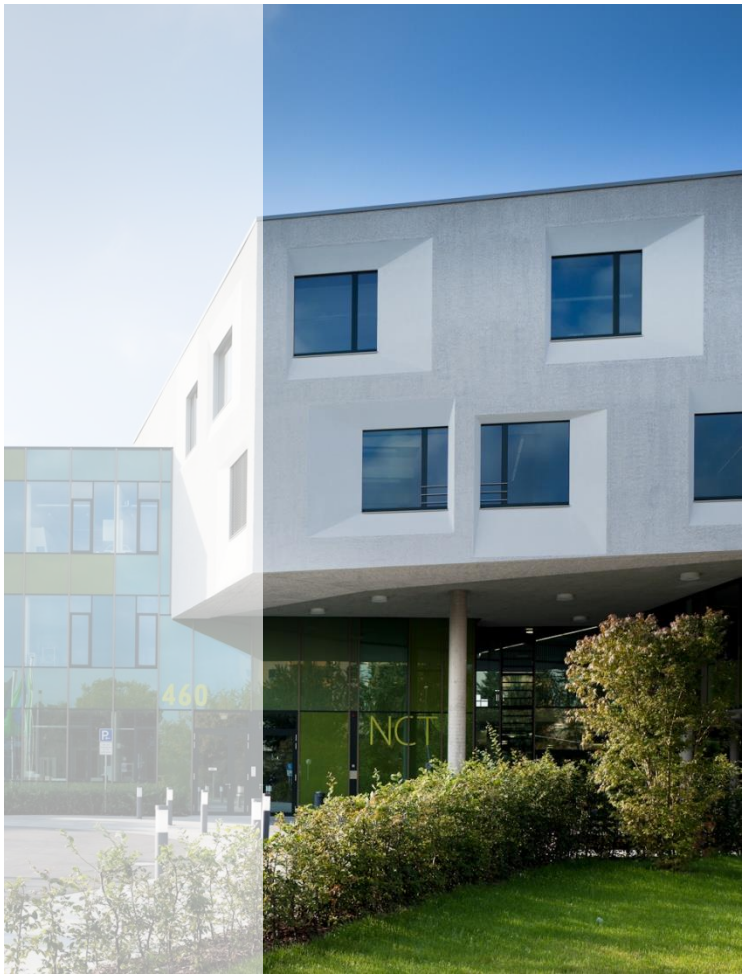
EVERY PATIENT

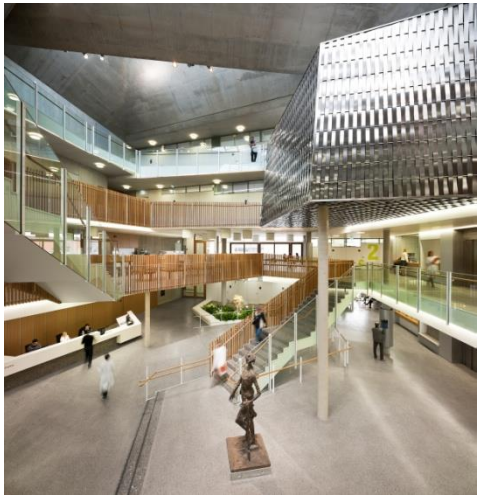
All
Translational Cancer Research Groups

EVERY TRIAL

Creating Interdisciplinarity

NCT 2.0 – New Building & Structures





IDENTITY & VISIBILITY

NCT 3.0 – The Next Level

DELIVER

Precision Oncology

EXCEL

Clinical and Translational Cancer Programs

GROW

Building

Partners

SCIENTIFIC & CLINICAL EXCELLENCE

NCT 3.0 - Strategic Aims

- Position NCT as a Leading Comprehensive Cancer Center in Europe
- Expand NCT Precision Oncology Program
- Deliver at the Point of Care
  Translation – Personalization – Precision
- Expand Internationally Recognized Clincial Cancer Programs & Profile Areas
- Employ Novel, Innovative Treatment Concepts

NCT Dresden

FUNDING

New Research Building
CCC Building funded by DKH

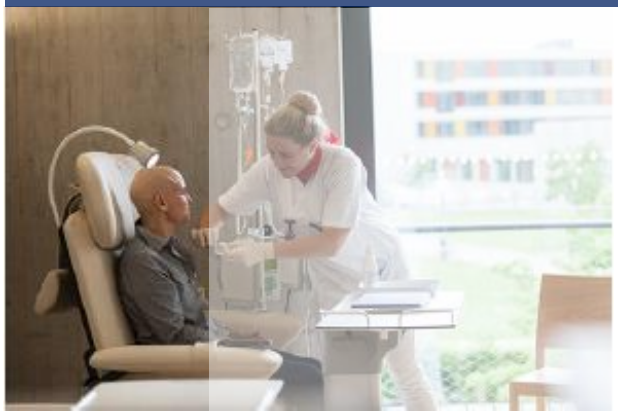
PROFILE AREAS / RECRUITMENTS

- Innovative Medical Oncology
- Translational Research
- Radioimaging
- Theragnostics
- Link-up DKFZ HIPO, NCT POP & NCT MASTER
- Immunotherapy
- Systems Biology
- Multidisciplinary Profile Areas

NCT 3.0 - Profile Areas to be Expanded

DELIVER

- NCT Precision Oncology
- Novel, Innovative Treatment Concepts
- Clinical Trials & Biobanking Infrastructure/Expertise

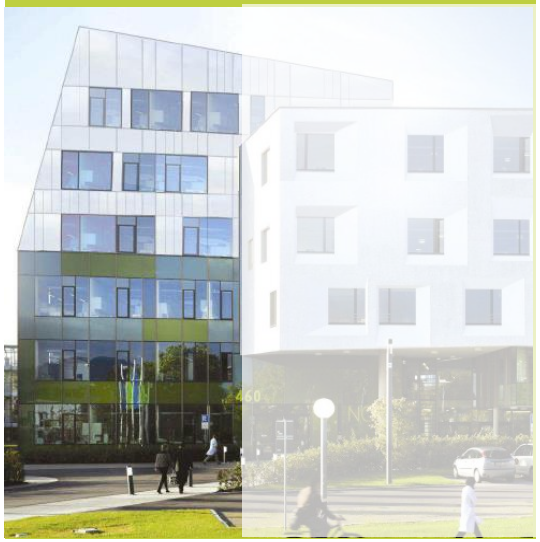


EXCEL

- Molecular Stratification
- Immunotherapy
- Profile Areas - Neurooncology Pancreatic Cancer, Radiooncology, Lung Cancer, Prostate Cancer
- NCT OncoCheck-Programm
- Innovative Oncological Imaging
- Molecular Tumor Pathology
- Biomarker Platform
- NCT DataThereHouse & Cancer Registry
- New Programs – CardiOncology, Palliative Oncology, Hematology
- NCT Basic Research Pipeline

GROW

- Partnerships
- Funding Programs
- Recruitments
- Talents
- Facilities



NCT Precision Oncology Program

STRATIFIED ONCOLOGY

CLINICAL EVALUATION & TRIALS

DATA INTEGRATION

TARGET EXPLOITATION

TARGET CHARACTERIZATION

TARGET IDENTIFICATION

NCT DataThereHouse

Organized in SAP HANA

NCT OMICS

PATIENT ADMISSION – DOCUMENTATION - BANKING

NCT DataThereHouse

Display Data from Various Sources for a Comprehensive Overview of Information Relevant for Personalized Treatment

