April 20 (Thu) - 22 (Sat), 2017 The Shilla Jeju Hotel, Jeju Island, Korea

obal Breast Cancer Conference

Education Session 1 New Issues in Cancer Research and Treatment 2017.4.20(Thu)4:00-5:10

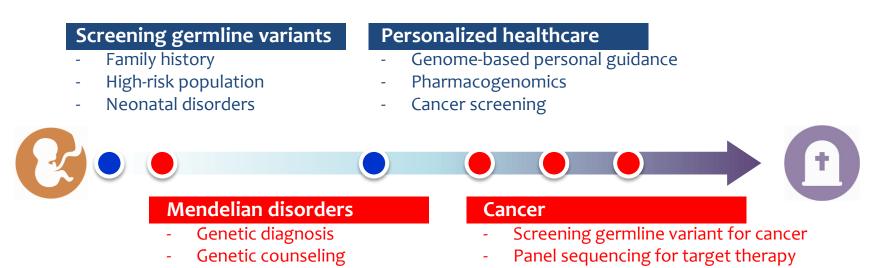
Actionable Genome Analysis for Human Cancer

Woong-Yang Park Samsung Genome Institute



Sequencing to save a life

Pre-clinical screening

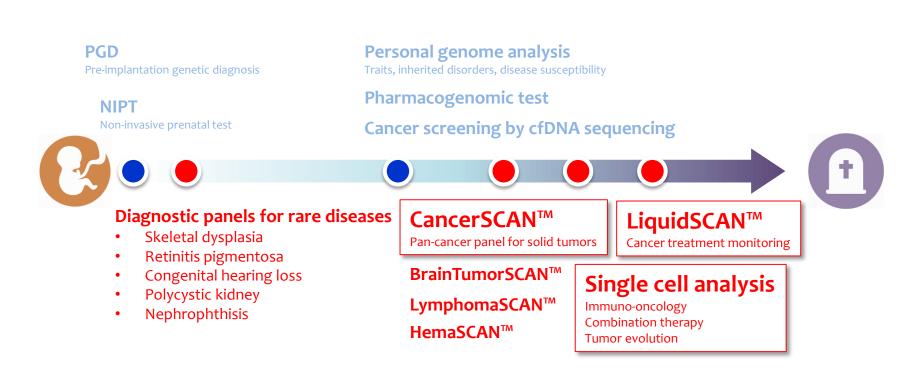


- Cell-free tumor DNA sequencing

Clinical diagnosis and monitoring

Actionable genome sequencing in hospital

Pre-clinical screening



Clinical diagnosis and monitoring

CancerSCAN[™], targeted deep sequencing for cancer

Panel information

Hybrid-capture on 375 cancer related genes

- Hotspot variants including 287 SNVs, 26 small indels, 17 CNVs, 13 fusions
- Detection of microsatellite instability using 113 target regions

Sample requirements and sequencing

- FFPE or fresh frozen samples
- >50ng of gDNA (tumor only)
- ~1,000x read depth in average

Analytical performance (Sensitivity)

- SNV/InDel: 99.1% / 96.4%
- CNV: 93.7%
- Fusion: 100% / 100%
- Microsatellite instability
- Tumor purity/tumor heterogeneity
- Chromosomal abnormality

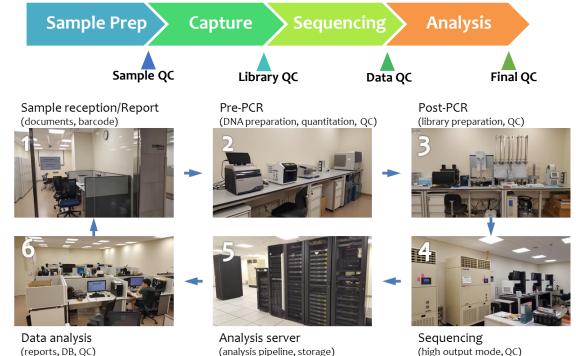
Report

- Class 1: Validated in target cancer
- Class 2: Clinical evidence in target cancer
- Class 3: Validated in other cancer
- Class 4: Clinical evidence in other cancer
- Class 5: Any evidence in all cancer types
- VUS (variant of unknown significance)



