2020年2月21日臨床評価部会総会２部

個別化医療実現に向けた臨床バイオマーカー戦略の State of the art

日本製薬工業協会
医薬品評価委員会　臨床評価部会
ブリストル・マイヤーズ　スクイブ株式会社
今井　康彦

製薬協

演題と演者に関わる開示事項

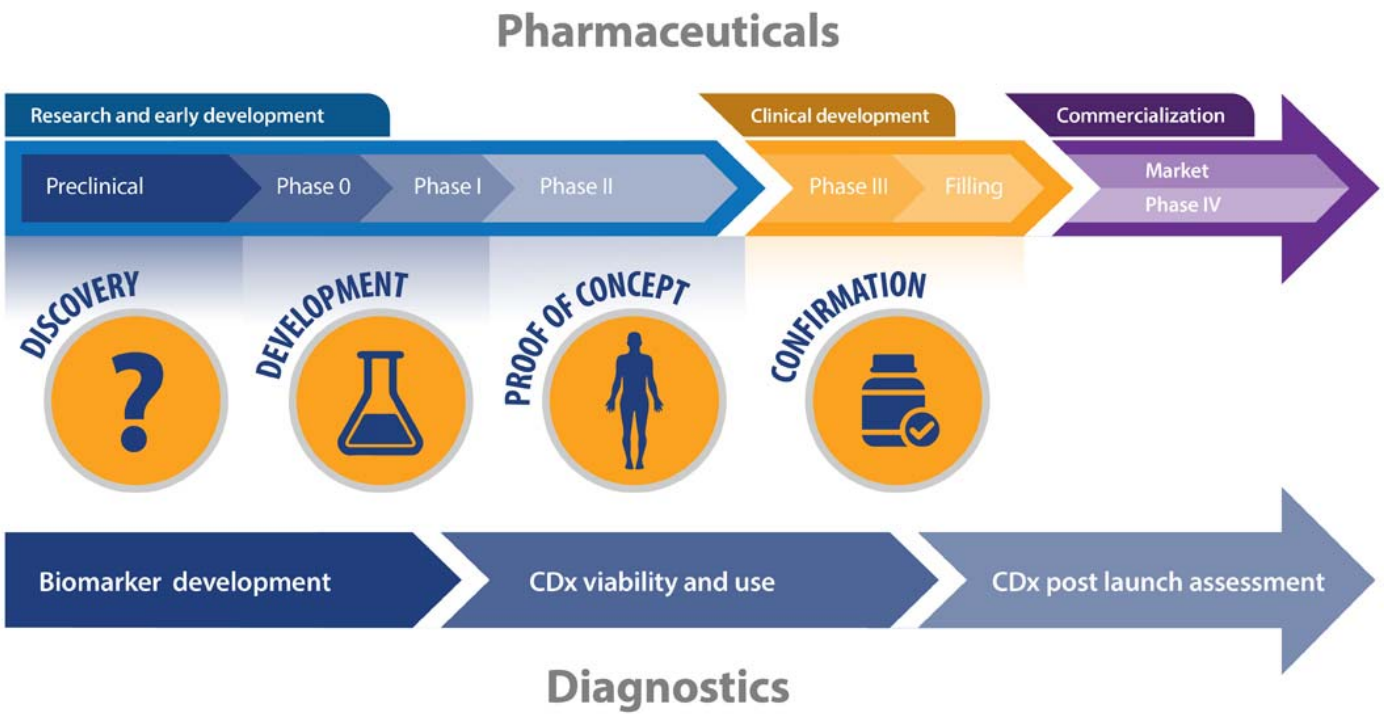
- 本発表内容は，一部演者の個人見解も含まれている可能性があります。

- 演者はブリストル・マイヤーズ　スクイブ（株）の社員でありますが，日本製薬工業協会医薬品評価委員会臨床評価部会員の立場で発表しており，企業活動とは無関係なものであり利益相反もありません。