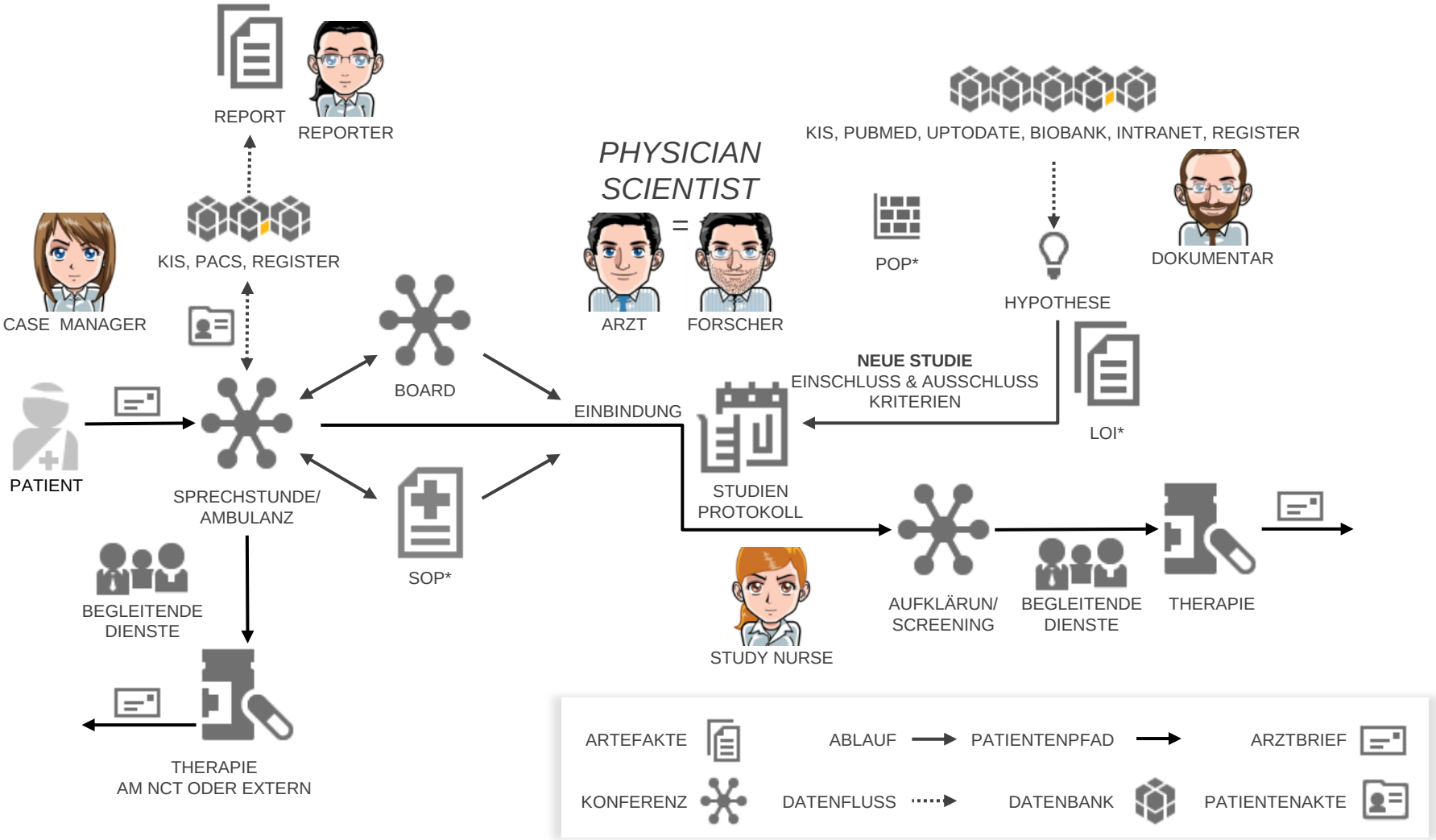
- SEQUENCING DATA
- ARRAY DATA
- CLINICAL PATHWAYS
- UNSTRUCTURED DATA
- DOCTOR'S LETTER
- STRUCTURED DATA