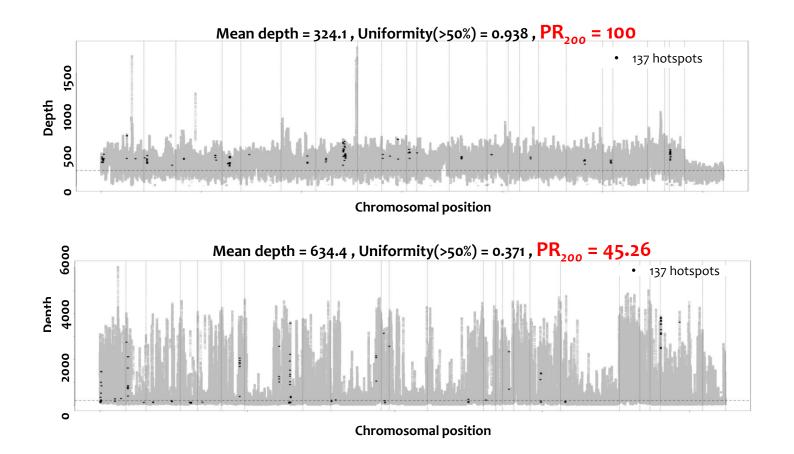
Quality management (QM) program

- Four quality control (QC) points per sample collected and reported to users; 1) genomic
 DNA samples, 2) sequencing library, 3) sequencing raw data, and 4) final report.
- We run a quarterly internal QC program for the bait, library, sequencers, additional machines, individual researchers.
- We undertake proficiency testing by several institutes such as College of American Pathologists (CAP) and The European Molecular Genetics Quality Network (EMQN).
- All experimental and bioinformatics process documented as standard operating procedure (SOP).



PR (Pass Rate) score for quality control of panel sequencing

A new scoring method for assessing the quality of clinical gene-panel sequencing data, specifically for the detection of a set of single nucleotide variants.



Shin SH et al. Journal of Molecular Diagnostics in revision

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PIK3CA (n=487)

100

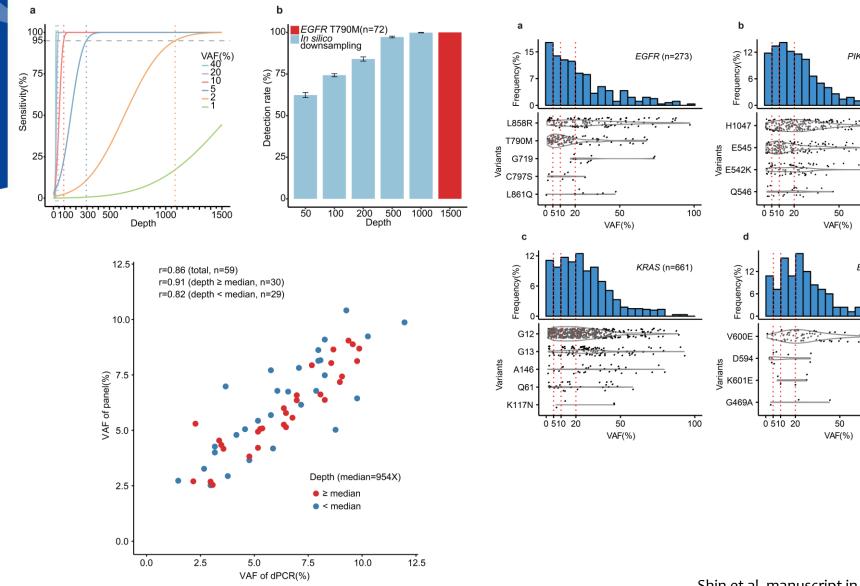
100

BRAF (n=86)