製薬協

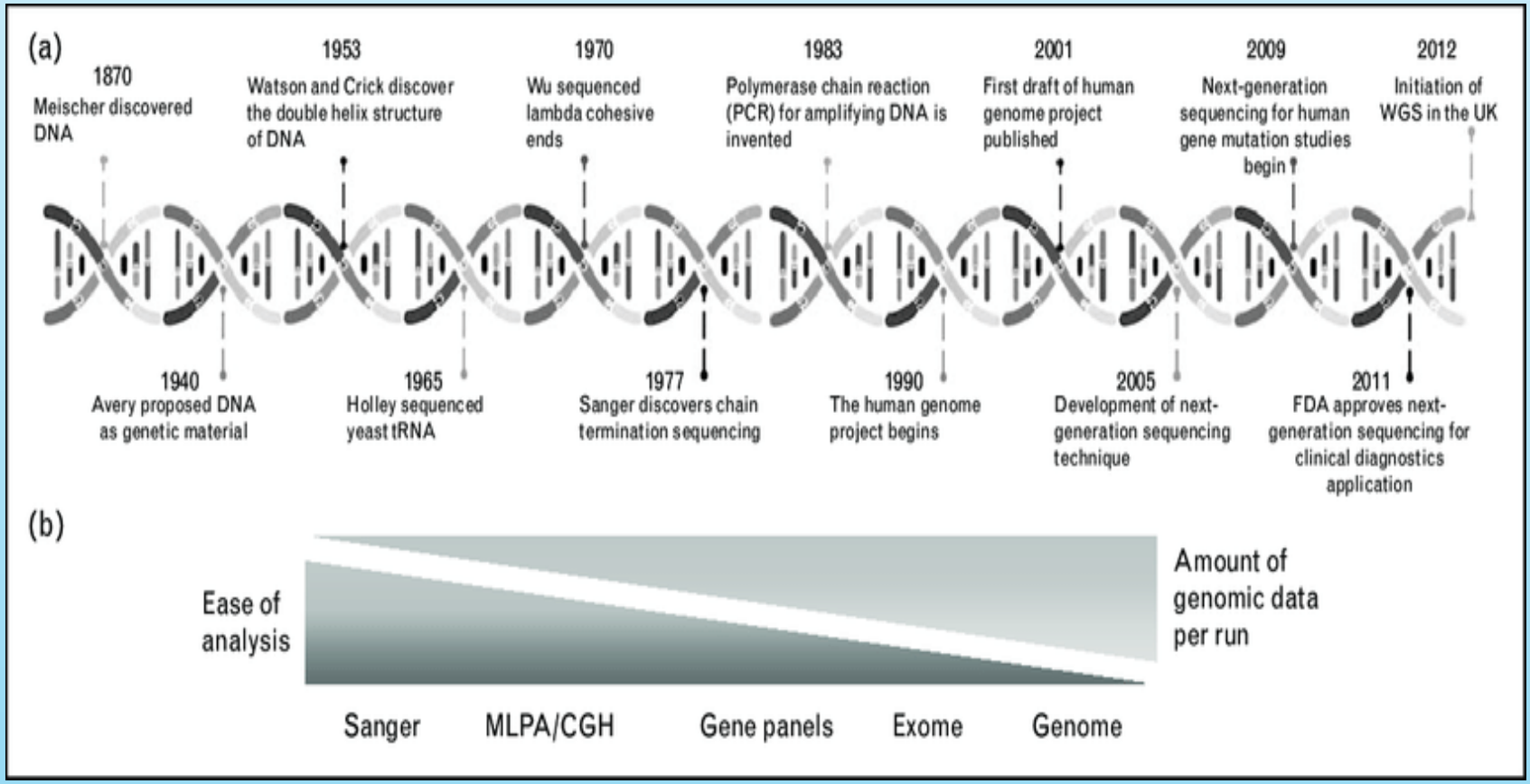
CDx and Drug Codevelopment Process

CrownBio
CONNECTING SCIENCE TO PATIENTS

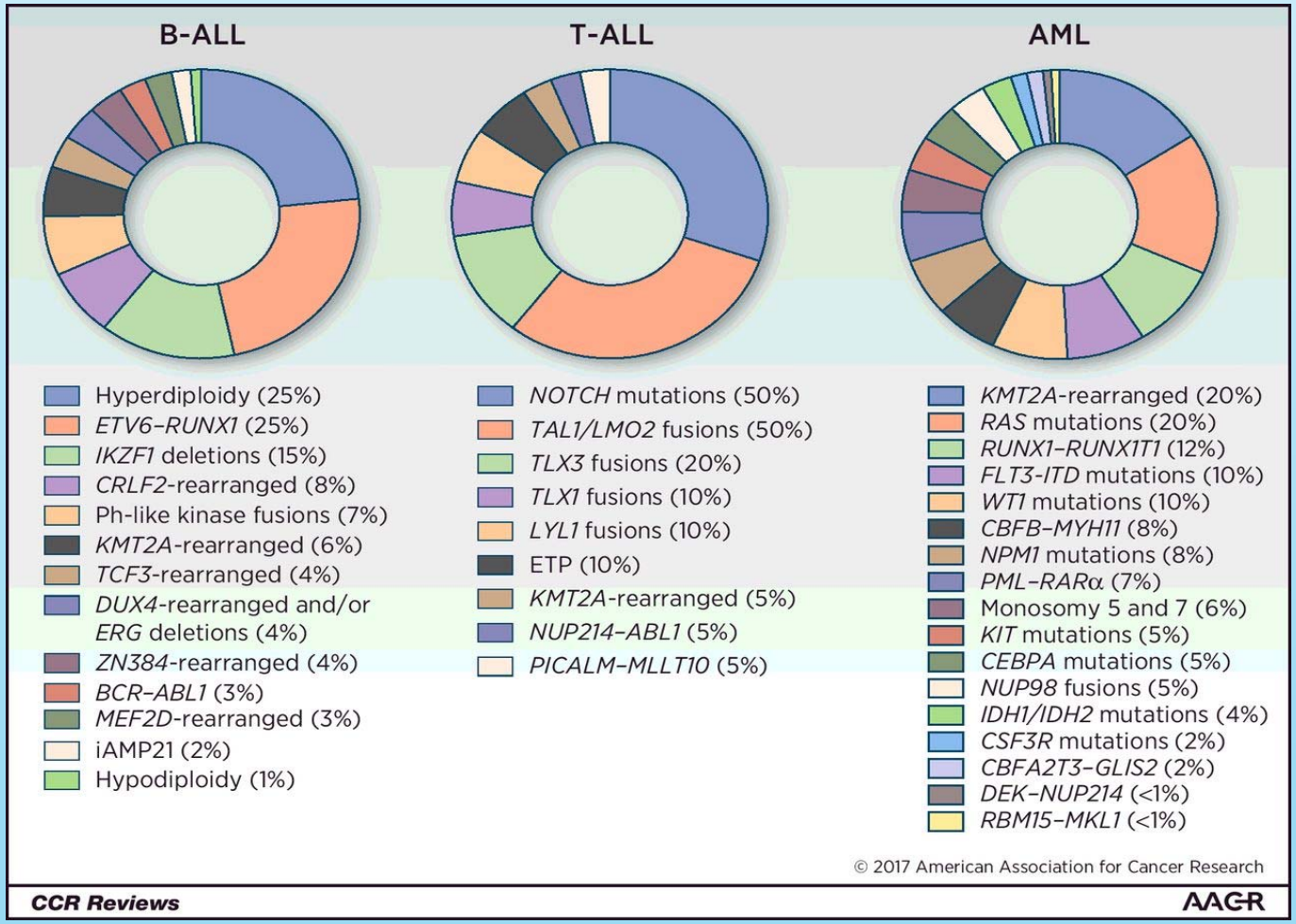


Brigitte Bruijns, Roald Tiggelaar and Han Gardeniers, Massively parallel sequencing techniques for forensics: A review, *Electrophoresis* 2018, *39,* 2642–2654

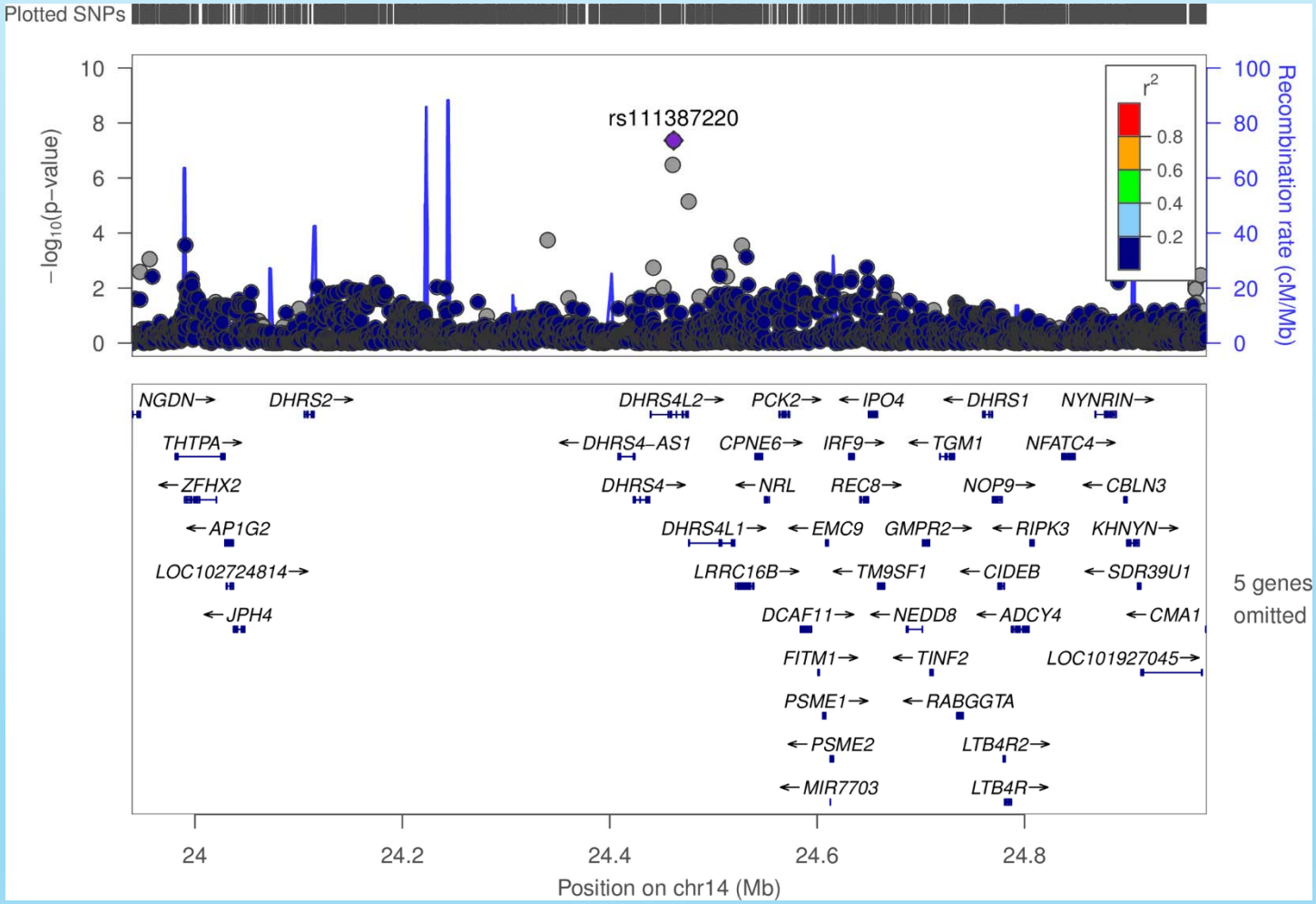
Genome Sequencingの技術革新



Next-generation sequencing in neuromuscular diseases - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/a-A-timeline-depicting-the-key-events-in-the-history-of-genomics-Genetic-research-and_fig4_306025523 [accessed 10 Jan, 2020]



