# Virtual Tumor Boards – challenges and opportunities

Christian Fegeler

IV Jornada de Oncología Médica , Puerto Varas, 23.08.2018

PAGEL
Partnerships for the Health Sector in Developing Countries

DAAD Research in Germany Land of Ideas

chip

SCOM
SOCIEDAD CHILENA DE ONCOLOGÍA MÉDICA

Ministerio de Salud
Gobierno de Chile

CIMT CENTRO DE INFORMATICA MEDICA Y TELEMEDICINA

UNIVERSIDAD DE CHILE

UNIVERSIDAD DE LA REPÚBLICA URUGUAY

HOCHSCHULE HEILBRONN

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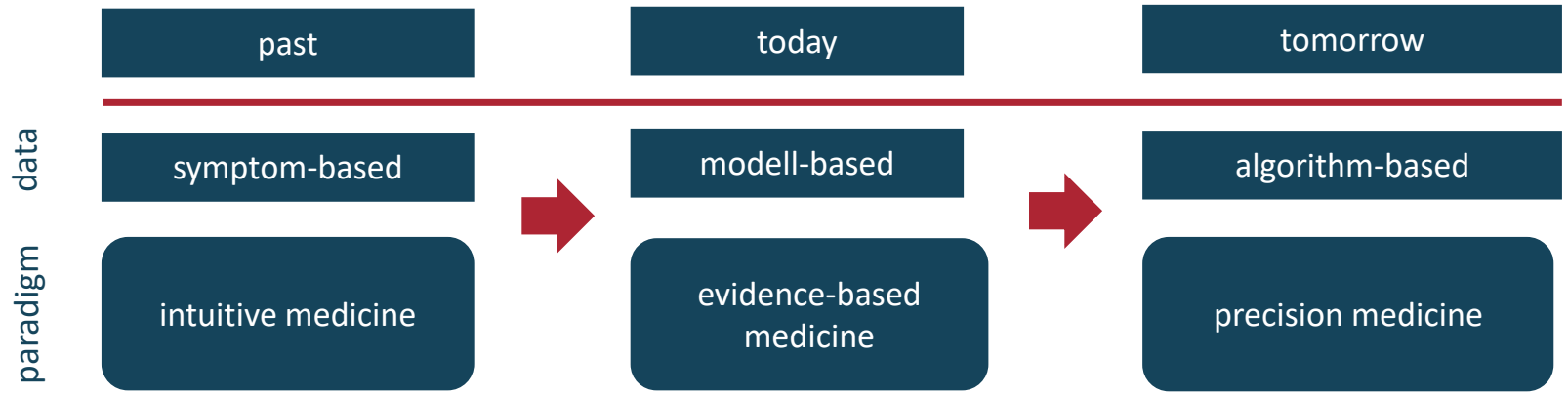
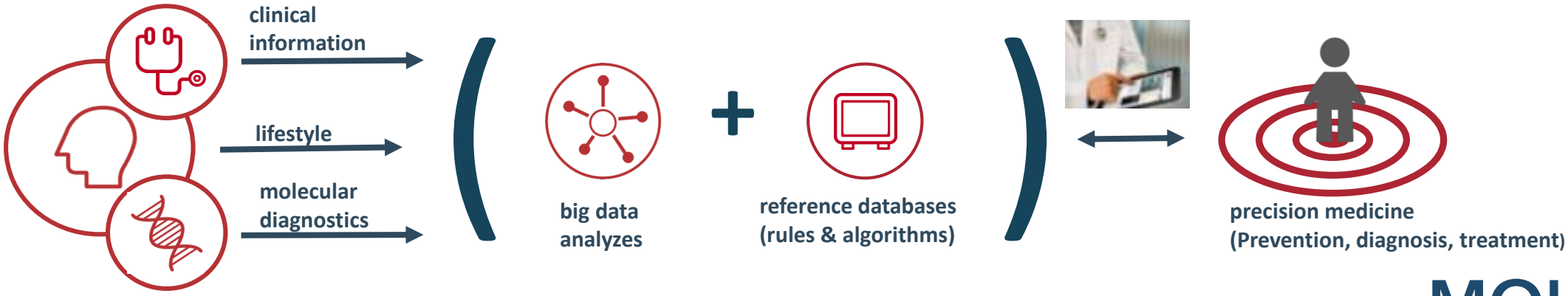
# Paradigm shift to precision medicine




source vgl.: Wilkens 2016

**application of rules, algorithms and reference databases enable traceable clinical decision-making aids and precise and efficient care**

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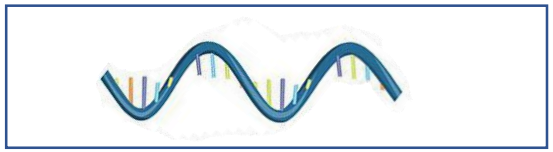
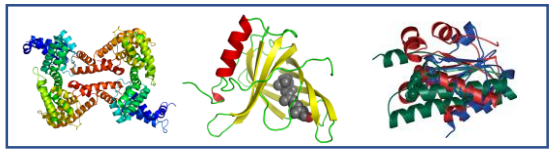
# The Scientific Challenge: molecular revolution in medicine is just beginning