INDIVIDUALIZED TREATMENT PLAN

- PHYSICIAN
- SCIENTIST
- TUMOR BOARD
- CASE MANAGER
- STUDY NURSE
- DOCUMENTALIST

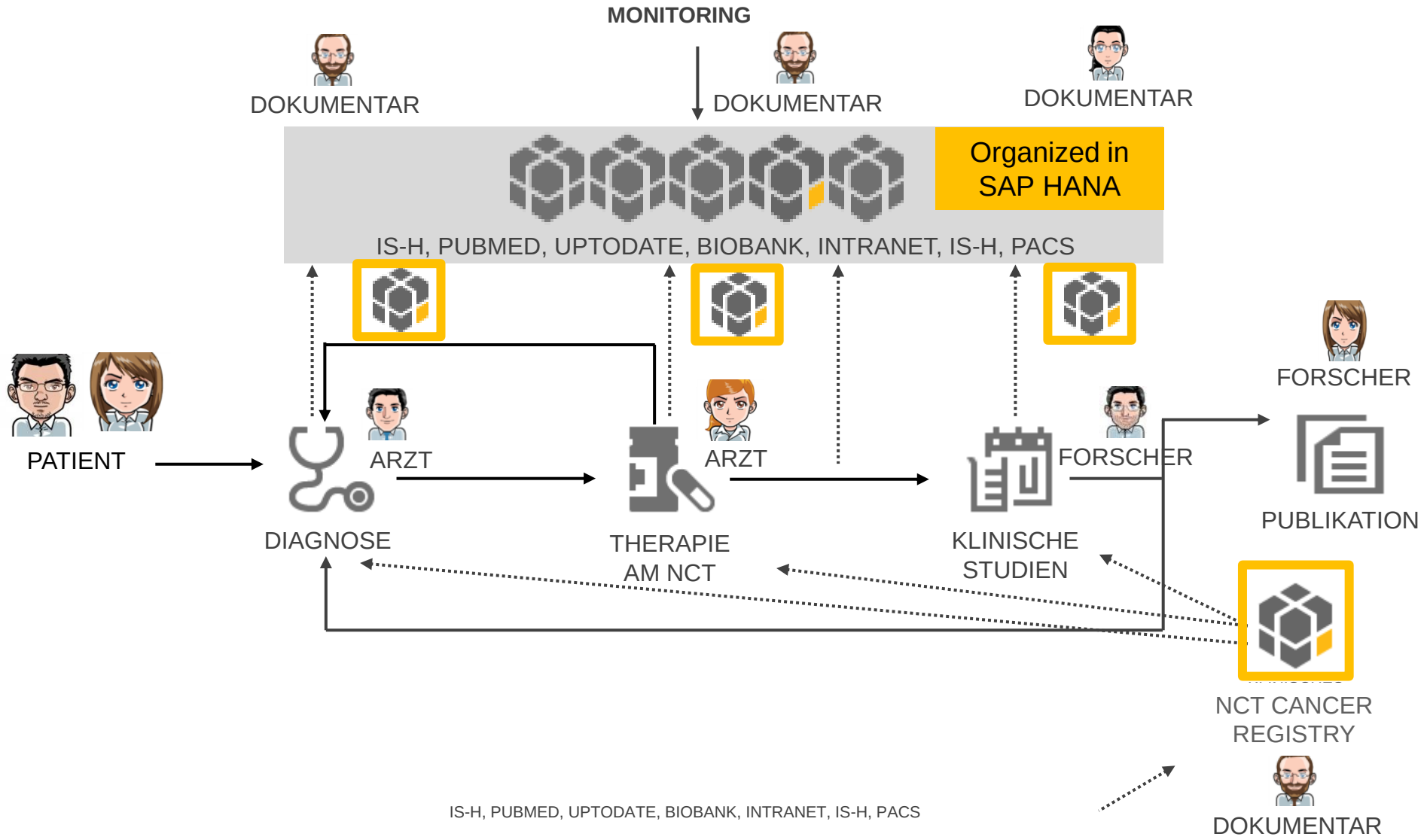
NCT DataThereHouse

Current Scenario

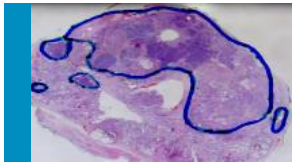


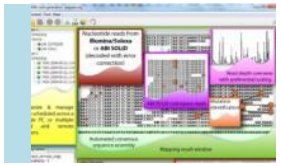
NCT DataThereHouse

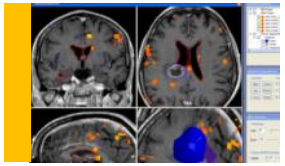
NCT Clinical Development Strategy



NCT MASTER Workflow







PATIENT ADMISSION
ENROLLMENT
CLINICAL DATA

DIAGNOSIS &
SAMPLING

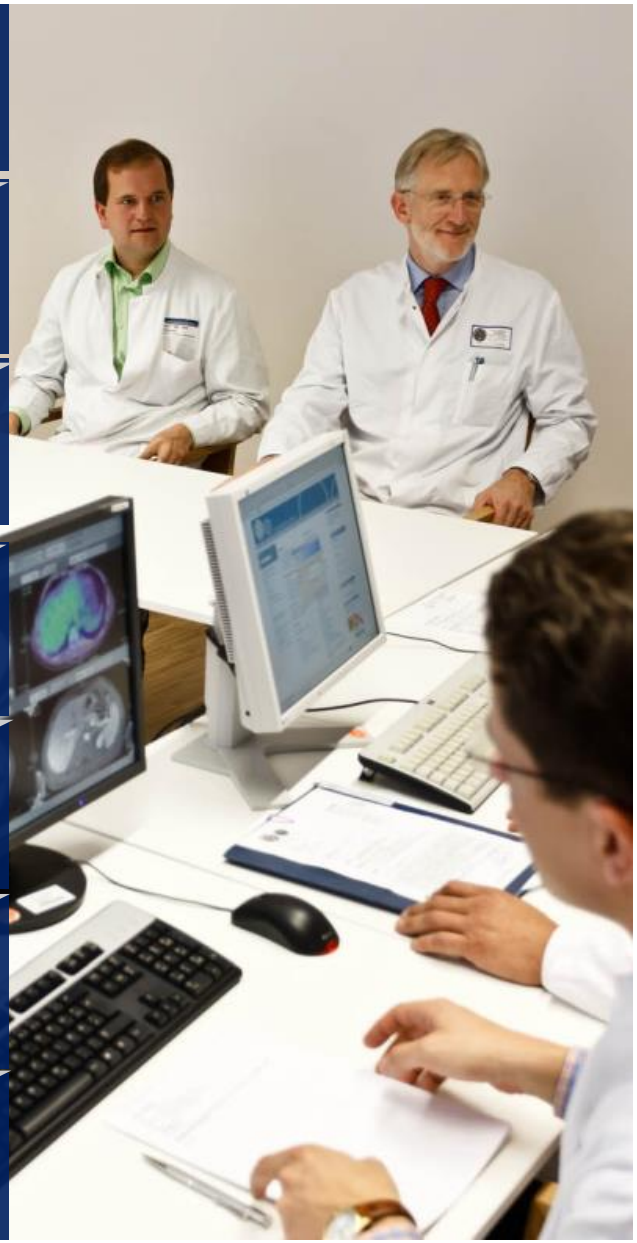
NCT OMICS

BIOINFORMATICS
CLINICAL REPORT

MOLECULAR
TUMOR BOARD

INDIVIDUALIZED
THERAPY &
TRIALS

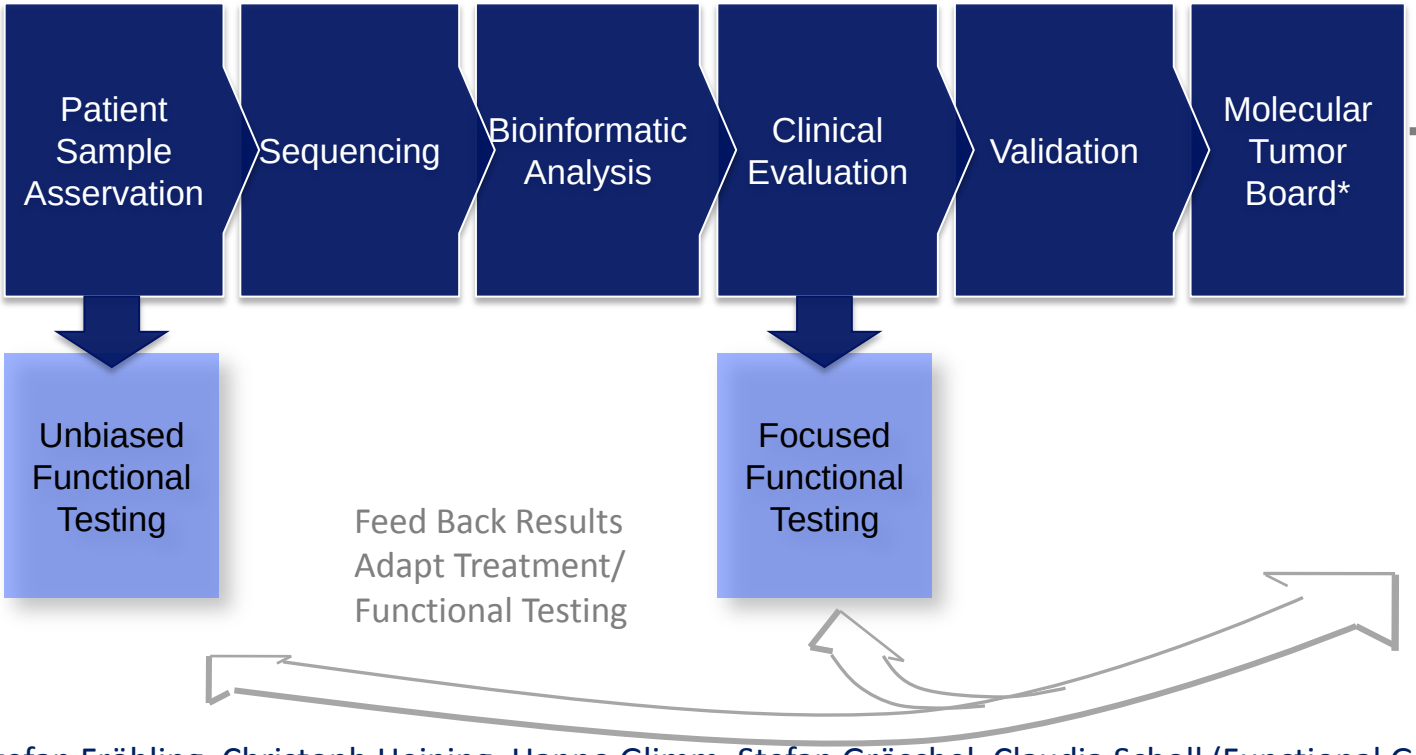
RESPONSE
RESISTANCE
PREVENTION



NCT DataThereHouse (SAP HANA)