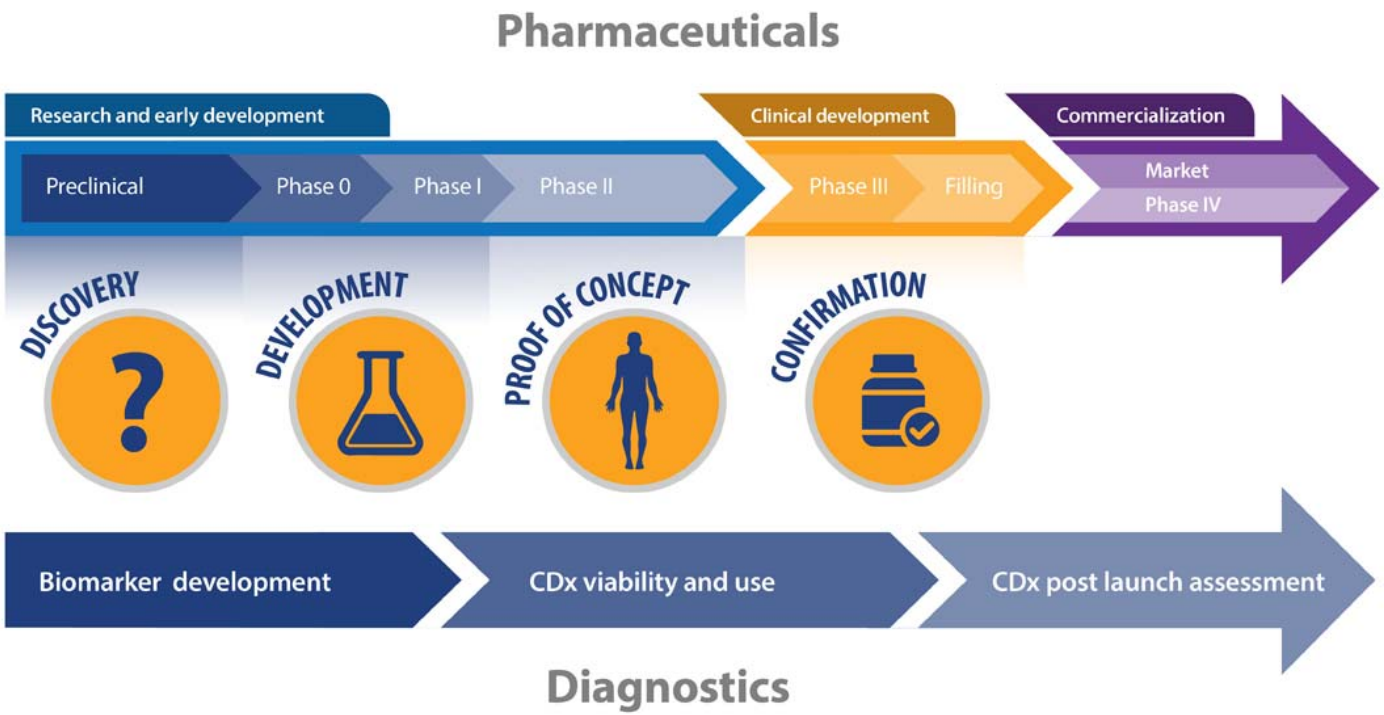
Thai Hoa Tran, Avanthi Tayi Shah and Mignon L. Loh, **Medicine in Pediatric Oncology: Translating Genomic Discoveries into Optimized Therapies,** **DOI:** 10.1158/1078-0432.CCR-16-0115 Published September 20


Plotted SNPs
rs111387220
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
NGDN→
DHRS2→
DHRS4L2→
PCK2→
←IPO4
←DHRS1
NYNRIN→
THTPA→
←DHRS4−AS1
CPNE6→
IRF9→
←TGM1
NFATC4→
←ZFHX2
DHRS4→
←NRL
REC8→
NOP9→
←CBLN3
←AP1G2
DHRS4L1→
←EMC9
GMPR2→
←RIPK3
KHNYN→
LOC102724814→
LRRC16B→
←TM9SF1
←CIDEB
←SDR39U1
←JPH4
DCAF11→
←NEDD8
←ADCY4
←CMA1
FITM1→
←TINF2
LOC101927045→
PSME1→
←RABGGTA
←PSME2
LTB4R2→
←MIR7703
LTB4R→
5 genes omitted
24
24.2
24.4
24.6
24.8
Position on chr14 (Mb)

製薬協

CDx and Drug Codevelopment Process

CrownBio
CONNECTING SCIENCE TO PATIENTS

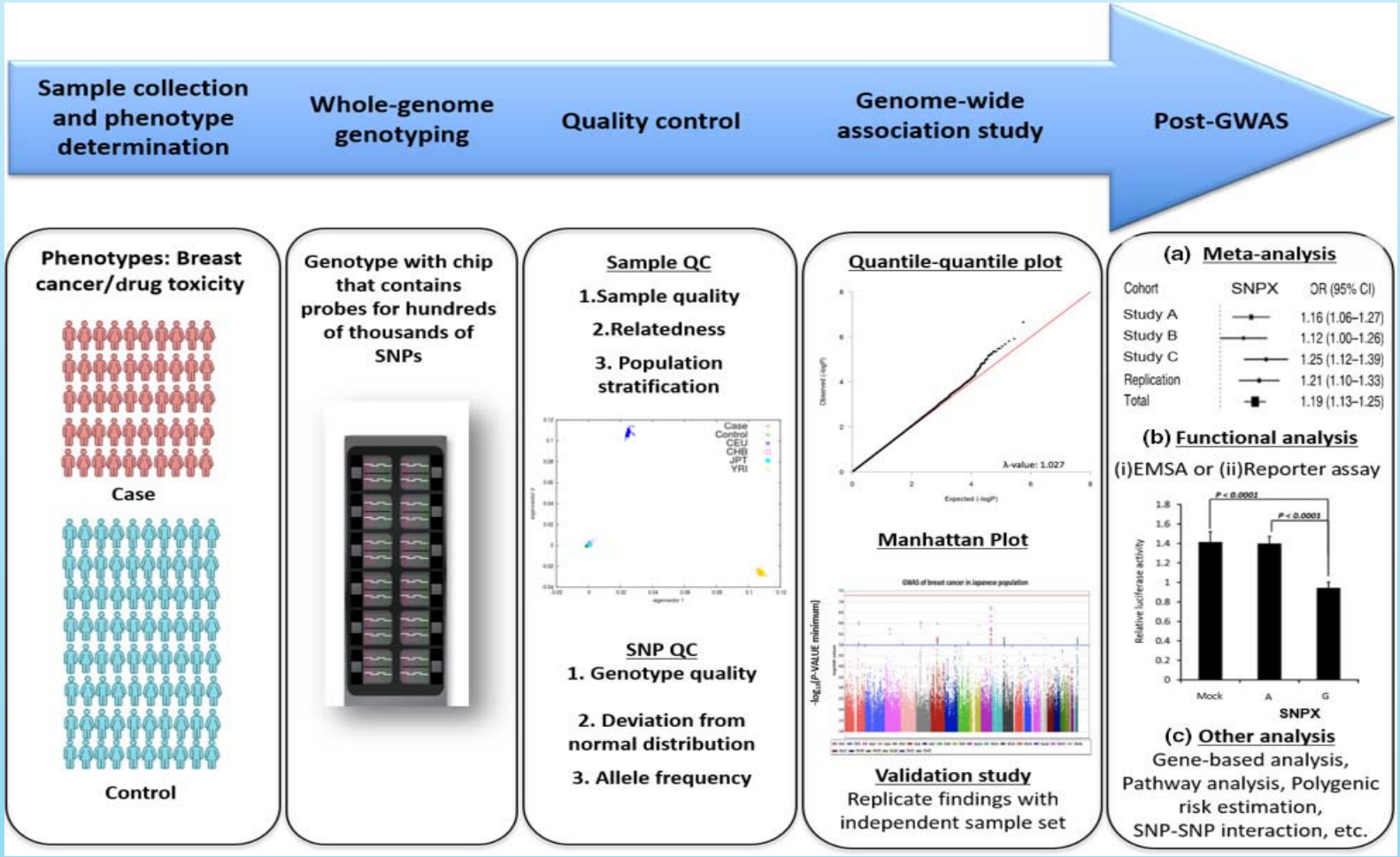


Brigitte Bruijns, Roald Tiggelaar and Han Gardeniers, Massively parallel sequencing techniques for forensics: A review, *Electrophoresis* 2018, *39,* 2642–2654