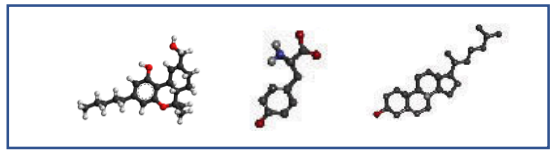
Genomics
≈ 25.000 Gene



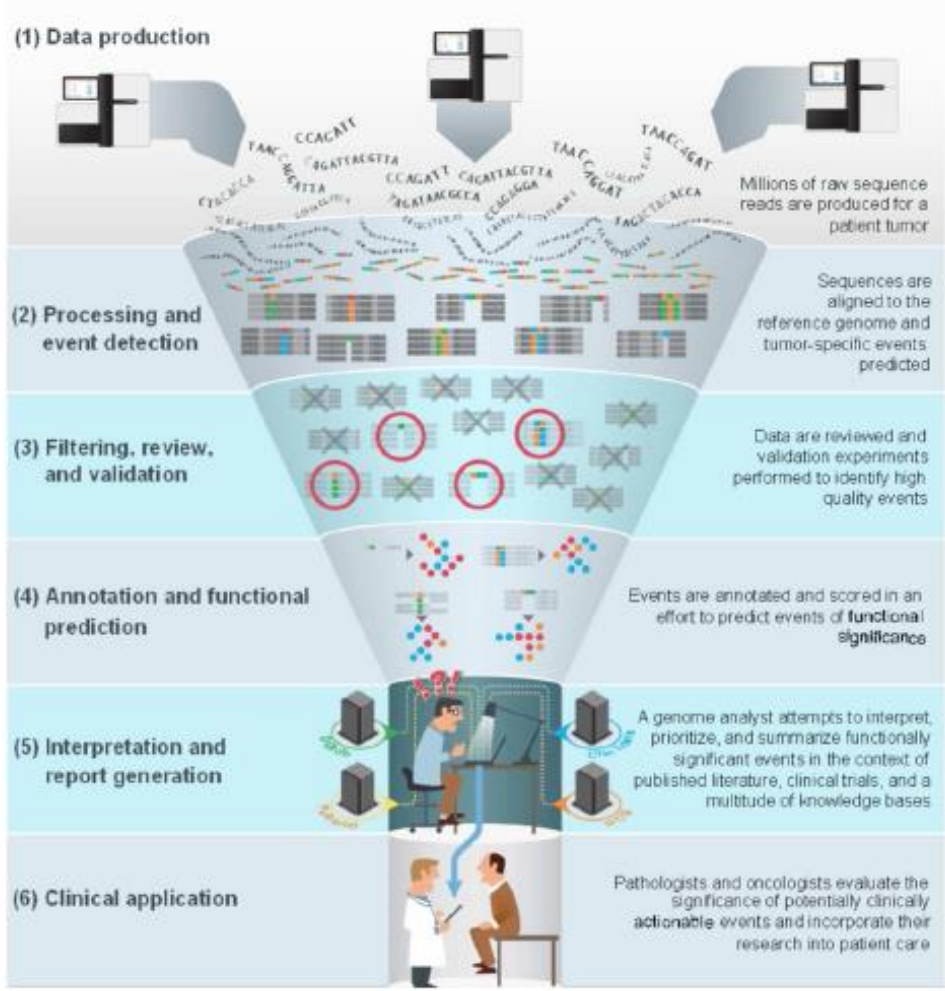
Transcriptomics
≈ 100.000 Transkripte



Proteomics
≈ 1,000.000 Proteine



Metabolomics
≈ 3.000 Metaboliten




Good *et al. Genome Biology* 2014, 15:438

# data + context = information

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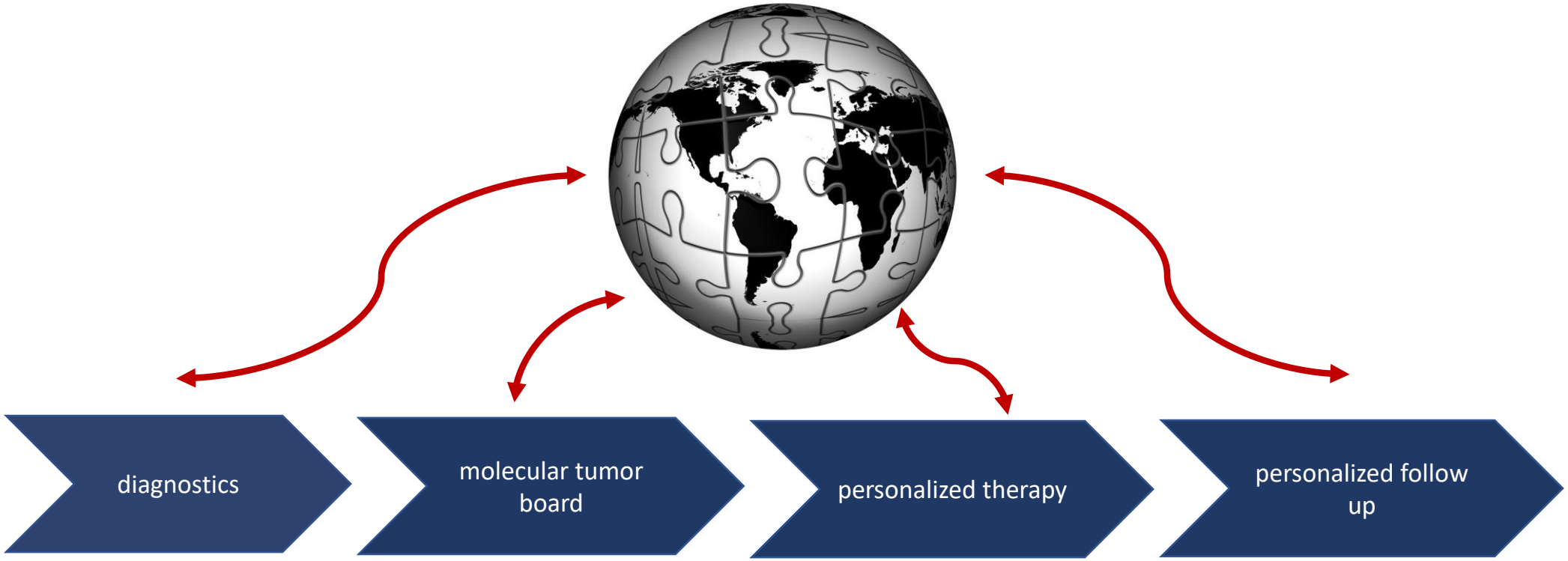
# The medical challenge:

## Make globally distributed knowledge …




… available for local patient care

# Challenges and Opportunities

- Paradigm shift in knowledge management
- Digitalisation
- Data and information quality
- Individualisation ("n of 1 cohort")
- Big Data

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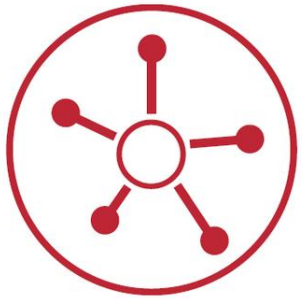
# Challenges to Opportunities

From individuality…

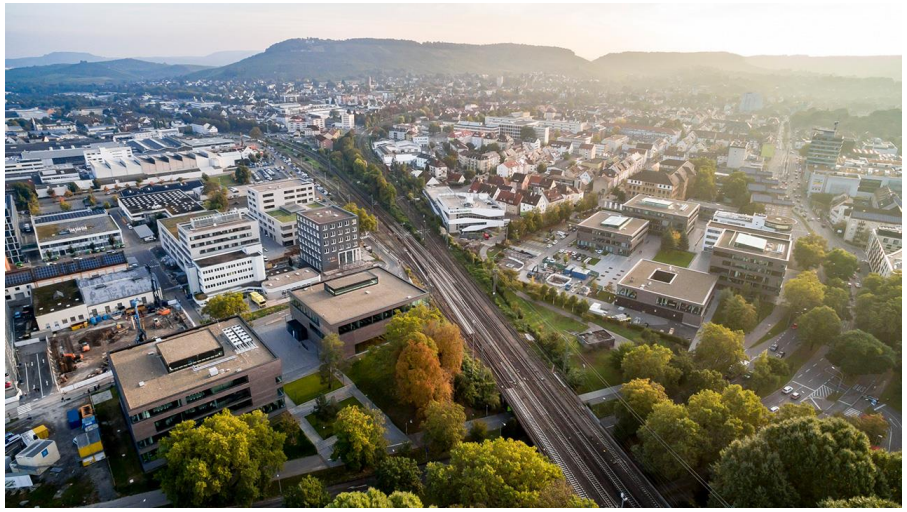


To Knowledge network

…and individualized therapy

# MOLIT Institute for Personalized Medicine

- founded in 2016
- Non-Profit-Organisation
- located in Heilbronn
- supported by Dieter Schwarz Foundation
- 12 own staff
- Applied science cluster and translation



TUMORZENTRUM
CANCER CENTER | heilbronn-franken

HOCHSCHULE HEILBRONN

SLK Kliniken

AACR American Association for Cancer Research
ANNUAL MEETING 2017 WASHINGTON, DC
Abstract Number CT074

# Non-comparative, Open-label, Multiple Cohort, Phase 1/2 Study to Evaluate Nivolumab in Patients With Virus-associated Tumors (CheckMate 358): Efficacy and Safety in Merkel Cell Carcinoma

Suzanne L. Topalian,[1] Shailender Bhatia,[2] Antoine Hollebecque,[3] Ahmad Awada,[4] Jan Paul De Boer,[5] Ragini R. Kudchadkar,[6] Anthony Goncalves,[7] Jean-Pierre Delord,[8] Uwe M. Martens,[9] Jose Maria Lopez Picazo,[10] Ana Oaknin,[11] William C. Spanos,[12] Raid Aljumaily,[13] William H. Sharfman,[1] Shangbang Rao,[14] Ibrahima Soumaoro,[14] Z. Alexander Cao,[14] Paul Nghiem,[15] Dirk Schadendorf[16]

[1]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [2]Univeristy of Washington, Seattle, WA, USA; [3]Gustave Roussy Cancer Institute, Villejuif, France; [4]Jules Bordet Institute, Brussels, Belgium; [5]Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [6]Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA, USA; [7]Institut Paoli-Calmettes, Marseille, France; [8]University Department of Oncology, Toulouse University Cancer Institute IUCT-Oncopole, Toulouse, France; [9]SLK-Clinics, Cancer Center Heilbronn-Franken, Heilbronn, Germany; [10]Clinica Universidad de Navarra, Navarra, Spain; [11]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [12]Sanford Health, USD Sanford School of Medicine, Sioux Falls, SD, USA; [13]Stephenson Cancer Center, University of Oklahoma, Oklahoma City, OK, USA; [14]Bristol-Myers Squibb, Princeton, NJ, USA; [15]Seattle Cancer Care Alliance, Seattle, WA, USA; [16]University of Essen, Essen, Germany

VITU
VirtuellesTumorboard

DE Impressum

# VITU - Virtuelles Tumorboard

Melden Sie sich an, um an einer Konferenz teilzunehmen.