NCT MASTER – Registry & Interventional Trial

Hanno Glimm **Stefan Fröhling**

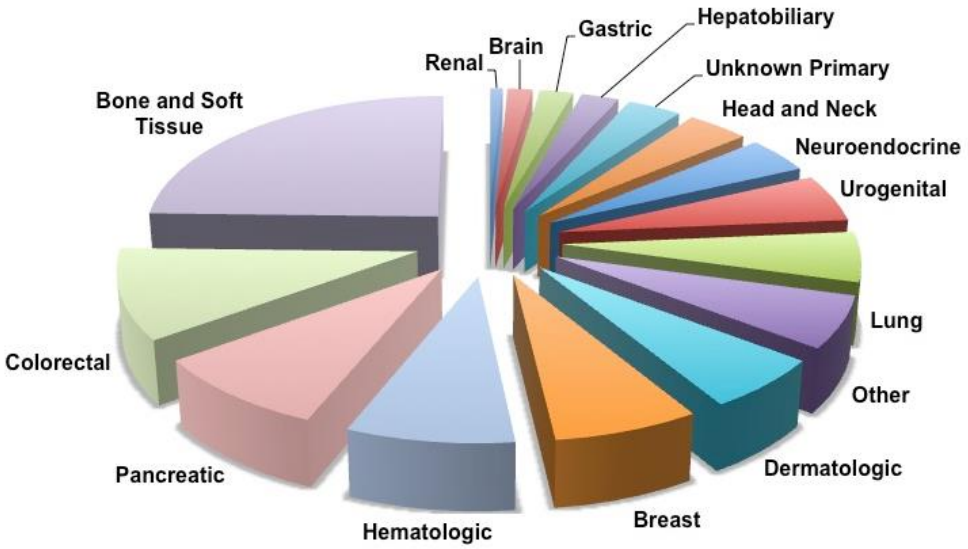


Stefan Fröhling, Christoph Heining, Hanno Glimm, Stefan Gröschel, Claudia Scholl (Functional Genomics)
DKTK – LMU München, Frankfurt, Dresden, Essen/Düsseldorf, Freiburg, Berlin

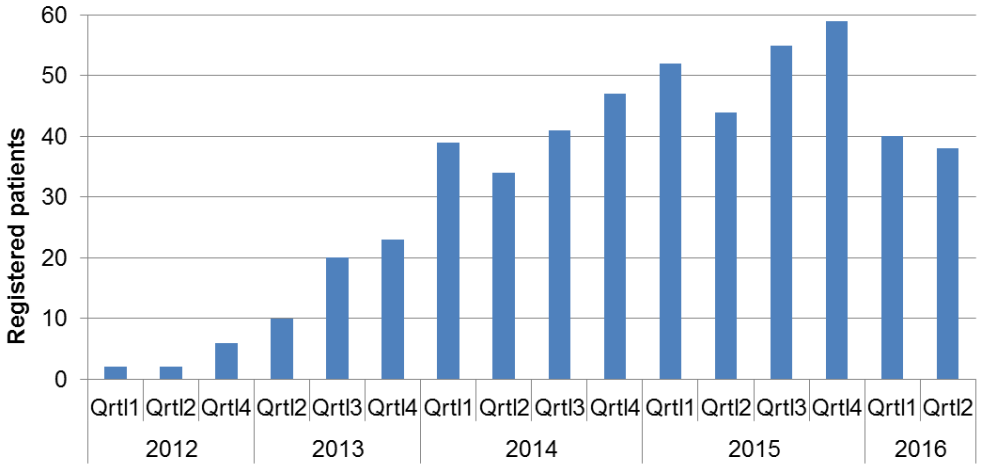
NCT MASTER – Registry & Interventional Trial

CURRENT STATUS

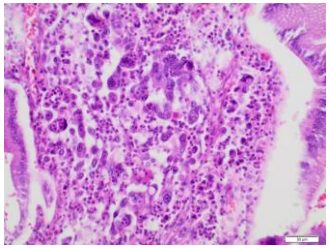
Entities



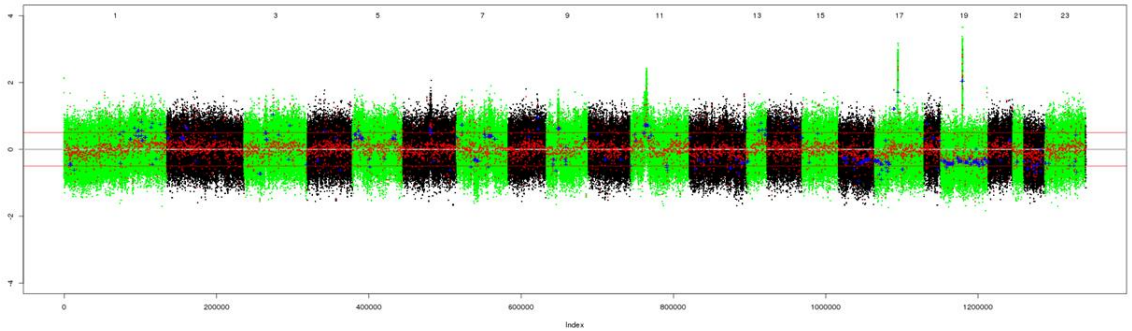
Recruitment (May 2016)

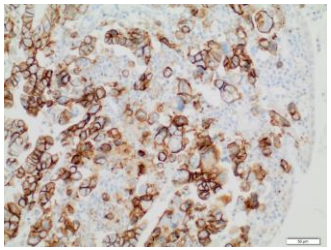


NCT MASTER – Case Report I)



H&E





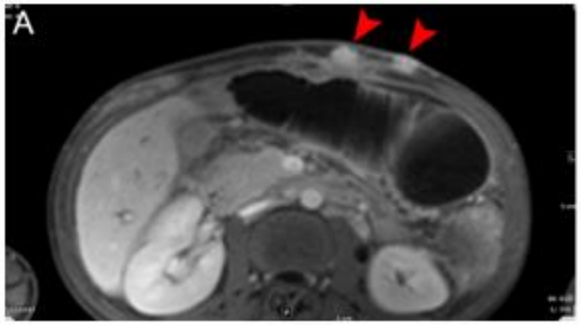
ERBB2

Metastatic gallbladder carcinoma

- **Peritoneal and cutaneous metastasis during adjuvant chemotherapy with oxaliplatin/gemcitabine**