50

50

Detection of low allele fraction variants

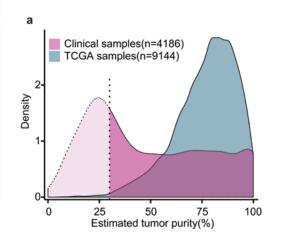


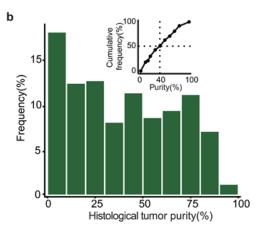
SAMSUNG GENOME INSTITUTE

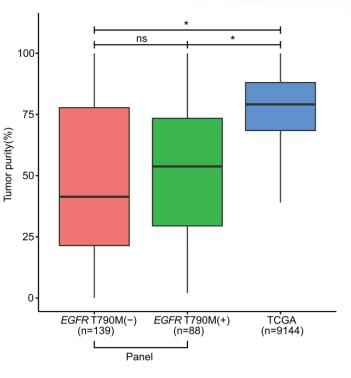
Shin et al. manuscript in review

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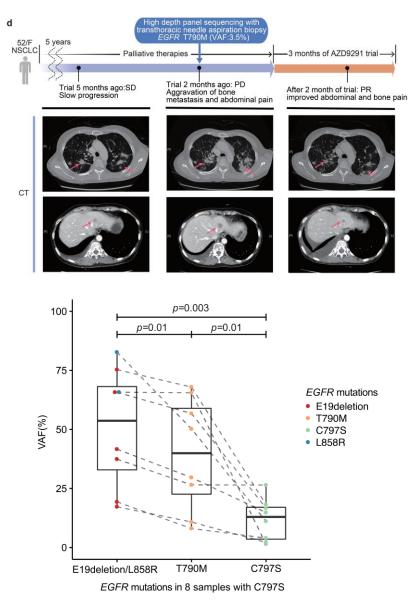
Low tumor purity of clinical samples

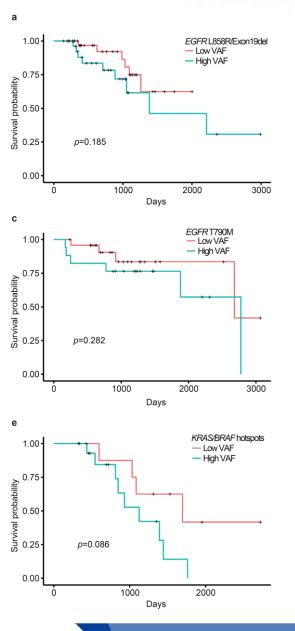




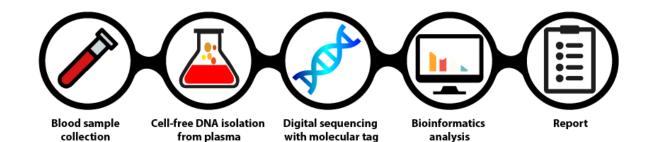


Response to target therapy for low allele fraction variants





LiquidSCAN[™], targeted ultra-deep sequencing for liquid biopsy



Sample requirement	Plasma (5ml) or whole blood (10ml)
Sequencing Method	Illumina NGS using a proprietary library construction method
Variants	SNV/Indel/CNV/Fusion
Report	Summary of variants with therapy options including clinical trials
Turn around time	3 weeks

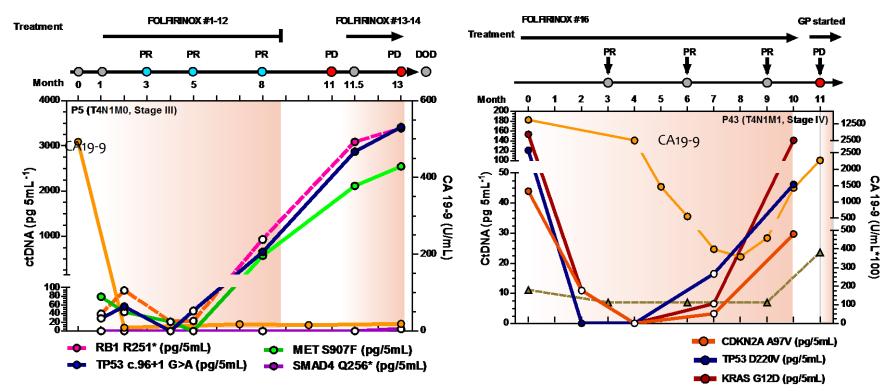
Performances (17.1Q)

Limit of detection	
SNV	>0.1%
Indel	>0.5%
Amplification	>4-fold; 20%
Fusion	>0.1%

>95% sensitivity and >95% specificity

Patient monitoring with LiquidSCAN[™] in pancreatic cancer

- Pancreatic ductal adenocarcinoma (PDAC) is a devastating disease and the seventh leading cause of cancer death in the world. Although carbohydrate antigen 19-9 (CA 19-9) has been tested for its clinical usefulness in pancreatic cancer, the sensitivity and specificity of CA 19-9 are not sufficient for an early detection marker.
- The levels of ctDNAs measured by LiquidSCAN[™] better correlated with clinical responses to therapy and disease progression than serum CA 19-9. Moreover, the alterations in ctDNA level were on average 2.1 months ahead of imaging changes.