Mit MOLIT anmelden

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Institut für personalisierte Medizin

# … our molecular tumor board (MTB)

- started in May 2017
- weekly conference
- Multidisciplinary (Research + Clinic)
- supplements organ-specific tumor conferences as needed

| | RH | TJ | RT | WS | KG | ND | KV | WSt | RS |
|---|---|---|---|---|---|---|---|---|---|
| **TMB** | 60 | 50 | 40 | 50 | 80 | n-a- | n.a. | n.a | 1500 |
| KRAS | | | | | | | | | |
| TP53 | | | | | | | | | |
| p16/CDKN2A | | | | | | | | | |
| SMAD4 | | | | | | | | | |
| SMAD2 | | | | | | | | | |
| BRAF | | | | | | | | | |
| BRCA1 | | | | | | | | | |
| BRCA2 | | | | | | | | | |
| FANCD2 | | | | | | | | | |
| FANCB | | | | | | | | | |
| ATR | | | | | | | | | |
| ABL1 | | | | | | | | | |
| ATM | | | | | | | | | |
| ARID1B | | | | | | | | | |
| ARID1A | | | | | | | | | |
| SMARCA4 | | | | | | | | | |
| KDM6A | | | | | | | | | |
| SETD2 | | | | | | | | | |
| RYR1 | | | | | | | | | |
| PRX | | | | | | | | | |
| MTHFR | | | | | | | | | |
| NOTCH3 | | | | | | | | | |

**1500 non-synonymous mutations**

**DNA damage repair genes**

R.S. 76 J.
Hepatisch metastasiertes Pankreaskarzinom
ED 12/2015

Therapie:
12/2015 – 07/2016 Gem + nabPaclitaxel
Progress
**07/2016 Molekulargenetik**
- *BRAF V600E-Mutation*
- *BRCA2- u. FANCB-Mutation*
- *Hypermutationsphänotyp*

08 -10/2016 Pembrolizumab + Trametinib
10/2016 – 04/2017 Pembrolizumab
PR

Tumorzentrum
Cancer Center Heilbronn-Franken

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SLK Kliniken

case report in

JCO® Precision Oncology
An American Society of Clinical Oncology Journal

case report

# Sustainable Response of a Patient With Metastasized Pancreatic Cancer and a Hypermutational Phenotype to Immunotherapy. New Therapeutic Concept for a Rare Subtype?

Stephanie Berger
Sylvia Bochum
Dora Finkeisen

## CASE REPORT

A 76-year-old woman was referred to our clinic with a suspicious lesion in liver segment VI after an abdominal ultrasound was performed in the routine setting. Besides occasional minor abdominal discomfort, the patient was asymptomatic. A biopsy specimen of the liver lesion revealed a poorly differentiated carcinoma, with tumor cells displaying a partly pleomorphic, signet ring or spindle cell appearance, fitting to the metastatic presentation of either a carcinoma of the bile duct or pancreatico-biliary system.

for whole-exome sequencing and sequenced on an Illumina HiSeq next-generation sequencing platform (Illumina, San Diego, CA) by CeGaT (Tuebingen, Germany). After bioinformatic filtering of germline variants and manual assertion of the called variants, a high tumor mutational burden (TMB) with 18 mutations/Mb was detected. The most relevant somatic driver mutations were a loss-of-function stop mutation within *FANCB* (E472*) and an activating mutation in *BRAF* (V600E). No mutations in *KRAS* and genes involved in DNA mismatch repair

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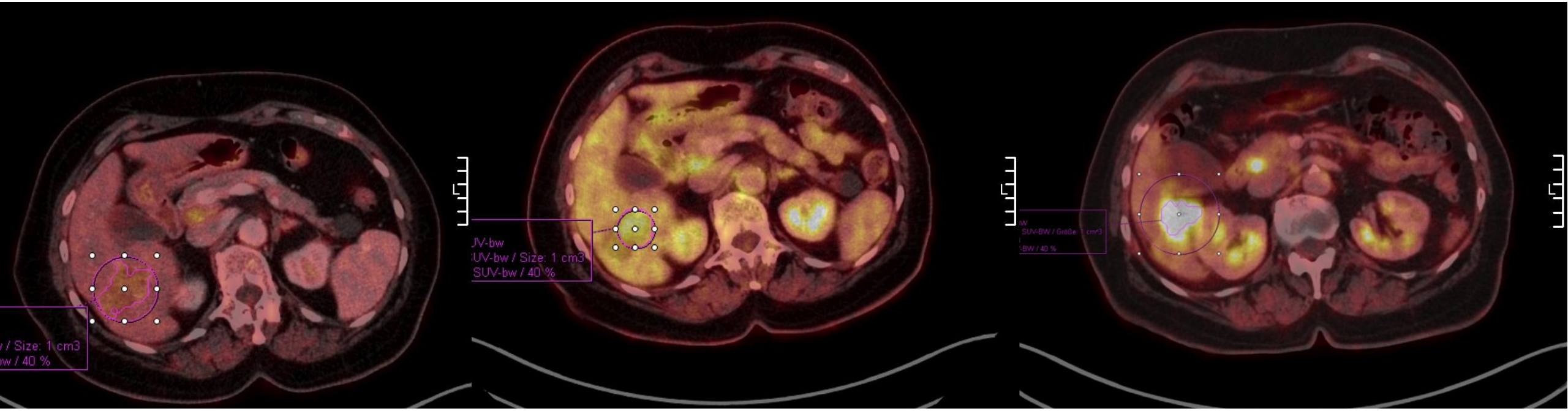
# personalized immunotherapy leads to tumor regression




**05/2017** **01/2017** **08/2016**

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# Workflow from tumor tissue to MTB report

treatment case

molecular diagnostics

molecular tumor board

**Obtaining the tumor material of the patient (CT or sonographically controlled or surgical specimen)**

**sample shipment**

**DNA sequencing (NGS)**

**Bioinformatics**

**clinical evaluation**

**validation**

**MTB-treatment recommendations**

**Patient**

**„Tissue team“**

**Labor team**

**bioinformatician**

**clinical oncologists, human geneticists, biologists, study physicians**

# Virtual Tumor Board as an IT tool set

data collection and preparation

MTB conference

follow-up individual case

Report of molecular diagnostics

↓

Supplement to relevant data from the clinic

↓

Search for similar cases in the literature

↓

Search for available therapy options (studies)

↓

validation

↓

MTB-treatment recommendations

↓

Review

dynamic integration of information, queries as needed

source independent search tool

Teleconference

Follow-up workflow

VITU
VirtuellesTumorboard

Home | Arbeitsliste | Konferenzplaner | Videokonferenz | Dokumentation

DE

aktuell | abgeschlossen

Einträge filtern: Einträge filtern

129 Einträge « ‹ 1 2 3 4 ... › »

Einträge pro Seite: 25

| Erstelldatum | Fallnummer | Patient | Geburtsdatum | Diagnose | Status | Statusbeschreibung |
|---|---|---|---|---|---|---|
| 26.3.2018 | 4c1592ee | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Bereit zur Terminierung |
| 26.3.2018 | 83d4b42b | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Bestätigung |
| 26.3.2018 | 85f71a31 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Befund |
| 26.3.2018 | be8076bf | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Dokumentation |
| 3.4.2018 | 1ff69f6f | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Bereit zur Terminierung |
| 3.4.2018 | e9c361f5 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Bestätigung |
| 3.4.2018 | 583d74e9 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Befund |
| 3.4.2018 | e7a466fb | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Dokumentation |
| 3.4.2018 | 96038fc3 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Bereit zur Terminierung |
| 3.4.2018 | c283fb9c | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Bestätigung |
| 3.4.2018 | 2c050fdd | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Befund |
| 3.4.2018 | d24a752b | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Dokumentation |
| 26.3.2018 | 01486f85 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Bereit zur Terminierung |
| 26.3.2018 | 9f295142 | Charles C. Chartington | 1.1.1970 | Bösartige Neubildung der Prostata | | Warten auf Bestätigung |