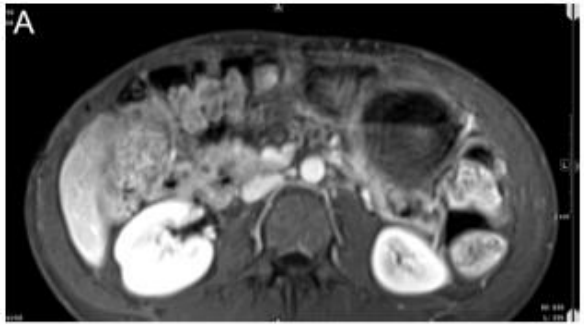
Amplification of chromosome 17q12, including *ERBB2*

- **Outlier *ERBB2* mRNA expression**
- **ERBB2 protein expression by immunohistochemistry (3+ according to ASCO guidelines)**



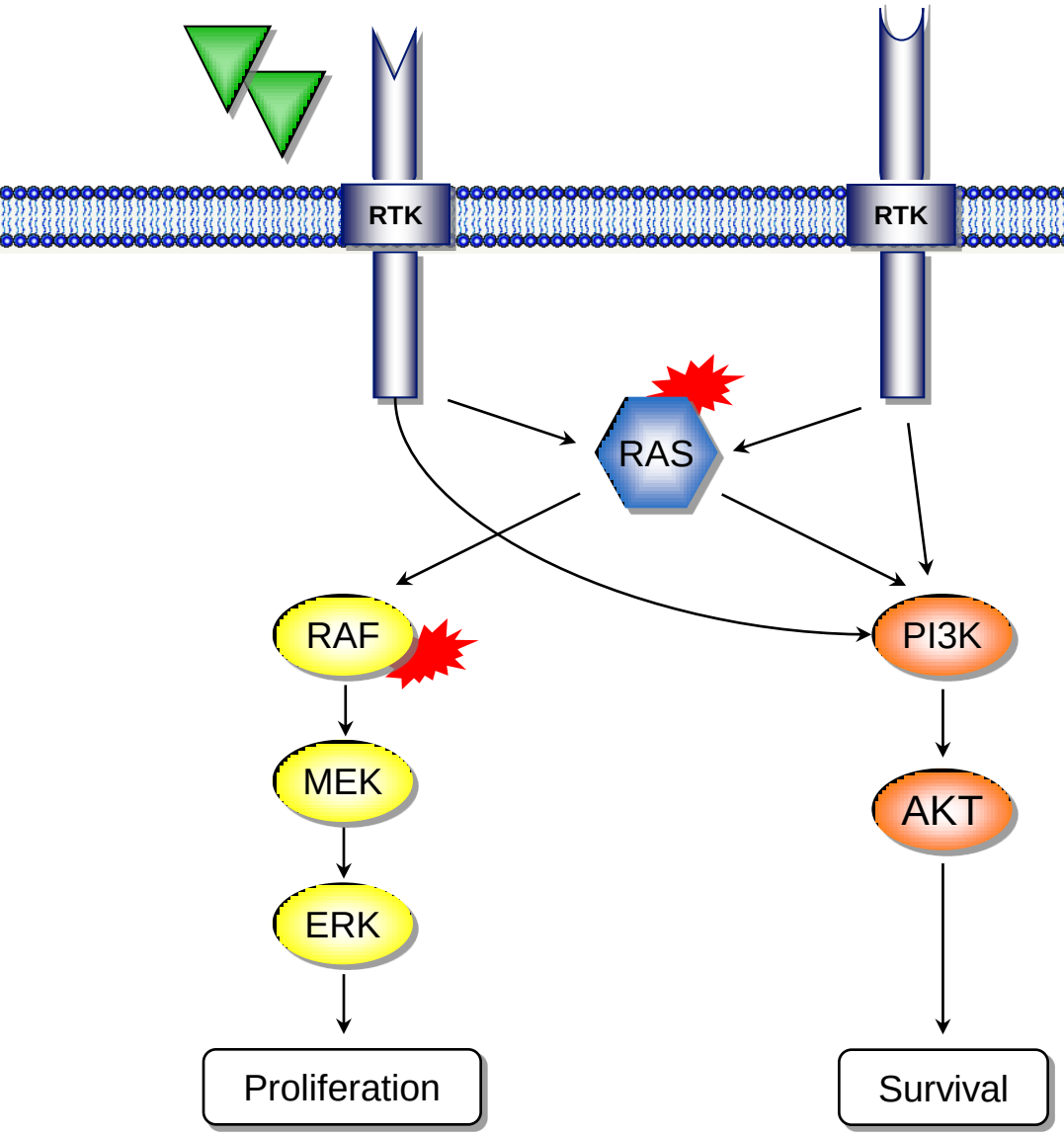
Dual ERBB2 blockade: trastuzumab/pertuzumab

Complete remission for >12 months



Czink et al. Z Gastroenterol 2016

NCT MASTER – Case Report II)



Rationale for Experimental Targeted Treatment

35-year-old patient with **bladder tumor**, bilateral **pulmonary masses**, enlarged hilar **lymph nodes**, and disseminated **bone lesions**
- Histology inconclusive
- Refractory to cyclophosphamide, doxorubicin, vincristine, and prednisone

Co-existence of **HRAS p.Q61R** and **BRAF p.F595L** within single clone

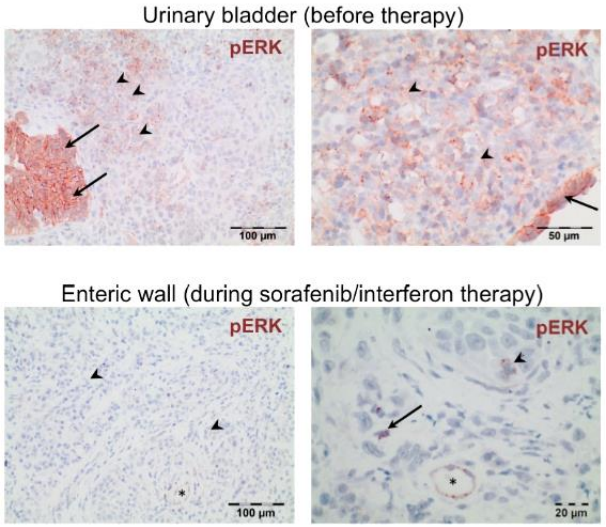
Mutational spectrum highly suggestive of **non-Langerhans histiocytosis**

Rationale for MAPK pathway blockade using **sorafenib** or **MEK inhibitor**

No rationale for vemurafenib or dabrafenib due to **risk of paradoxical MEK/ERK activation**