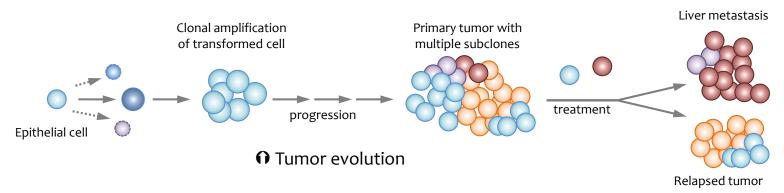


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Park G, Park JK et al Genome Biology in revision

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Single cell genome analysis



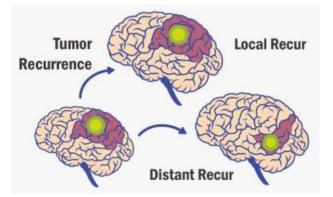
O Tumor heterogeneity

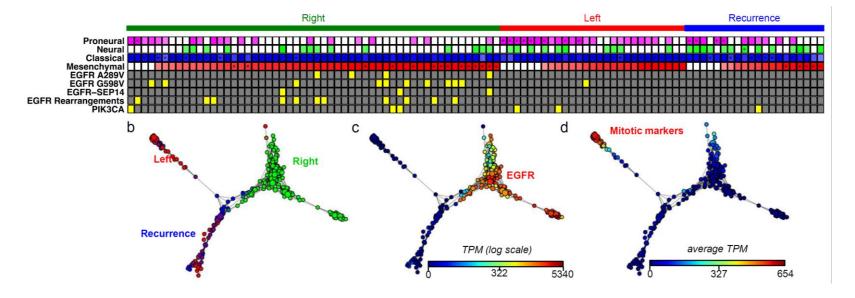
• Circulating tumor cells

Cancer stem cells(rare cell population)Subclonal differencesin drug response

O Tumor microenvironment

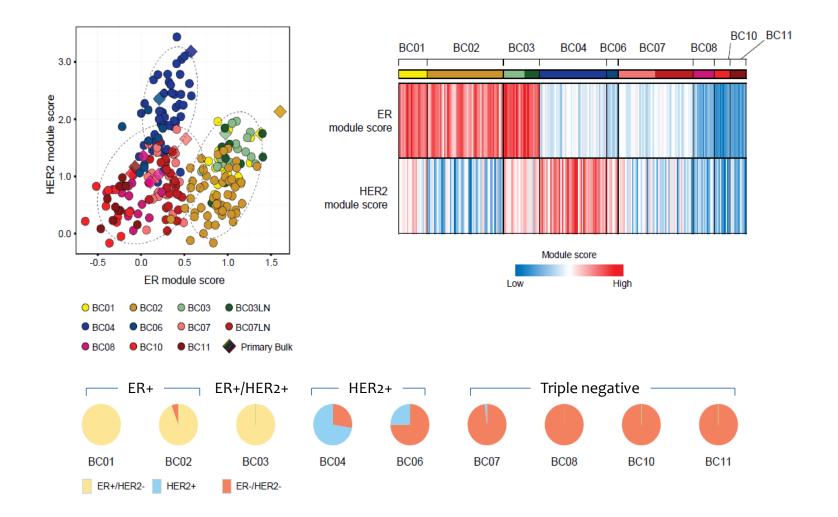
Single cell analysis to understand tumor evolution