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**Terminierbare Fälle**

Fall suchen

**Fall 4c1592ee**
Charles C. Chartington, 1.1.1970
Bösartige Neubildung der Prostata

**Fall 1ff69f6f**
Charles C. Chartington, 1.1.1970
Bösartige Neubildung der Prostata

**Fall 96038fc3**
Charles C. Chartington, 1.1.1970
Bösartige Neubildung der Prostata

**Fall 01486f85**
Charles C. Chartington, 1.1.1970
Bösartige Neubildung der Prostata

**Fall 23bbb7e4**
Charles C. Chartington, 1.1.1970
Bösartige Neubildung der Prostata

**Planer**

Konferenz suchen

**Neue Konferenz planen**

**Molekulares Tumorboard**
**15.6.2018, 14:21**
**0**
Fälle zugeordnet

**Molekulares Tumorboard**
**15.6.2018, 14:21**
**2**
Fälle zugeordnet

**Molekulares Tumorboard**
**15.6.2018, 14:21**
**1**
Fall zugeordnet

**Tumorboard**
**21.6.2018, 14:00**
**0**
Fälle zugeordnet

# Molekulares Tumorboard - 15.6.2018

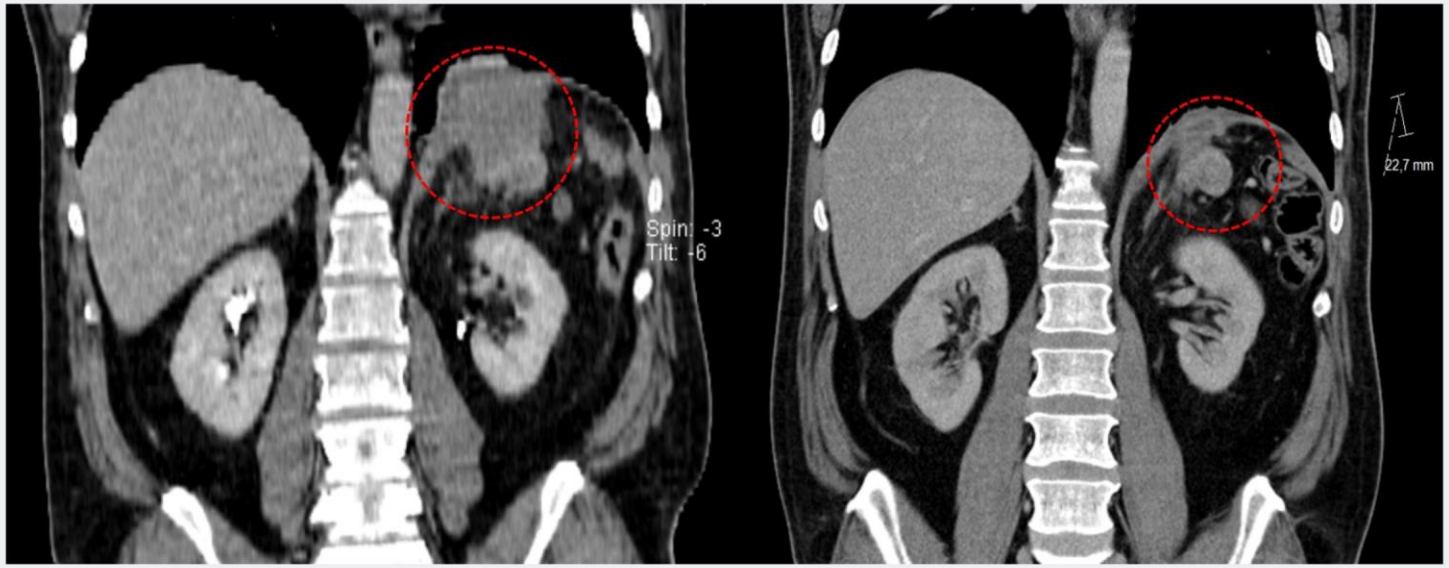
Konferenzansicht | Präsentationsansicht

## Videokonferenz

Teilnehmer 1

Teilnehmer 2

## Präsentation




## Falldaten

Dokument suchen

**Radiologie**
CT vom 20.03.2018

**Molekulardiagnostik**
Befund vom 03.04.2018

**Patient Reported Outcomes**
Patiententagebuch Januar 2018

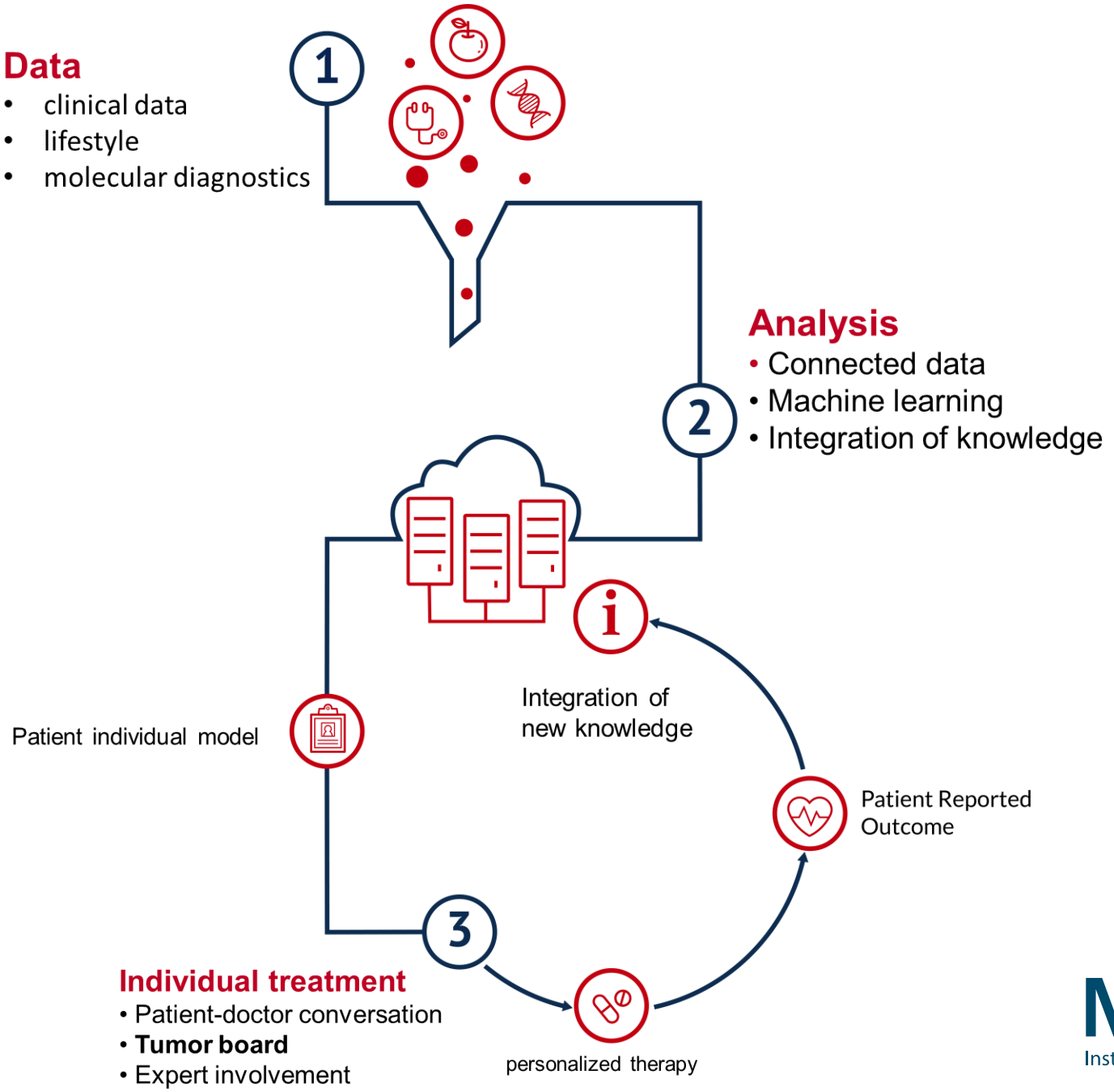
Nächster Fall

## Notizen

MOLIT Institut für personalisierte Medizin

# Opportunity 1:

from
digital data
to
digital workflows

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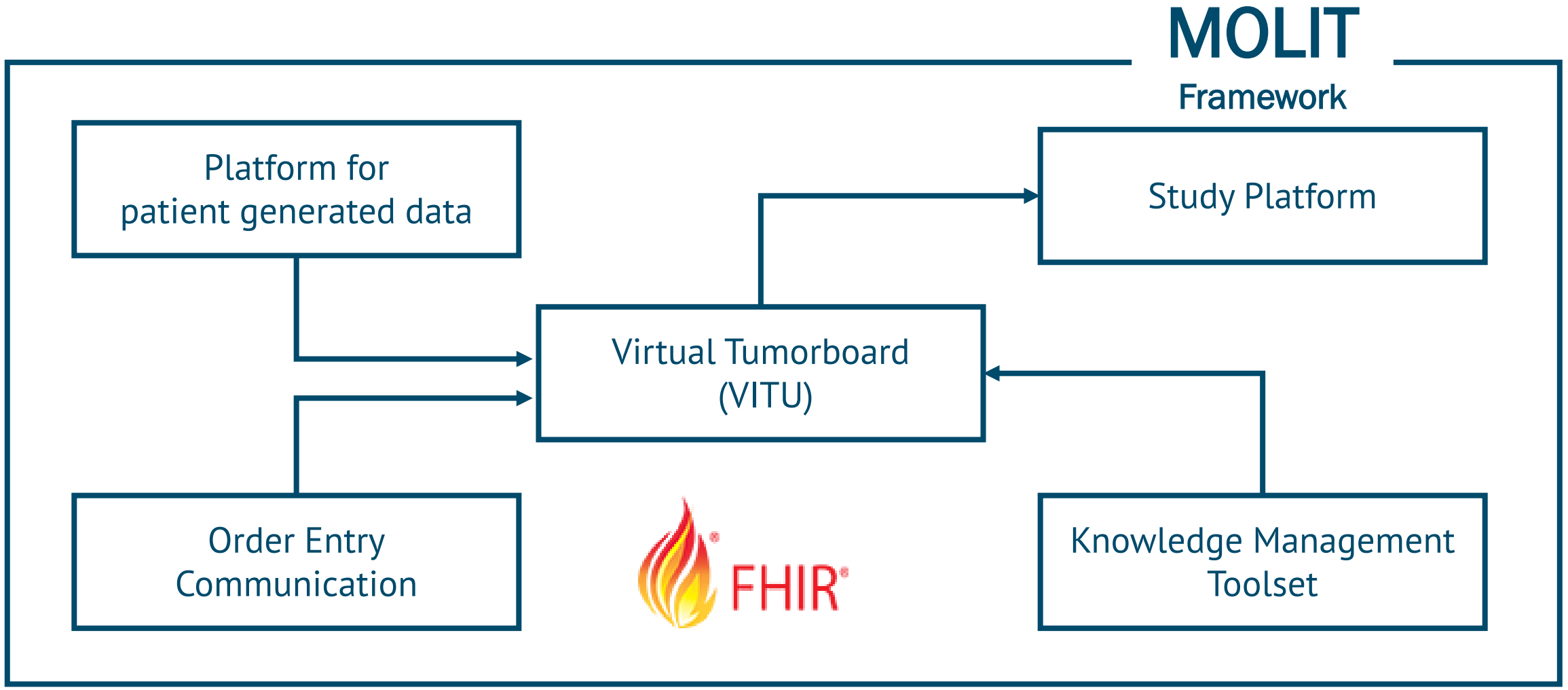
# MOLIT Framework an interoperable toolbox

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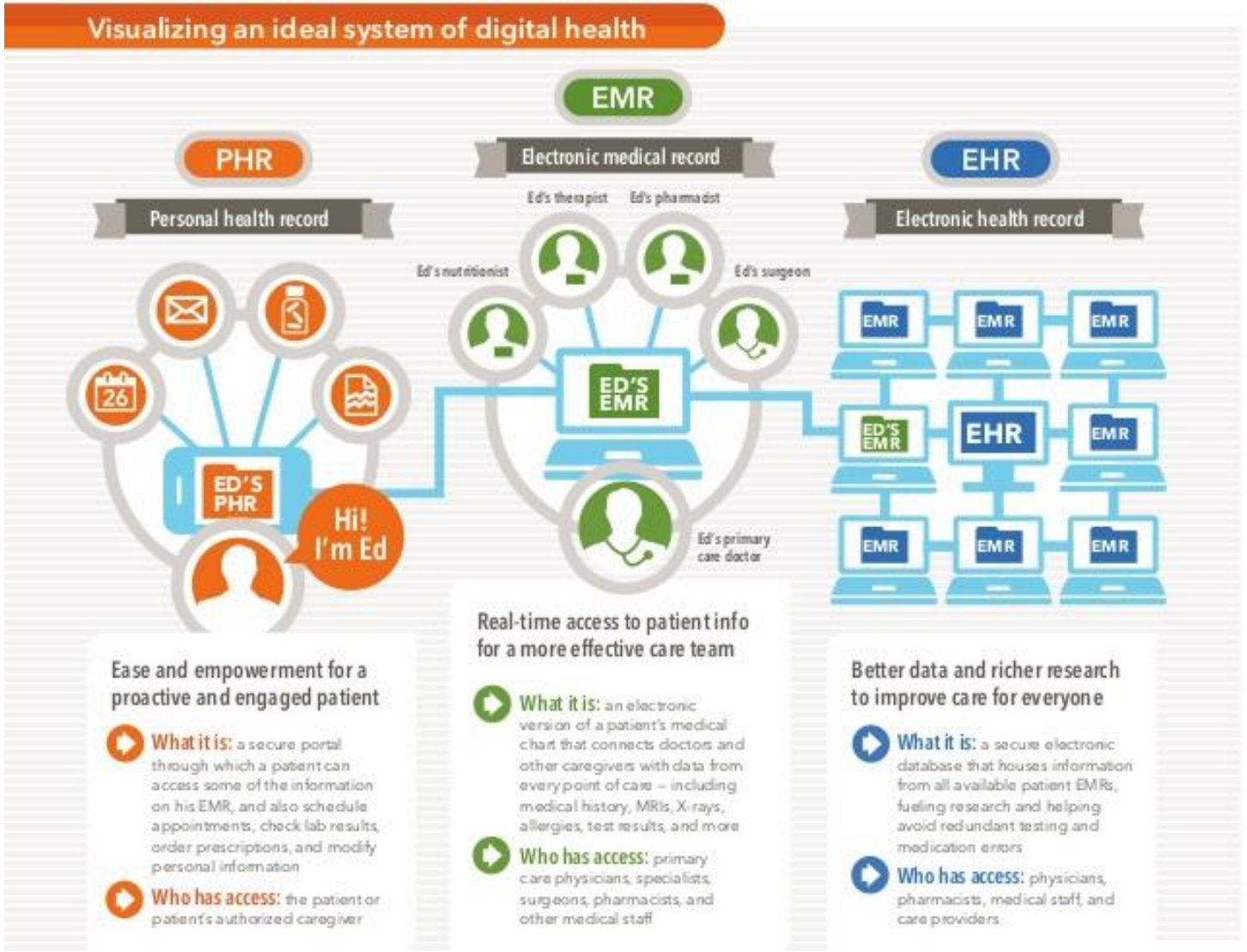
# Opportunity 2:

interoperability enables different usage contexts

## Example: Kaiser permanente

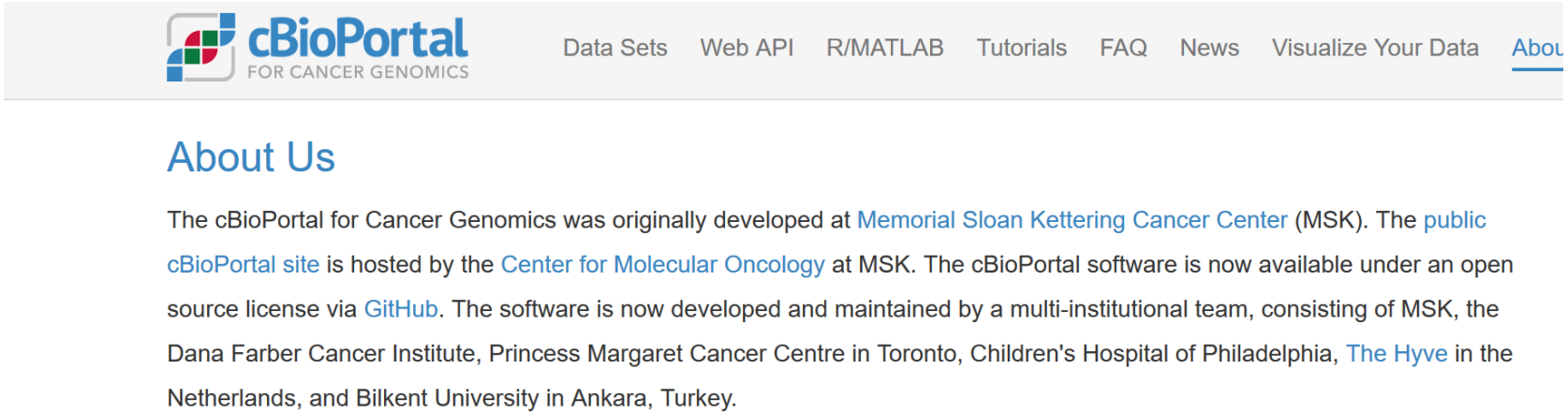



Source 08.03.2016 : http://image.slidesharecdn.com/kaiserpermanente-makingsenseofhealthinformationsystems-140826184840-phpapp01/95/making-sense-of-health-information-systems-1-638.jpg?cb=1418657425

# Opportunity 3:

# interoperability enables cooperation

# Example: www.cbioportal.org



cBioPortal FOR CANCER GENOMICS

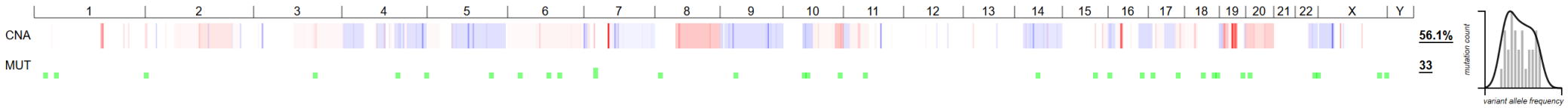
Data Sets | Web API | R/MATLAB | Tutorials | FAQ | News | Visualize Your Data | About | Login

Patient: TCGA-BK-A0CC, 69 years old, Endometrial Cancer (Uterine Serous Carcinoma/Uterine Papillary Serous Carcinoma), LIVING (10 months), DiseaseFree (10 months)

Uterine Corpus Endometrial Carcinoma (TCGA, Nature 2013)

Samples: TCGA-BK-A0CC-01, Stage III

Summary | Clinical Data | Pathology Report | Heatmap | Tissue Image




## 33 Mutations (page 1 of 4)

Columns

| Gene | Protein Change | Annotation ▼ | Mutation Type | Allele Freq | mRNA Expr. | Cohort | COSMIC |
|---|---|---|---|---|---|---|---|
| PPP2R1A | *S256F* | | Missense | 0.52 | 40% | 11.3% (M) | 17 |
| TP53 | *Q331** | | Nonsense | 0.65 | 2% | 27.8% (M) | 36 |
| FAT1 | *E314** | | Nonsense | 0.64 | 47% | 16.1% | 1 |
| EPHA7 | *H408Q* | | Missense | 0.15 | 84% | 3.2% | 1 |
| PHLPP2 | *R1206Q* | | | | | 5.2% | 1 |
| DHDDS | *A165V* | | Missense | 0.25 | 29% | 1.6% | 1 |
| NSUN4 | *R10L* | | Missense | 0.44 | 10% | 2.4% | 1 |
| OR2T33 | *L299Q* | | Missense | 0.13 | 64% | 3.2% | 1 |
| AMOTL2 | *Q558del* | | IF del | | 99% | 5.2% | 1 |
| FAT4 | *X3967_splice* | | Splice | 0.31 | 53% | 16.1% | |

13 samples (**5.2%**) in this study have mutated PHLPP2, out of which 1 (**0.4%**) have PHLPP2 R1206 missense mutations.

Showing 1-10 of 33 Mutations | Show more

## 380 Copy Number Alterations (page 1 of 38)

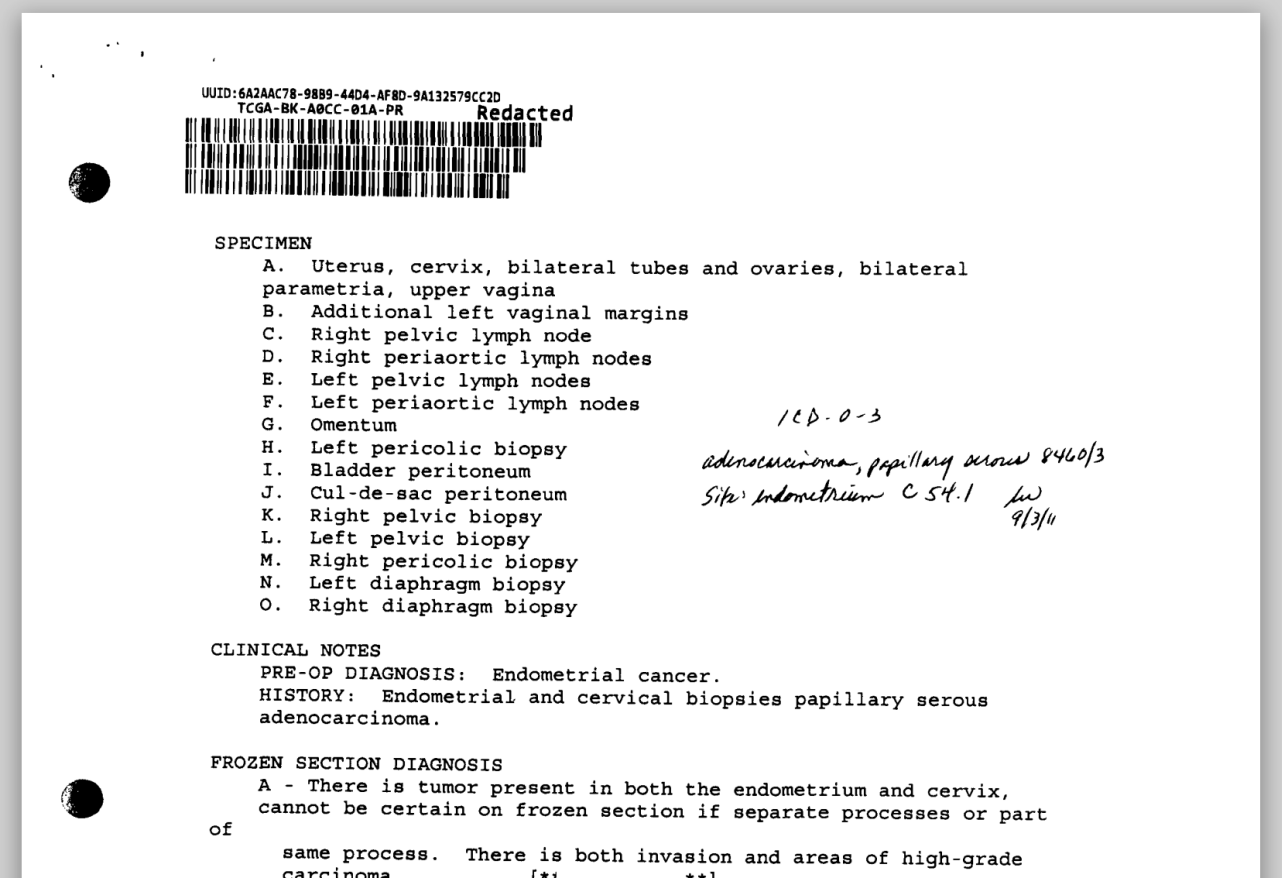
Columns

source, 21.08.2018: http://www.cbioportal.org/patient?studyId=ucec_tcga_pub&caseId=TCGA-BK-A0CC