表題： 医薬品開発におけるバイオマーカー戦略の現状と展望

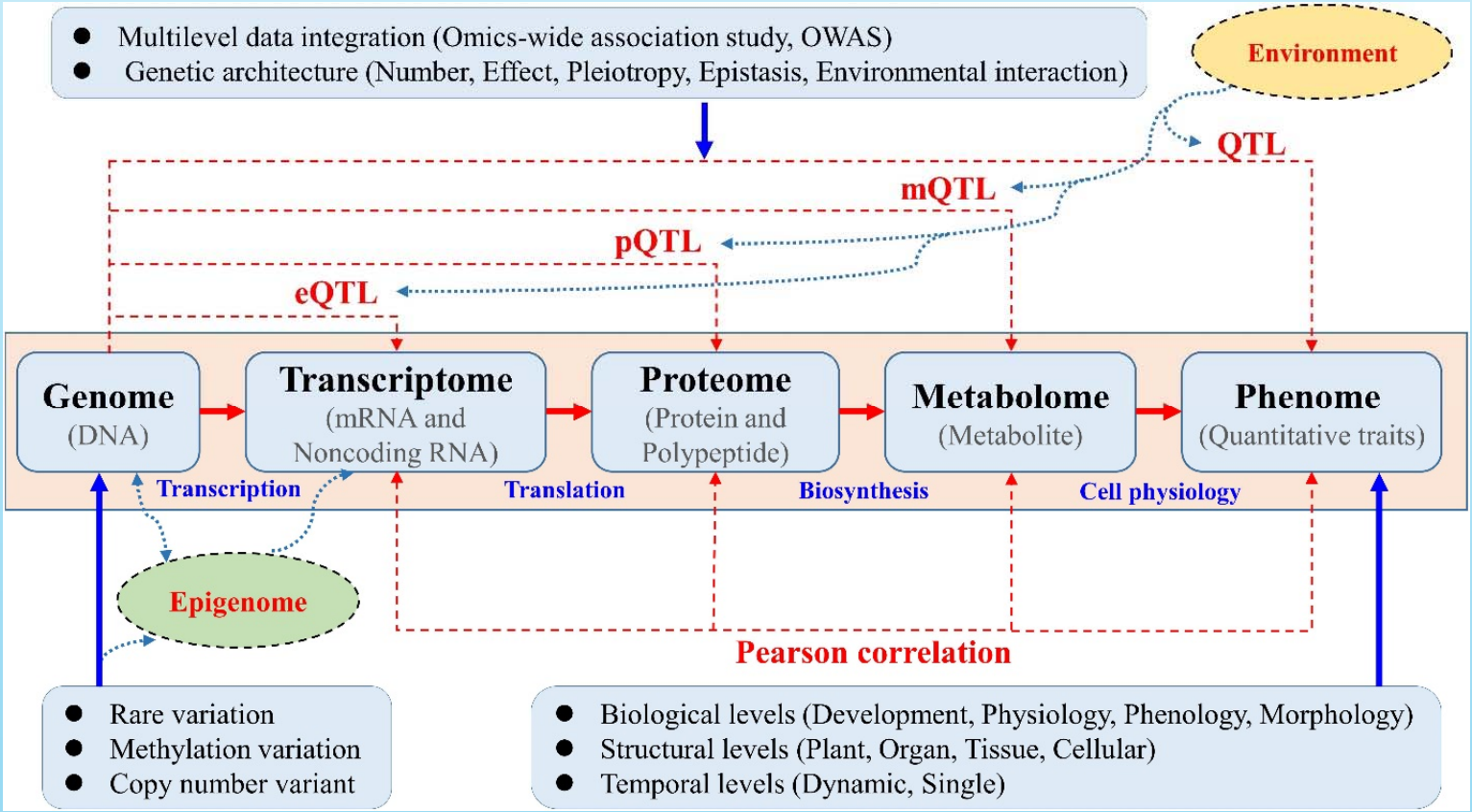
著者名: 上野貴代[1,2]， 松島信子[1,3]， 安藤裕崇[1,4]， 片島正貴[1,5]， 松野久美[1,6]，
今井康彦[1,2]

所属機関: 1 日本製薬工業協会 医薬品評価委員会 臨床評価部会,
2 ブリストル・マイヤーズ スクイブ株式会社， 3 ヤンセンファーマ
株式会社， 4 杏林製薬株式会社， 5 アステラス製薬株式会社， 6 バイ
エル薬品株式会社



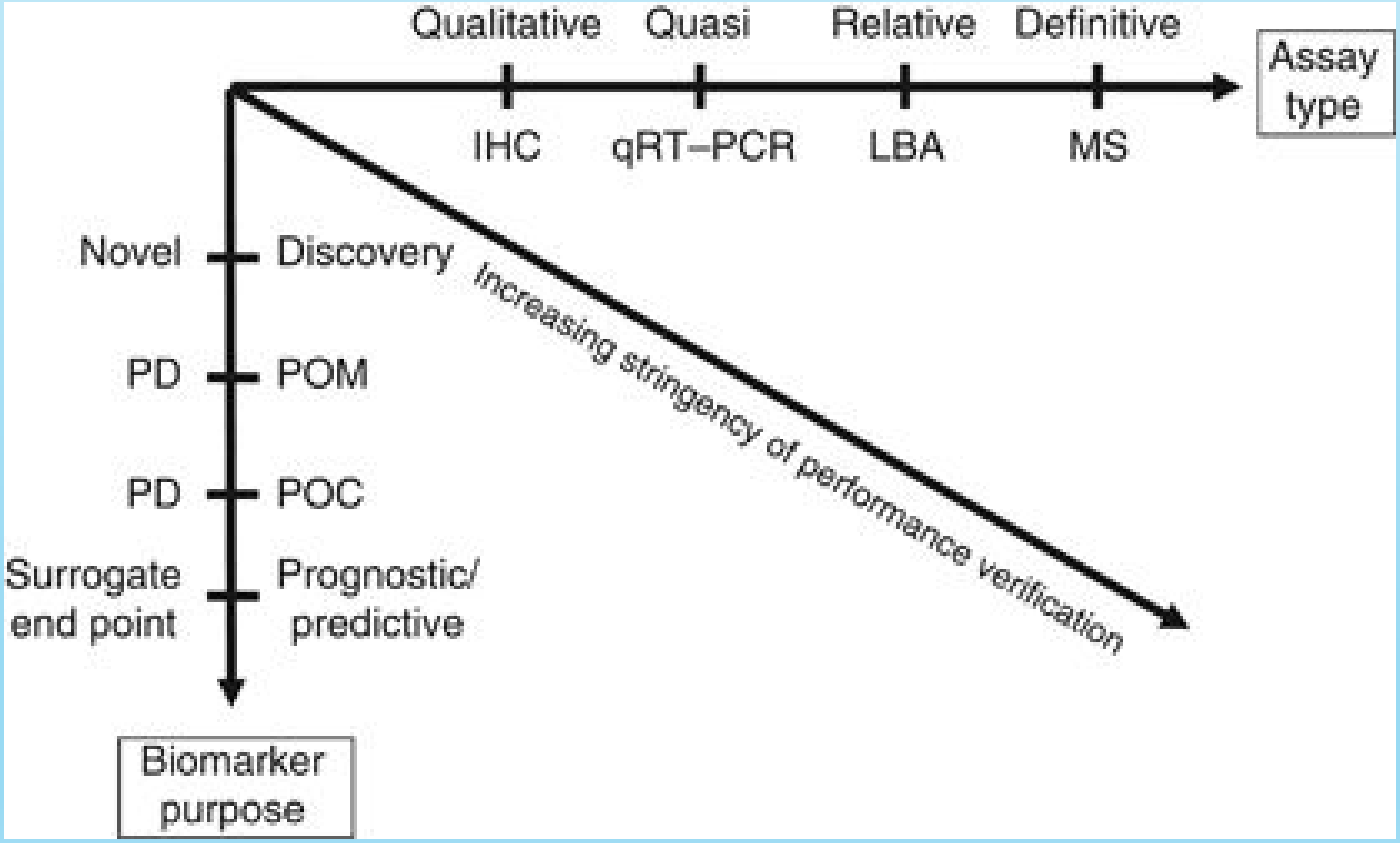
Breast cancer: The translation of big genomic data to cancer precision medicine Siew - Kee Low
Hitoshi Zembutsu, Yusuke Nakamura,First published: 07 December 2017
https://doi.org/10.1111/cas.13463