Kordes et al. Leukemia 2016

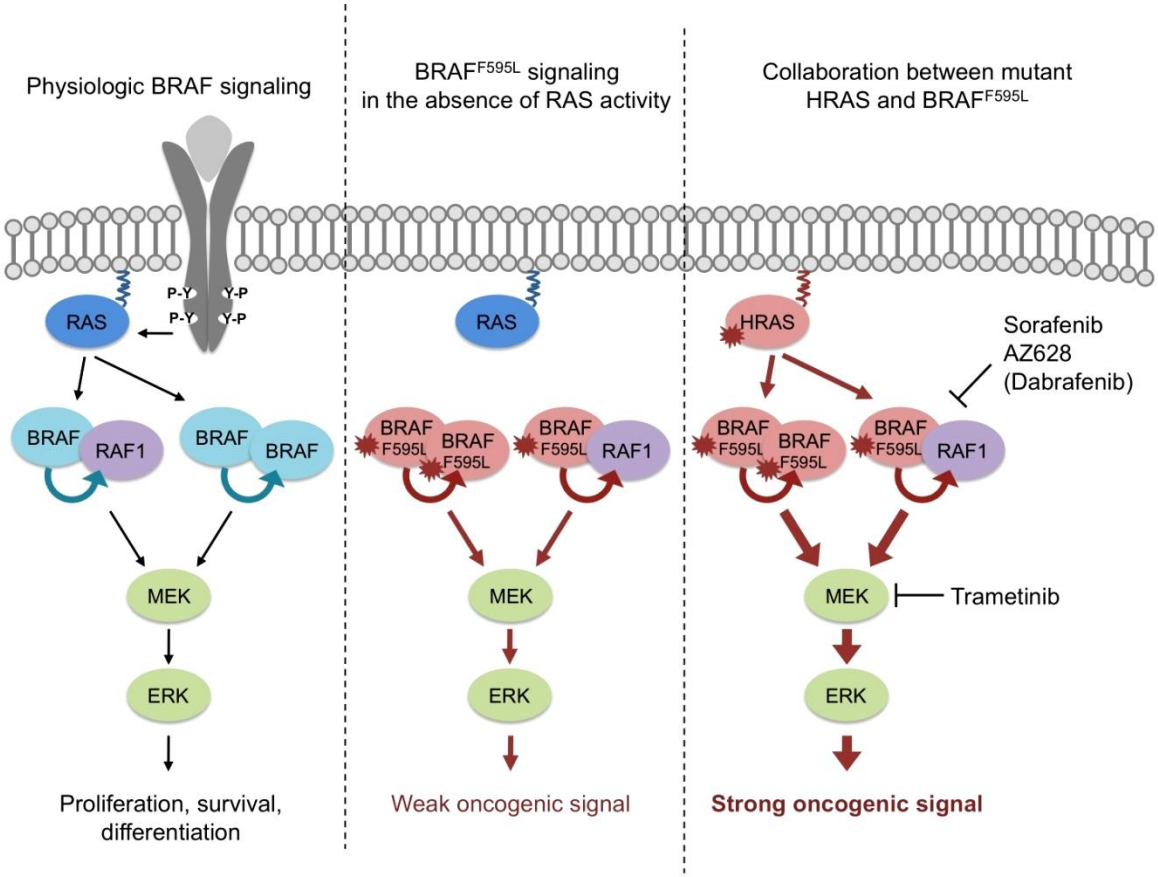
NCT MASTER – Case Report II)



Loss of phosphorylated ERK expression in tumor cells after 3 weeks of **sorafenib** and interferon alpha treatment

Frequent **coexistence of intermediate-activity BRAF mutations** and **oncogenic RAS** in various cancers
Wan et al. Cell 2004
COSMIC database

Rationale for Experimental Targeted Treatment

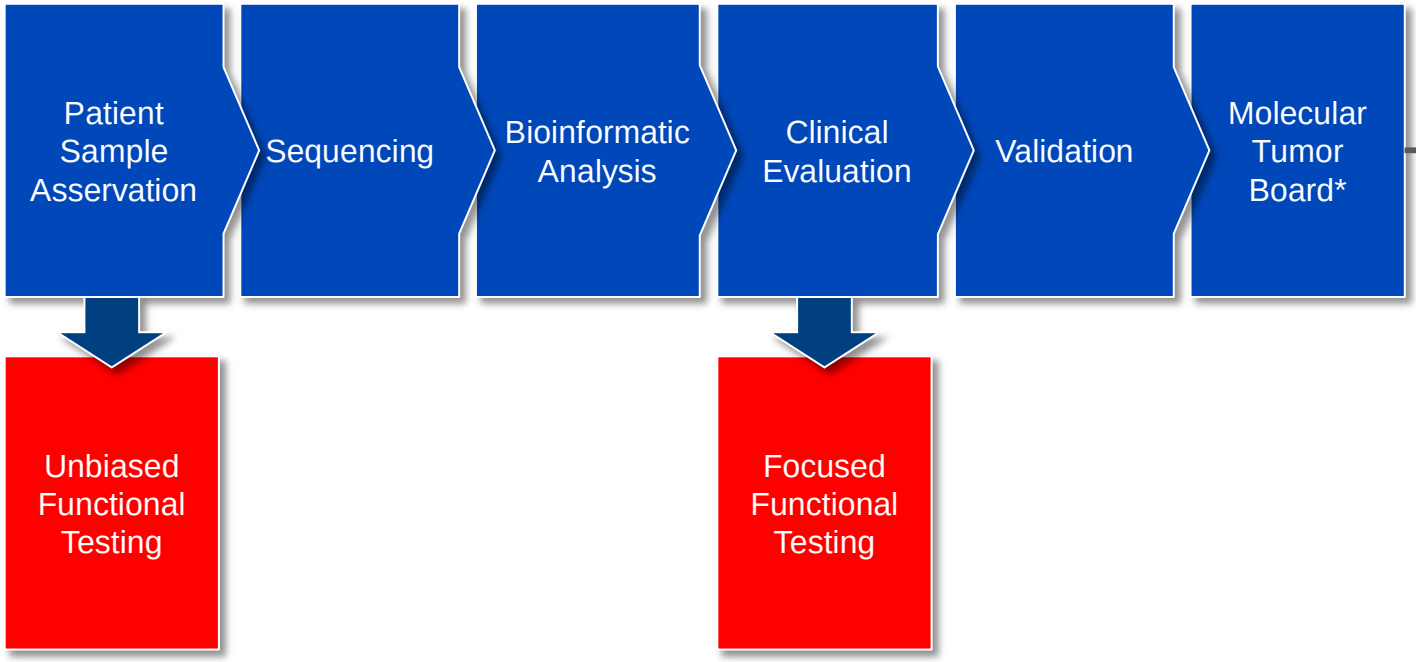


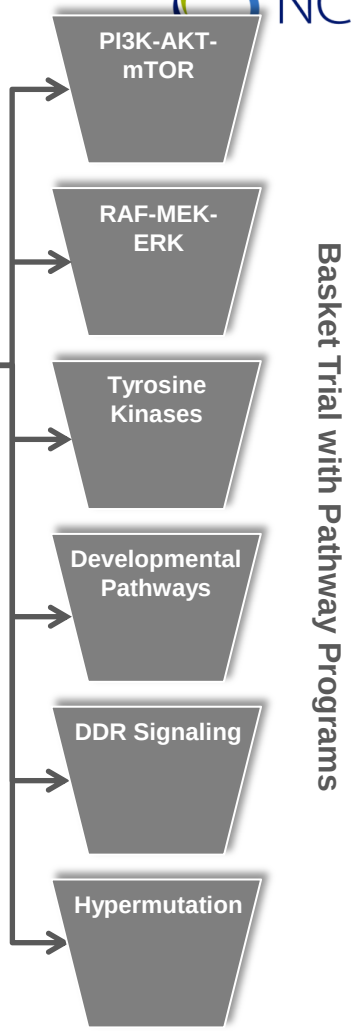
Cooperative activity of **BRAF p.F595L** and **HRAS p.Q61R** in aggressive histiocytic sarcoma