Patient: TCGA-BK-A0CC, 69 years old, Endometrial Cancer (Uterine Serous Carcinoma/Uterine Papillary Serous Carcinoma), LIVING (10 months), DiseaseFree (10 months) Uterine Corpus Endometrial Carcinoma (TCGA, Nature 2013)

Samples: 1 TCGA-BK-A0CC-01, Stage III





UUID:6A2AAC78-98B9-44D4-AF8D-9A132579CC2D
TCGA-BK-A0CC-01A-PR Redacted

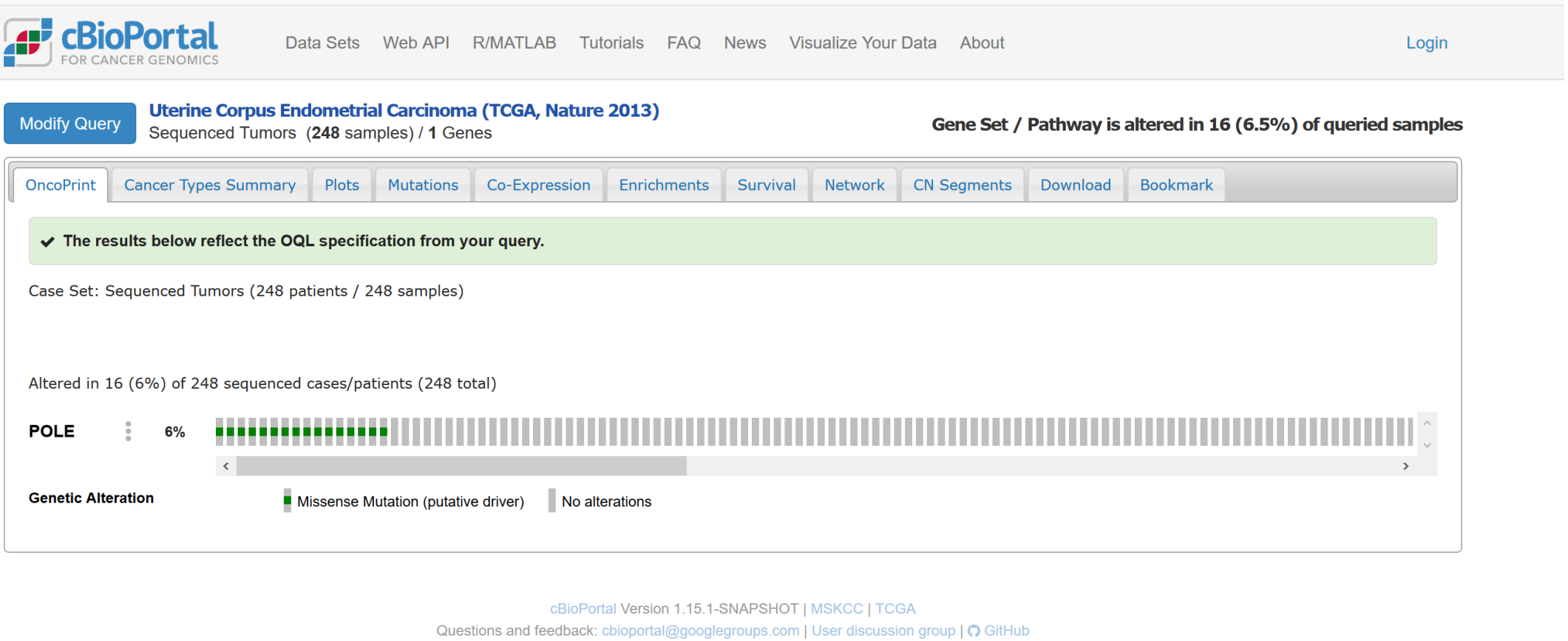
SPECIMEN
A. Uterus, cervix, bilateral tubes and ovaries, bilateral parametria, upper vagina
B. Additional left vaginal margins
C. Right pelvic lymph node
D. Right periaortic lymph nodes
E. Left pelvic lymph nodes
F. Left periaortic lymph nodes
G. Omentum
H. Left pericolic biopsy
I. Bladder peritoneum
J. Cul-de-sac peritoneum
K. Right pelvic biopsy
L. Left pelvic biopsy
M. Right pericolic biopsy
N. Left diaphragm biopsy
O. Right diaphragm biopsy

ICD-O-3
adenocarcinoma, papillary serous 8460/3
Site: endometrium C 54.1 [illegible]
9/3/11

CLINICAL NOTES
PRE-OP DIAGNOSIS: Endometrial cancer.
HISTORY: Endometrial and cervical biopsies papillary serous adenocarcinoma.

FROZEN SECTION DIAGNOSIS
A - There is tumor present in both the endometrium and cervix, cannot be certain on frozen section if separate processes or part of
same process. There is both invasion and areas of high-grade
carcinoma [illegible]