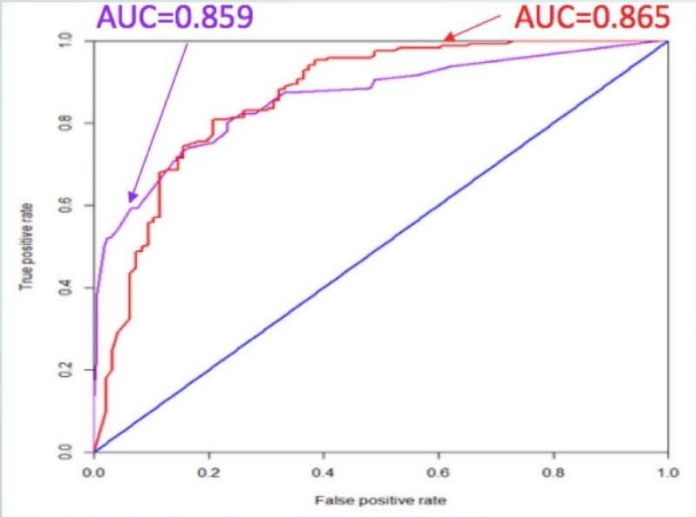
Omics, GWAS, QTL



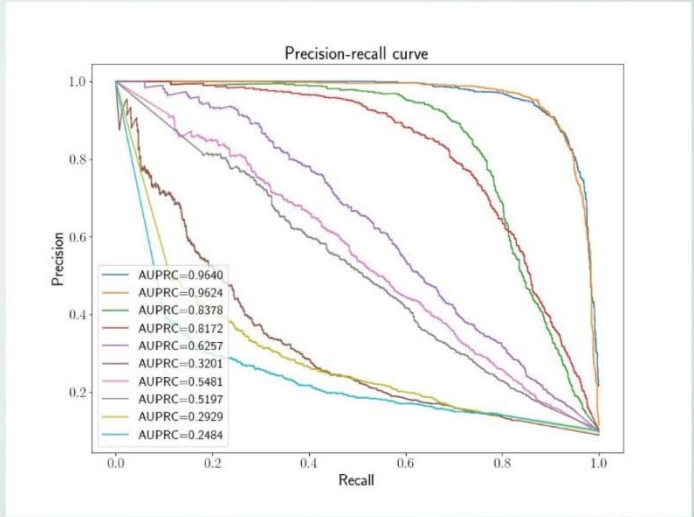
Qingzhang Du, Weniie Lu, Mingyang Quan, Liang Xiao, Fangyuan Song, Peng Li, Daling Zhou, Jianbo Xie, Longxin Wang and Deqiang Zhang, Genome-Wide Association Studies to Improve Wood Properties: Challenges and Prospects, Genome-Wide Association Studies to Improve Wood Properties: Challenges and ProspectsFront. Plant Sci., 21 December 2018 | https://doi.org/10.3389/fpls.2018.01912

Biomarkers assay validation　に求められるFit For the Purposeな Requirements



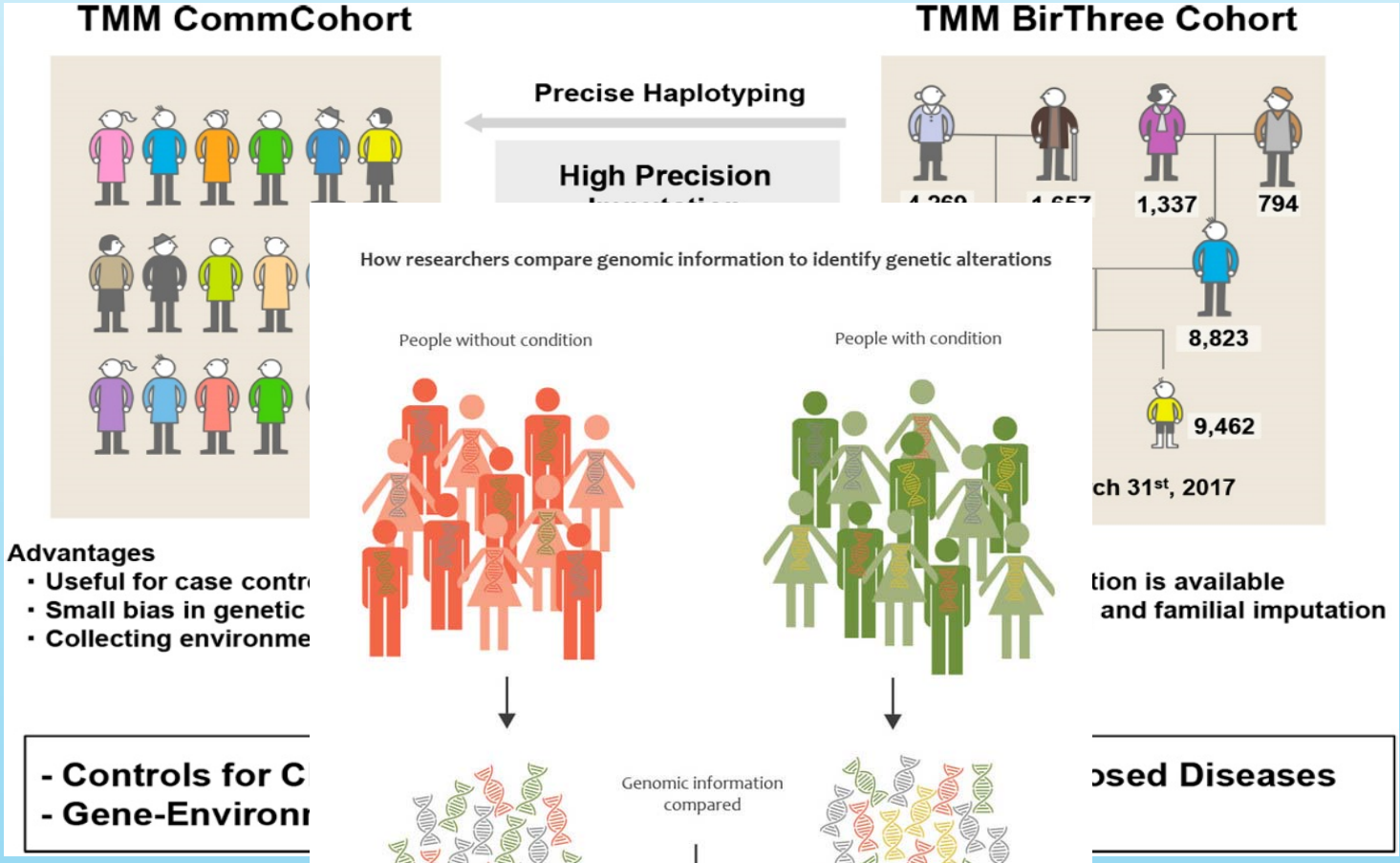


Receiver Operating Characteristic (ROC):
True positive rate: TP / (TP + FN)
False positive rate: FP / (FP + TN)



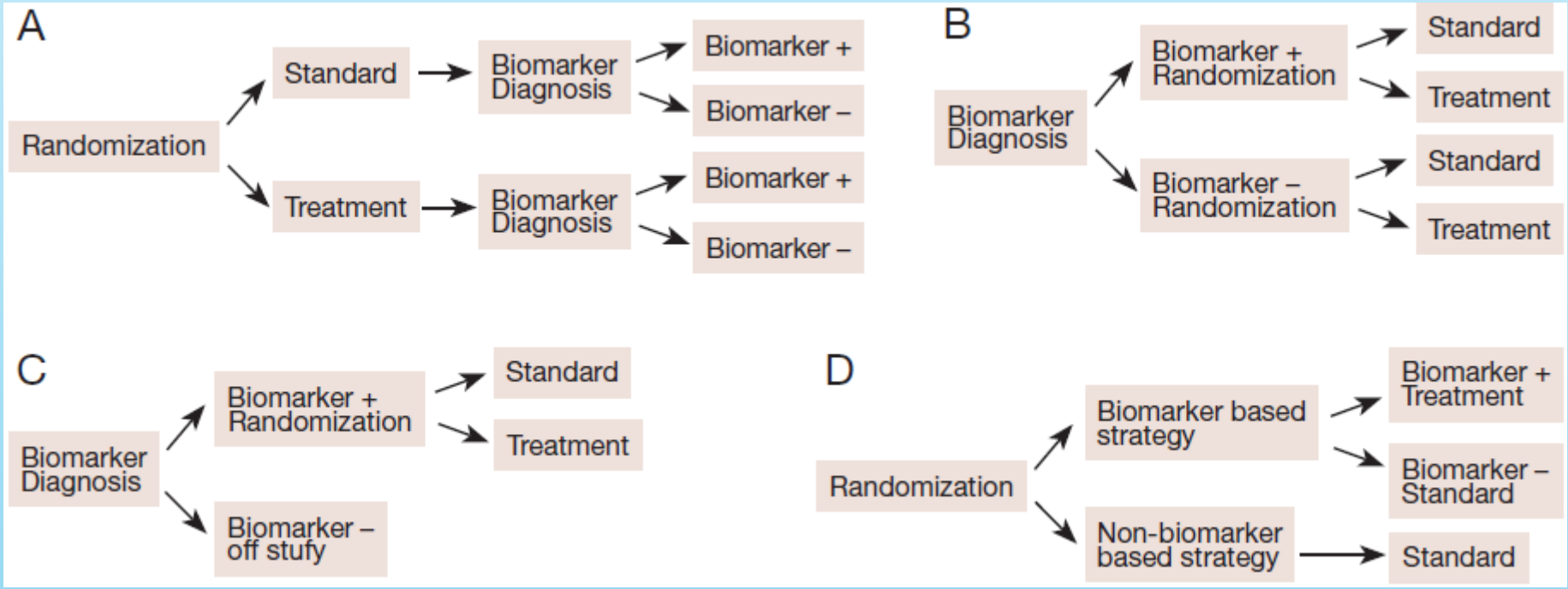
Precision Recall (PR):
Recall (completeness): TP / (TP + FN)
Precision (relevance): TP / (TP + FP)