Kordes et al. Leukemia 2016

DKTK MASTER

Critical Next Steps



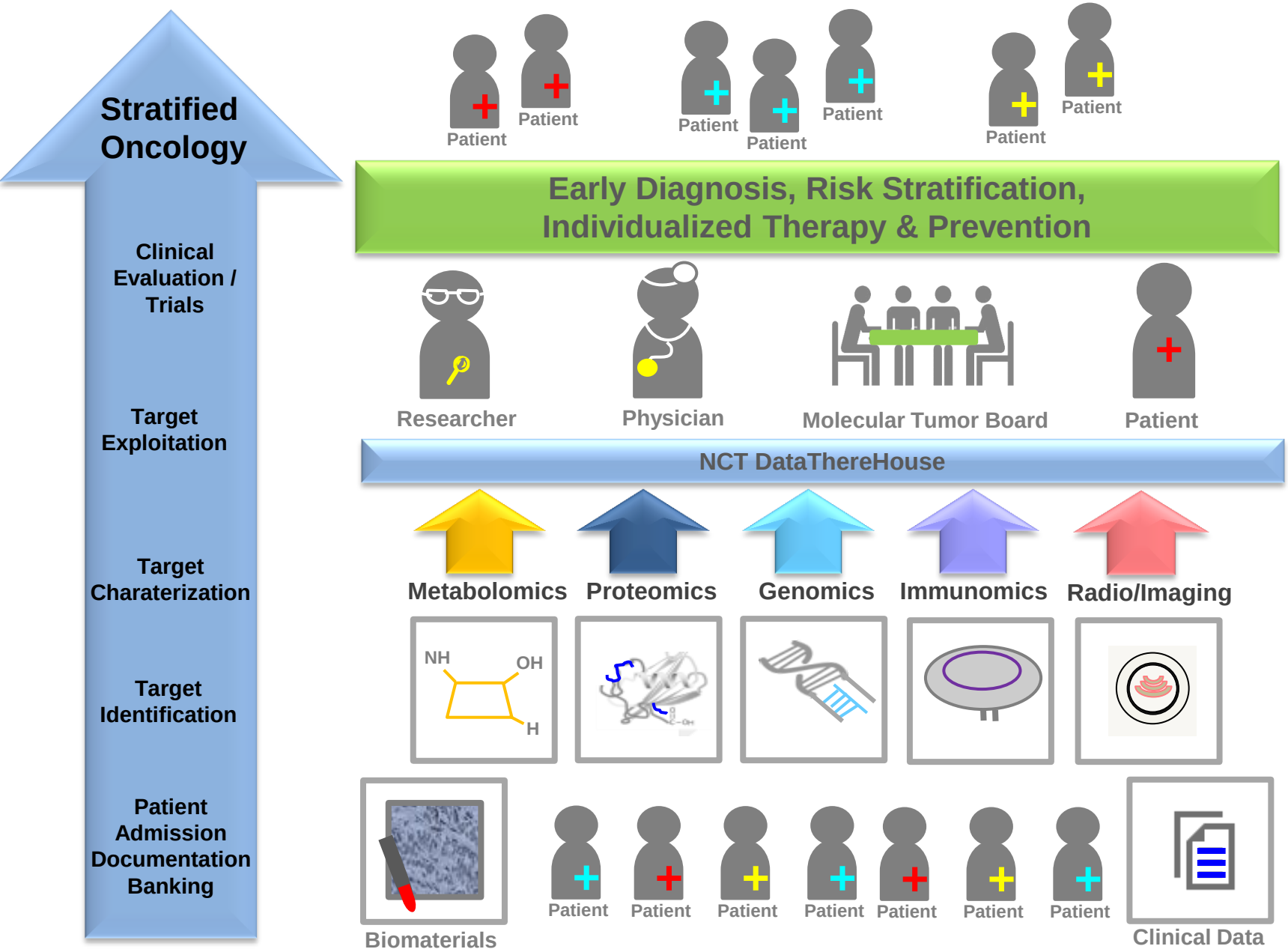


Development of a common path for clinical cancer genome sequencing and molecular stratification within DKTK

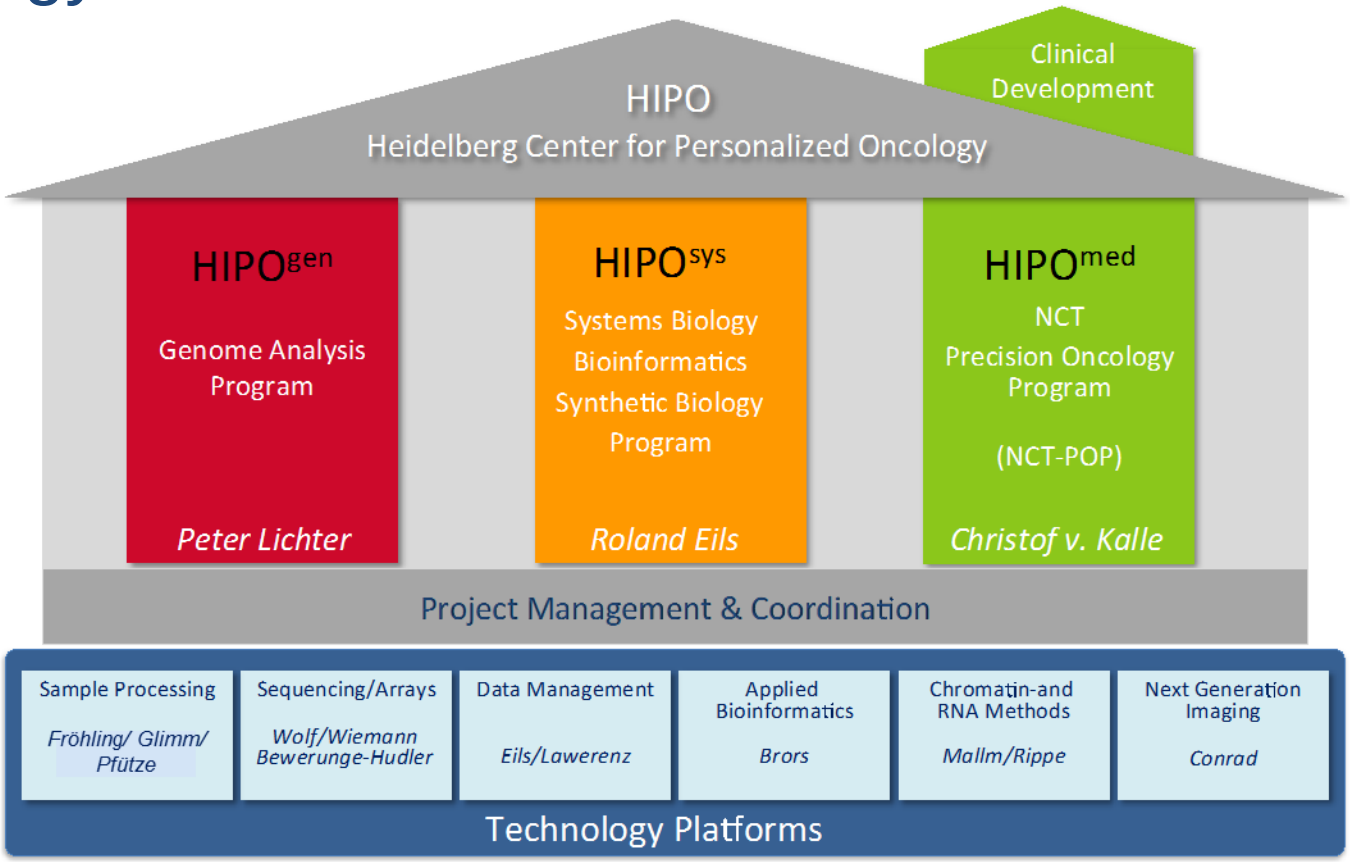
Further development of strategies for clinical translation