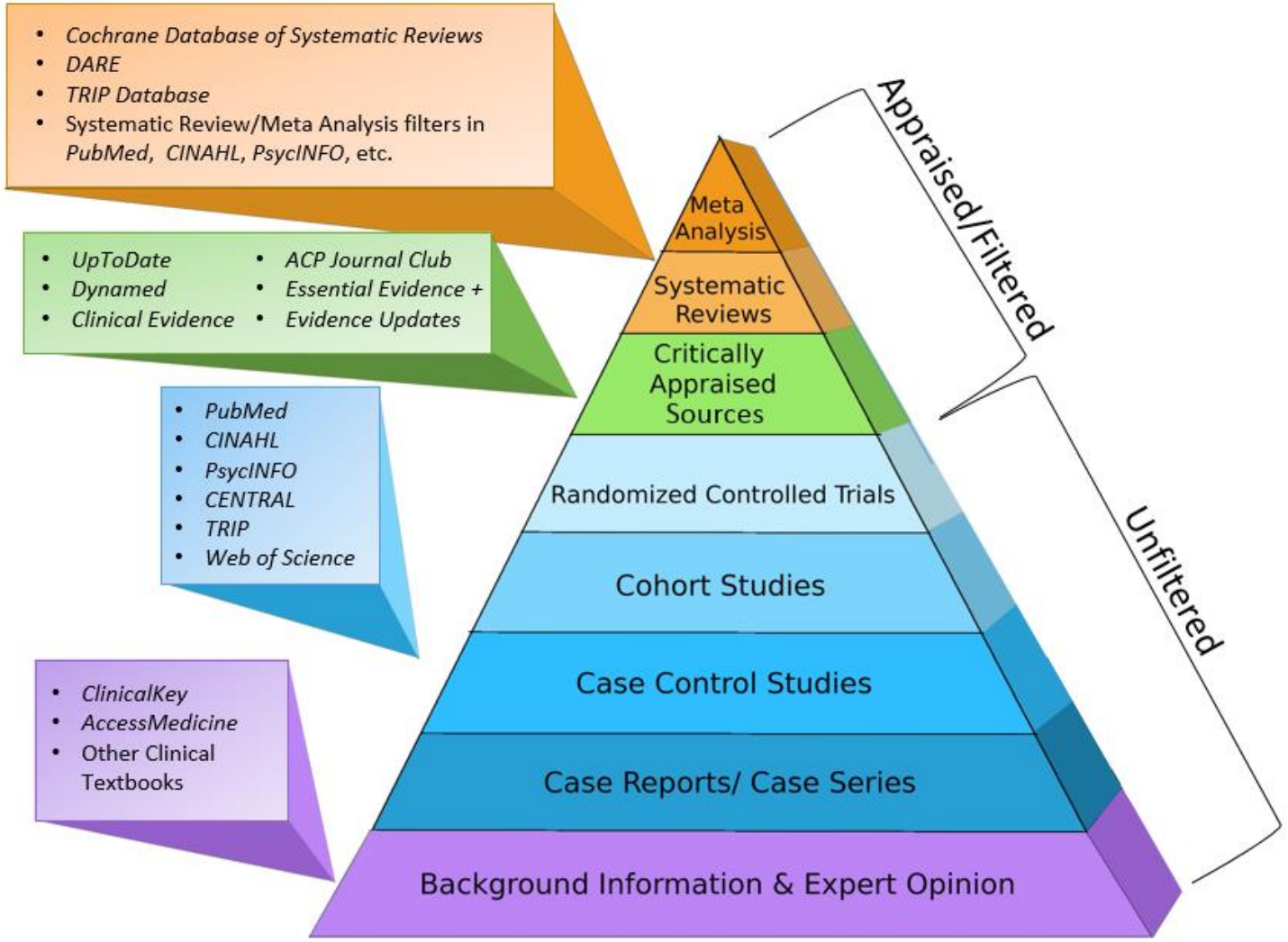
Source 21.08.2018: http://www.cbioportal.org/patient?caseId=TCGA-BK-A0CC&studyId=ucec_tcga_pub&tab=pathologyReportTab




Source, 21.08.2018:
http://www.cbioportal.org/index.do?cancer_study_list=ucec_tcga_pub&cancer_study_id=ucec_tcga_pub&genetic_profile_ids_PROFILE_MUTATION_EXTENDED=ucec_tcga_pub_mutations&Z_SCORE_THRESHOLD=2.0&RPPA_SCORE_THRESHOLD=2.0&data_priority=0&case_set_id=ucec_tcga_pub_sequenced&case_ids=&gene_set_choice=user-defined-list&gene_list=POLE%3A+MUT+%3D+P286+MUT+%3D+V411+MUT+%3D+L424+MUT+%3D param_selection=null&tab_index=tab_visualize&Action=Submit

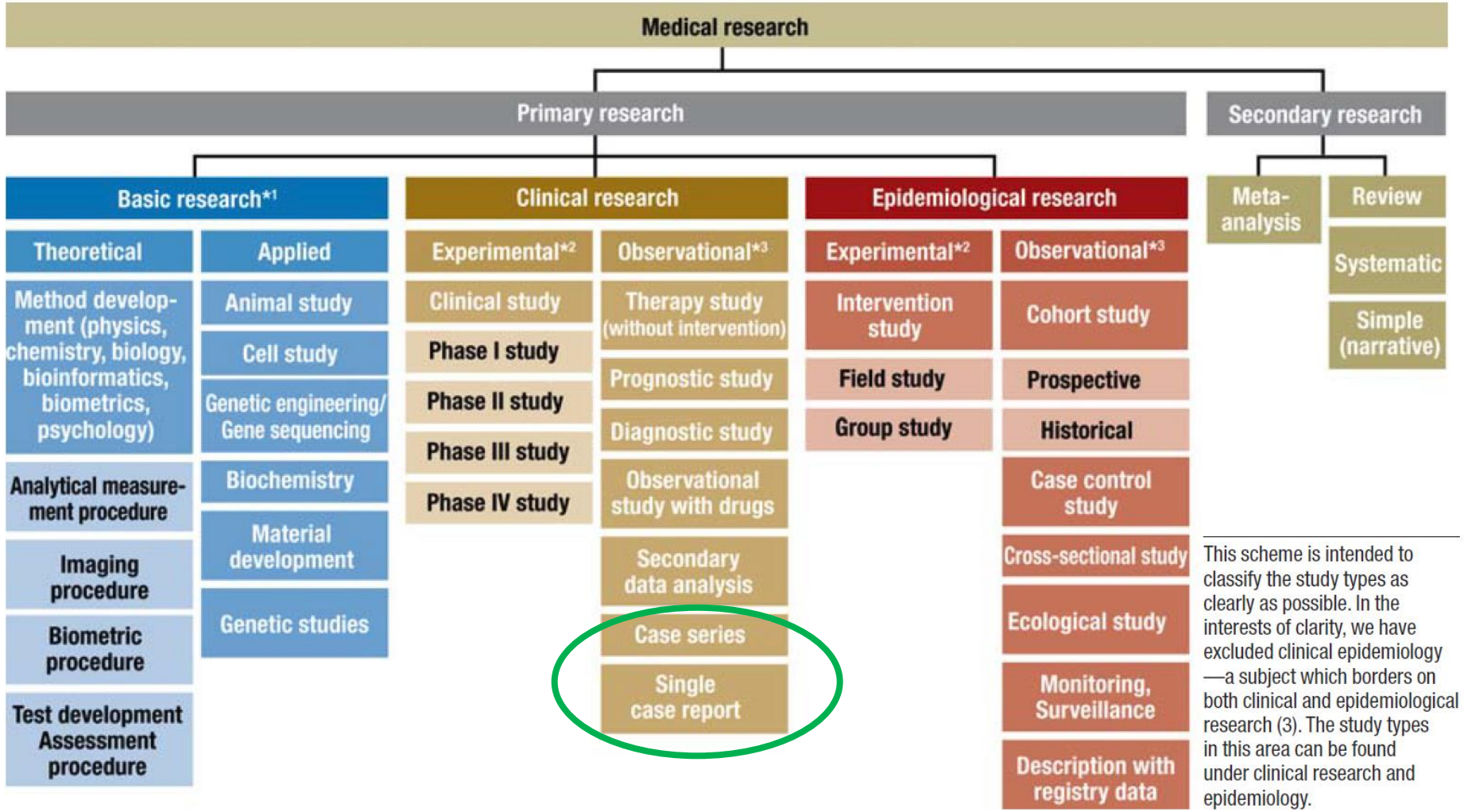
# Opportunity 4:

Case series are data with context




The EBM Pyramid of Evidence. Ebling Library, Health Sciences Learning Center
Downloaded from: http://researchguides.ebling.library.wisc.edu/EBM/acquire ; 21.082018

**FIGURE 1**




**Classification of different study types**

*1, sometimes known as experimental research; *2, analogous term: interventional; *3, analogous term: noninterventional or nonexperimental

Röhrig, Bernd; Prel, Jean-Baptist du; Wachtlin, Daniel; Blettner, Maria
Types of Study in Medical Research—Part 3 of a Series on Evaluation of Scientific Publications
Dtsch Arztebl Int 2009; 106(15): 262-8; DOI: 10.3238/arztebl.2009.0262

# draft characteristics of a good case series are:

- Clearly defined question.
- Well-described study population.
- Well-described intervention.
- Use of validated outcome measures.
- Appropriate statistical analyses.
- Well-described results.
- Discussion/conclusions supported by data.
- Funding source acknowledged.

Carey Timothy S., Scott D. Boden Scott D.
A Critical Guide to Case Series Reports
Spine 2003;28:1631–1634

# Challenges and Opportunities

- Paradigm shift in knowledge management
- Digitalisation
- Data and information quality
- Individualisation ("n of 1 cohort")
- Big Data

- Digital workflows
- Interoperability
- Case series

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# Gracias

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