Figure x. Receiver Operating Characteristics (ROC) and Precision Recall (PR) Curves, machine learning, and deep learning: Everything you need to know 22/02/2019 ;
ttps://clusterdata.nl/bericht/news-item/ai-machine-learning-and-deep-learning-everything-you-need-to-know/



Establishment of In onalized Healthcare: The To

Nobuo Fuse[1], Mika Ritsuko Shimizu[1,3], Gen Tam uchi[5], Kengo Kinoshita[1,6], S



http://investors.shire.com/~/media/Files/S/Shire-IR/agm-documents/agm-2017/annual-report-2016.pdf

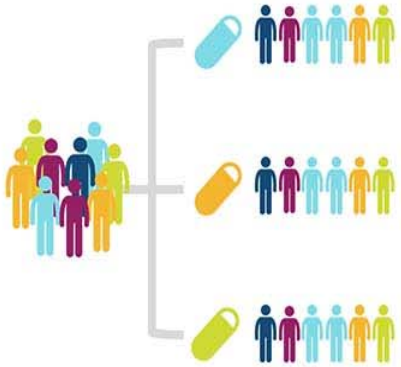
製薬協

Design concepts and terminology

Innovative clinical trial design to accelerate targeted combination therapies

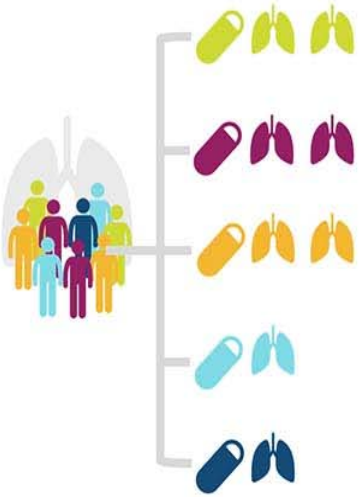
Conventional Multi-drug

A head-to-head study with no initial intent to add further therapies



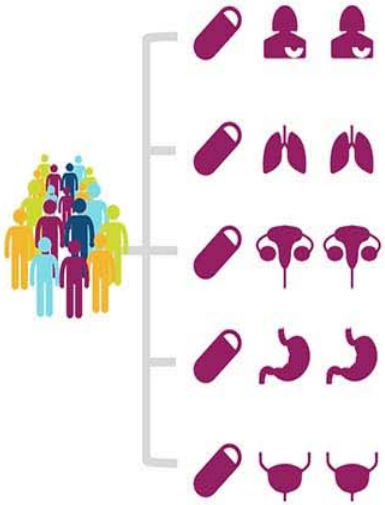
Umbrella trials

A study of therapies in the context of a single disease, often with prospective patient selection



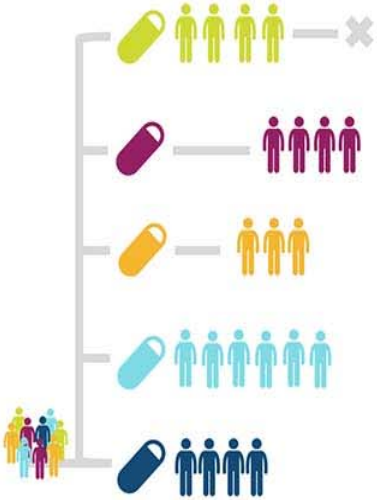
Basket Trials

A study of therapy/ies in the context of multiple diseases or disease subtypes



Platform Trials

A study of therapy/ies in an **open-ended manner,** with therapies allowed to enter or leave



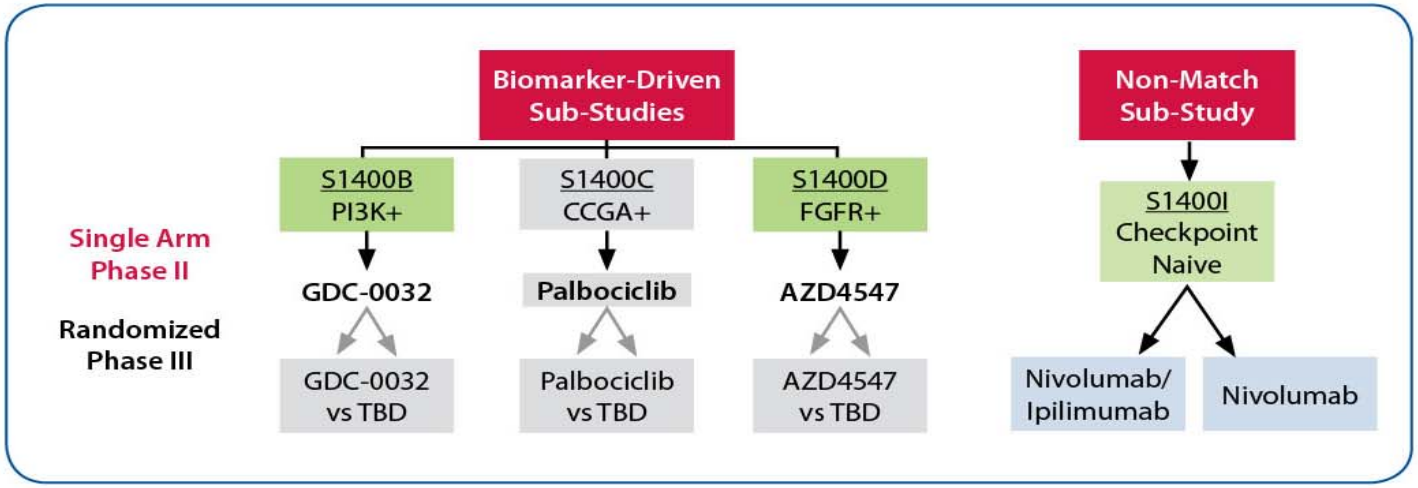


Figure 1. Current Lung-MAP schema. *CCGA = Cell Cycle Gene Alteration*

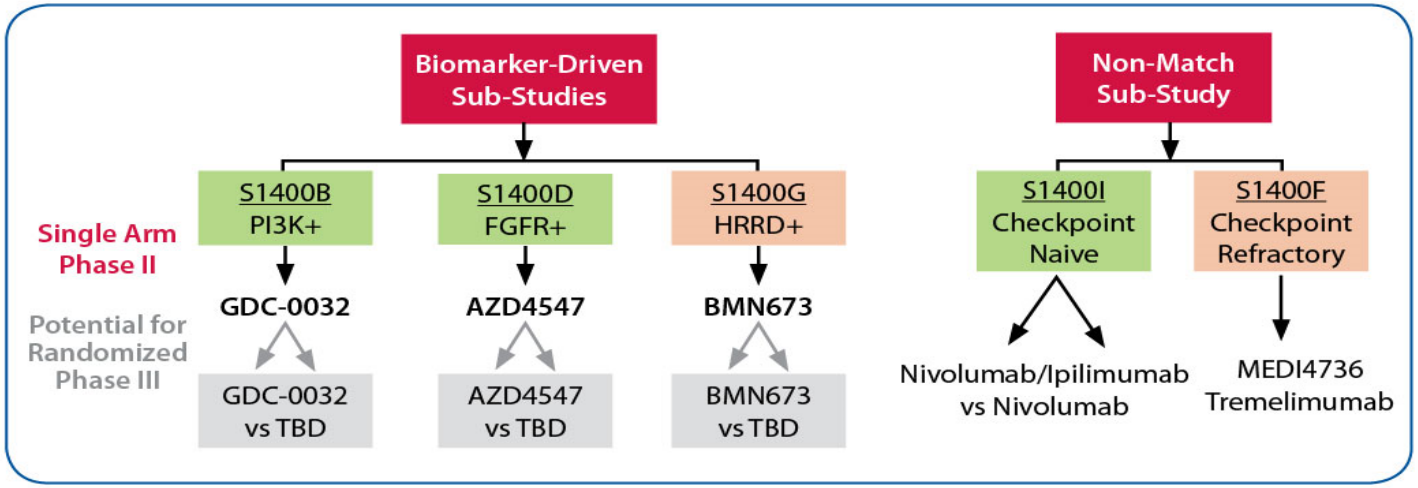


Figure 2. Lung-MAP upcoming protocol schema. *HRRD = Homologous Recombinant Repair Deficiency*