Refinement and expansion of strategies for functional annotation

NCT Precision Oncology Program



Heidelberg Center for Personalized Oncology



National High Throughput Sequencing Core Unit

Illumina
xten Cluster

2009 2010 2011 2012 2015

ICGC Sequencing

NCT Precision Oncology Program

ICGC

International Cancer Genome Consortium

INFORM

hipo

Deutsches Konsortium für Translationale Krebsforschung

Applied Bioinformatics

Benedikt Brors

PRIMARY ANALYSIS

SECONDARY ANALYSIS

TERTIARY ANALYSIS: „INTERPRETATION“

OneTouchPipeline

RNA sequences

DNA sequences

fastq QC

alignment

duplicates

lane merging

calculate coverage

genotype matching

Pathogen integration

Ploidy prediction

INDELs

SNVs

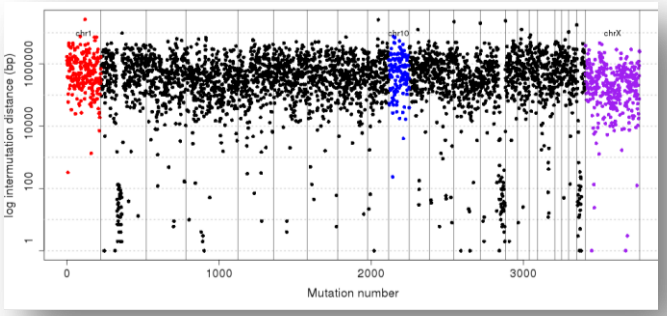
Copy number variants

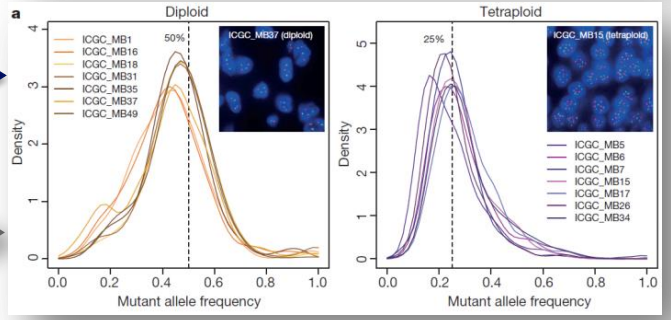
Structural Variants

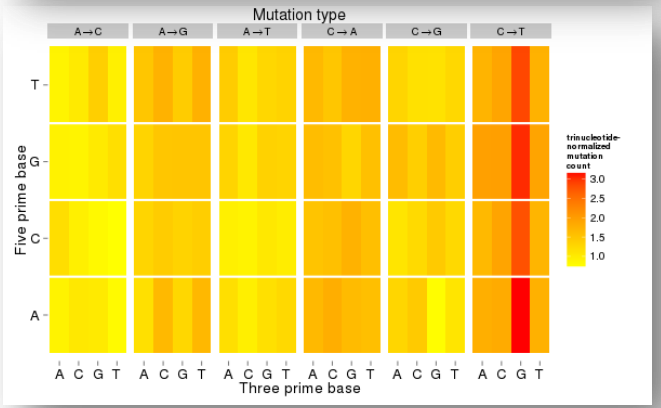
Alternative Splicing

Mutation in RNAseq?

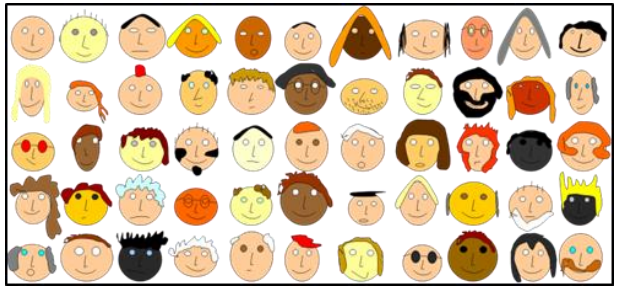
Mutation annotation







INFORM = INdividualized therapy FOr Relapsed Malignancies in childhood



Angelika Eggert

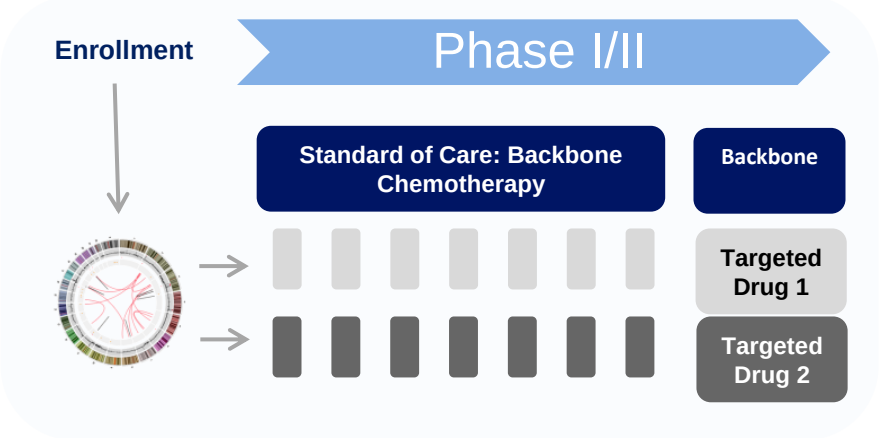
Olaf Witt

Peter Lichter

Stefan Pfister

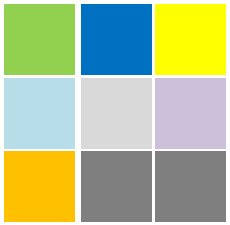
Feasibility-Registry Study (Year 1+2)	
ALL	AML
HGG (incl. DIPG)	Medullo/Ependym.
Ewing Sarcoma	Neuroblastoma
NHL	Osteosarcoma
Rhabdomyosarcoma	Rhabdoid Tumors

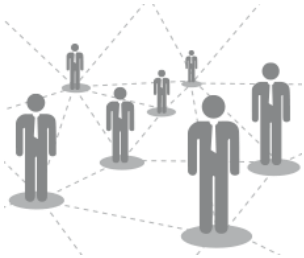
Clinical Trial (Year 3-5)



Big Data in Oncology for personalized medicine…

- needs to RETHINK the old & the new
- needs SMART Data
- is a TEAM Effort





NCT Partnerships

Academic Collaboration

iMed HELMHOLTZ ASSOCIATION

EMBL

DKFZ-ZMBH ALLIANCE

Joint Industry-Academia Collaboration

Roche

BAYER

SAP

Cancer Core Europe Consortium Centers

dkfz.

NCT

GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS

NKI-AVL The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital

Karolinska Institutet

VHIO

NATIONAL CENTER FOR TUMOR DISEASES

NCT HEIDELBERG

THANK YOU

dkfz.

NCT

UniversitätsKlinikum Heidelberg

50 Jahre – Forschen für ein Leben ohne Krebs