製薬協

Diagnostic Sequencing and Personalized Therapy

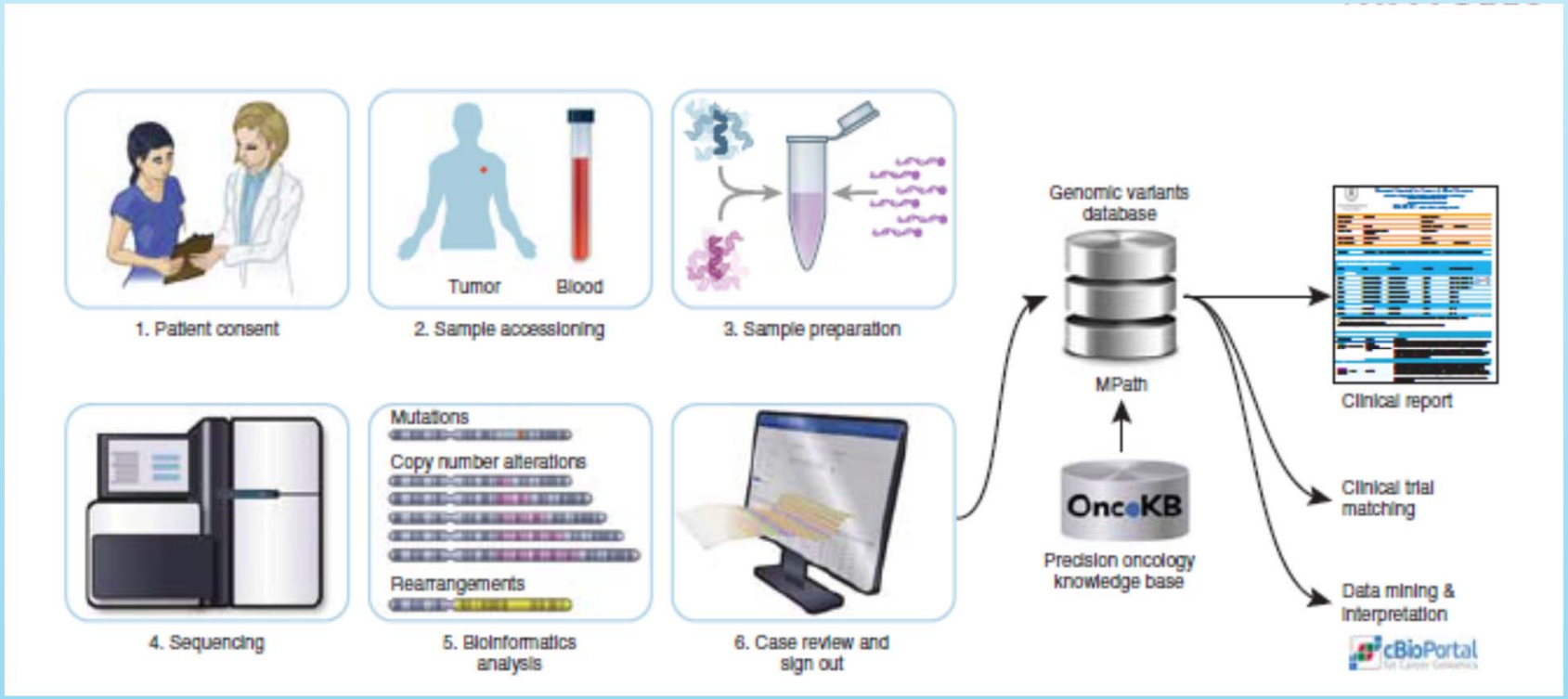
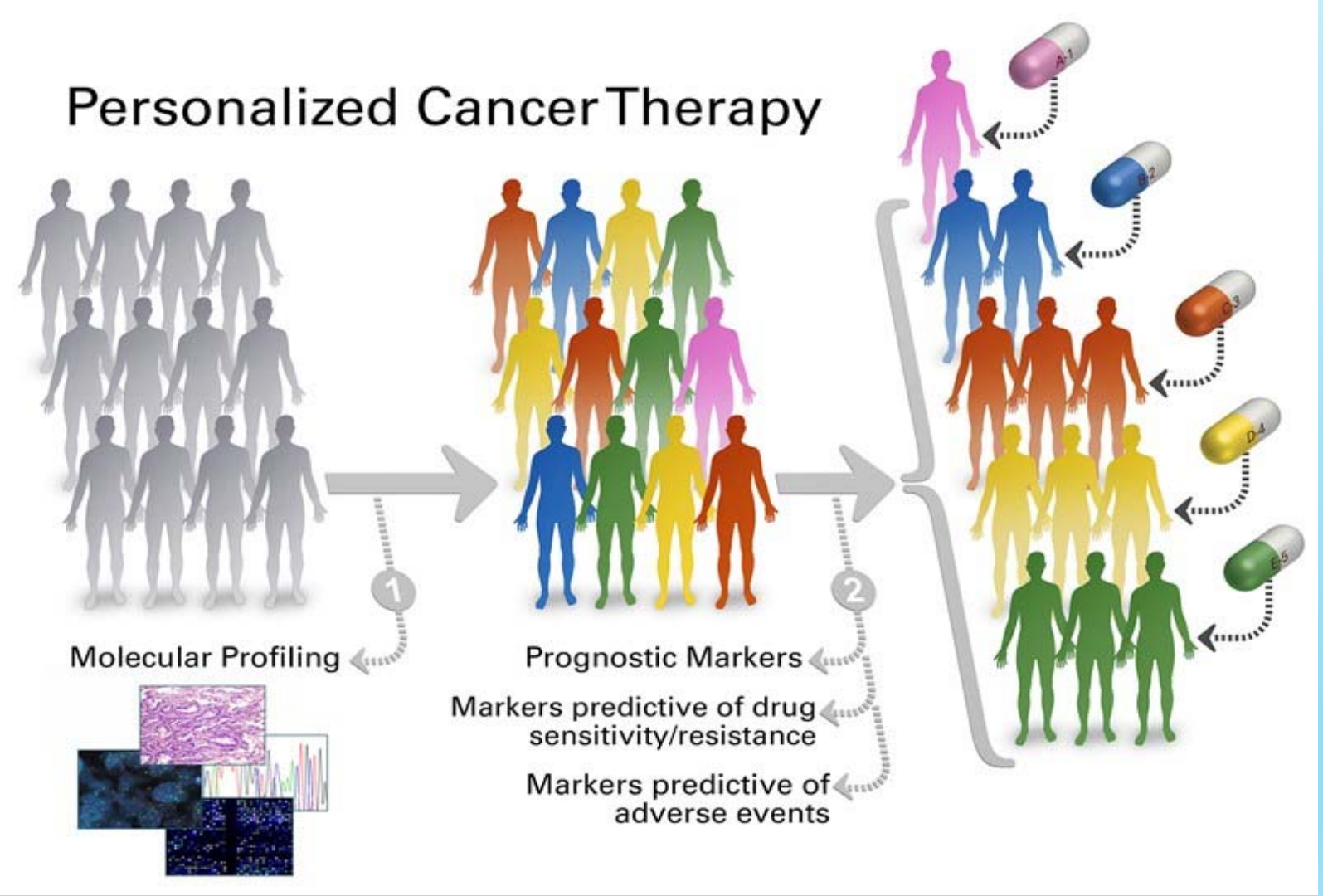


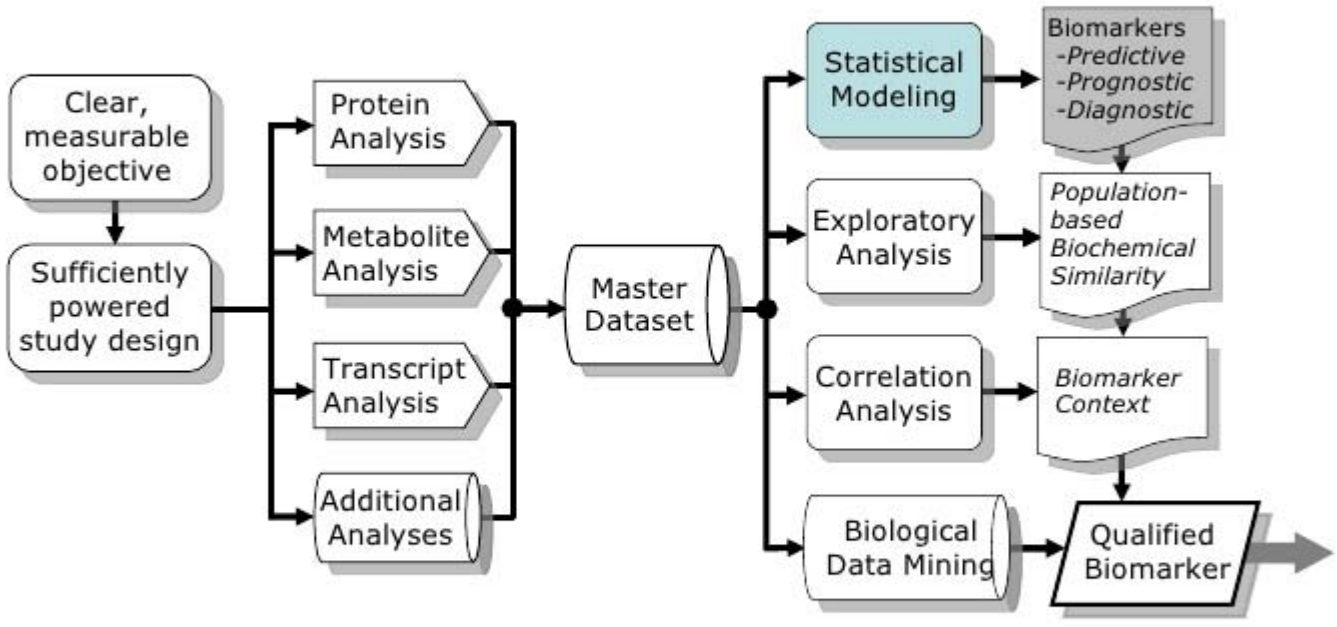
Figure 1 Overview of the MSK-IMPACT clinical workflow. Patients provide informed consent for paired tumor–normal sequence analysis, and a blood sample is collected as a source of normal DNA. DNA is extracted from tumor and blood samples using automated protocols, and sequence libraries are prepared and captured using hybridization probes targeting all coding exons of 410 genes and select introns of recurrently rearranged genes. Following sequencing, paired reads are analyzed through a custom bioinformatics pipeline that detects multiple classes of genomic rearrangements. Results are loaded into a genomic variants database developed in house, MPath, where they are manually reviewed for quality and accuracy. Genomic alterations are reported in the electronic medical record, transmitted to an institutional database (Darwin) that facilitates automated clinical trial matching and automatically uploaded to the cBioPortal for data mining and interpretation.

製薬協


Personalized Cancer Therapy
1
Molecular Profiling
2
Prognostic Markers
Markers predictive of drug sensitivity/resistance
Markers predictive of adverse events
A-1
B-2
C-3
D-4
E-5

製薬協

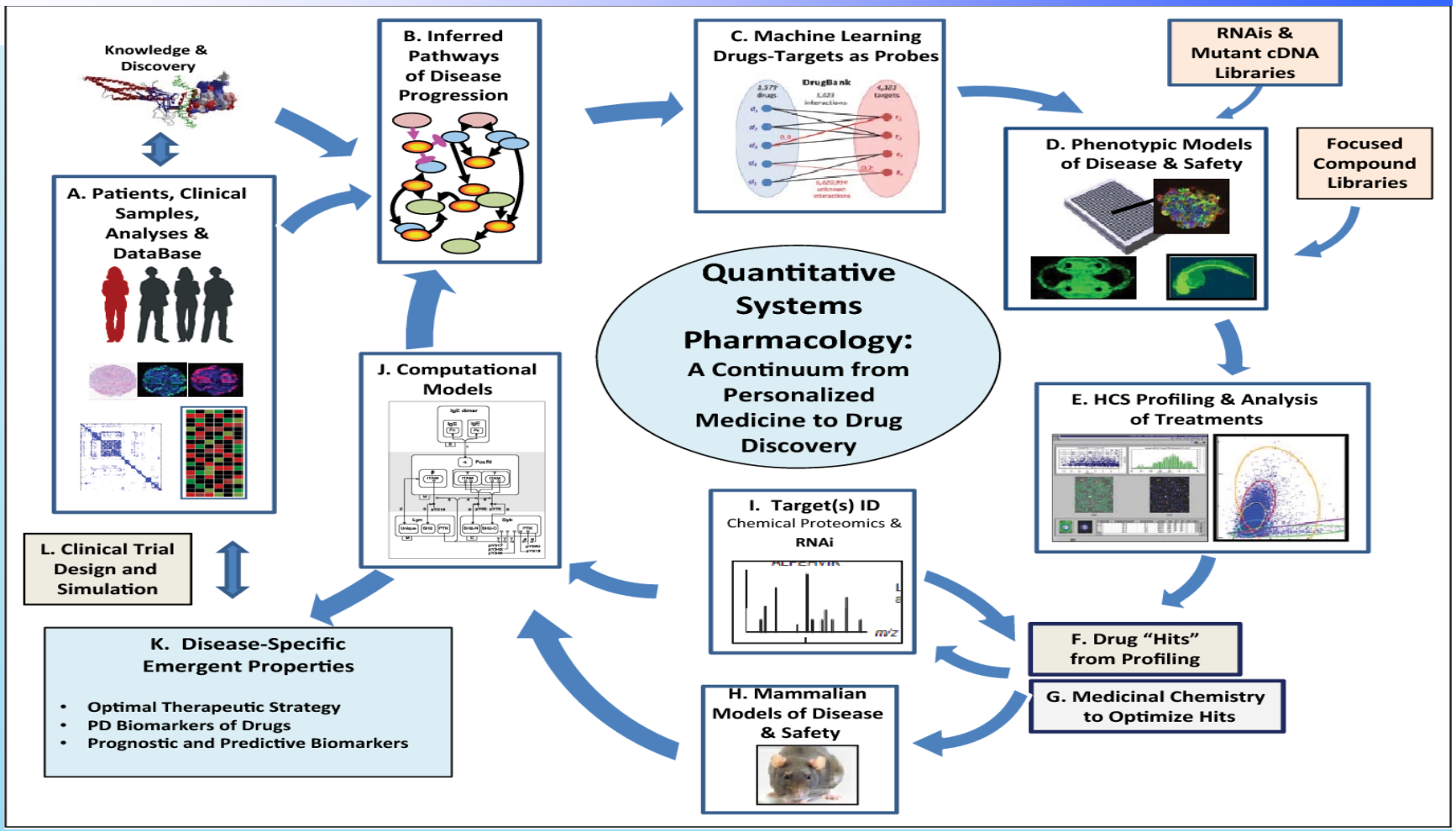
Molecular Systems Analysis – BGM Workflows



Fully Integrated Operations, QA/QC, IT
Data Mgmt, LIMS & Oracle Pipeline

The PRISM Forum

BGMEDICINE



Quantitative systems pharmacology platform for drug discovery and the advancement of personalized medicine being implemented at the University of Pittsburgh Drug Discovery Institute.

Published in Journal of biomolecular screening 2016, A Perspective on Implementing a Quantitative Systems Pharmacology Platform for Drug Discovery and the Advancement of Personalized MedicineAndrew M Stern, Mark E. Schurdak, Ivet Bahar, Jeremy M. Berg, D. Lansing Taylor