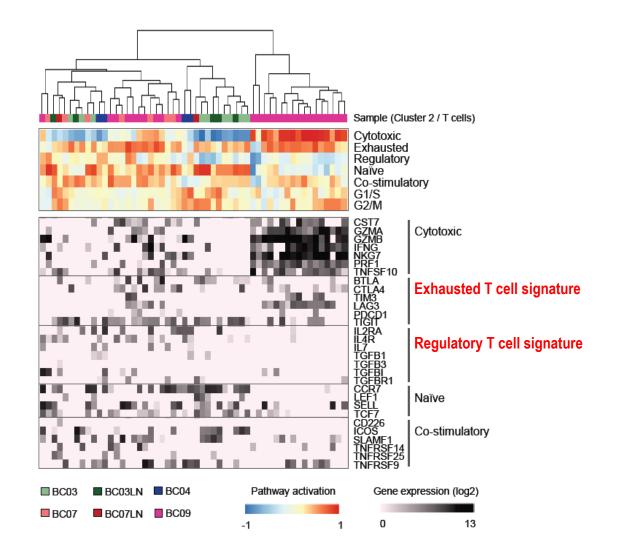


Lee JK et al. Nature Genetics 2017

Mixed subtype single cells in breast cancer

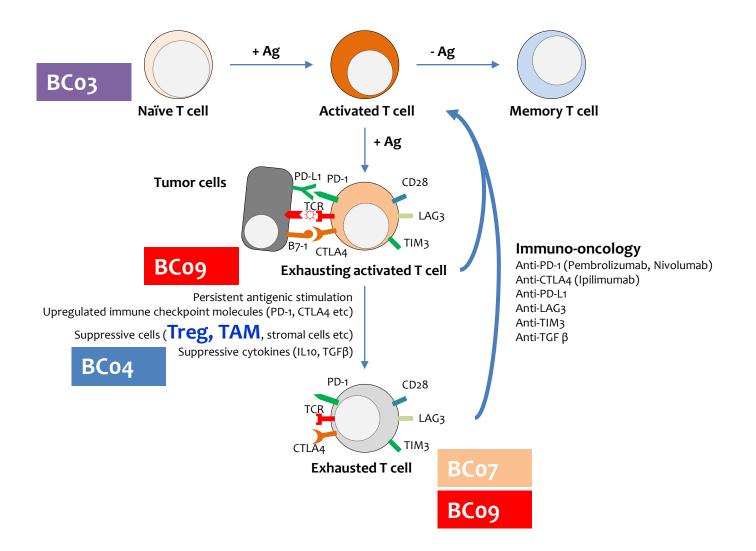


Tumor-infiltrating T cells in breast cancer

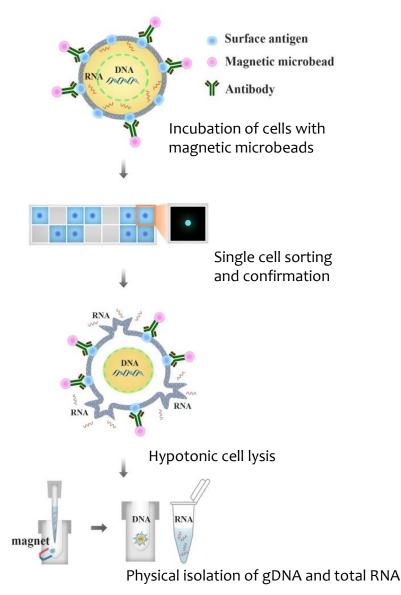


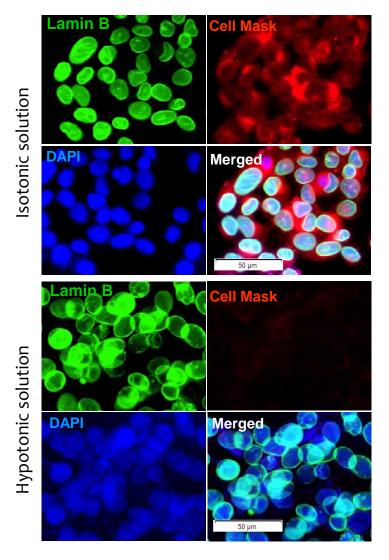
Chung WS, Eum HH, Lee HB et al. Nature Communications 2017

Exhaustion of tumor-infiltrated T lymphocytes



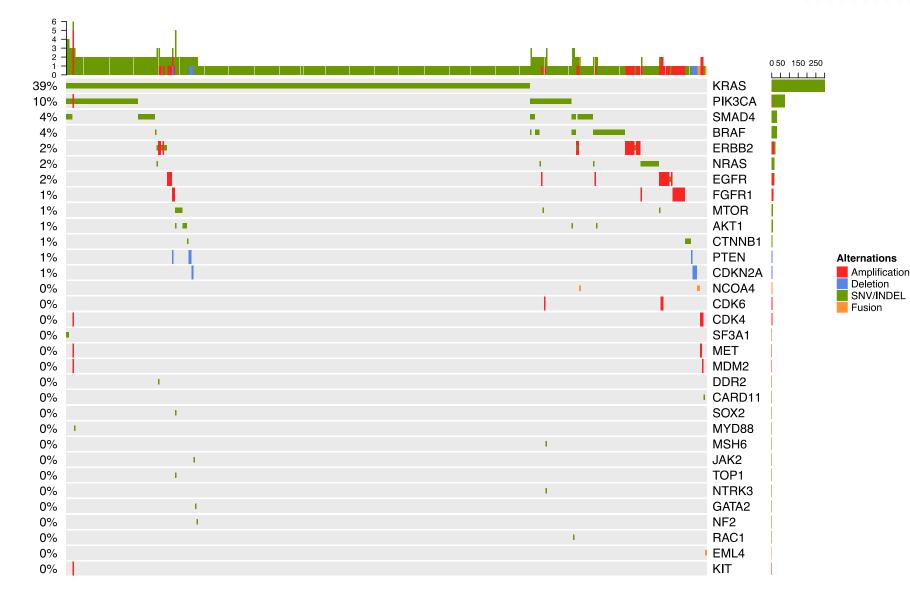
SIDR, Simultaneous isolation of DNA/RNA from single cells



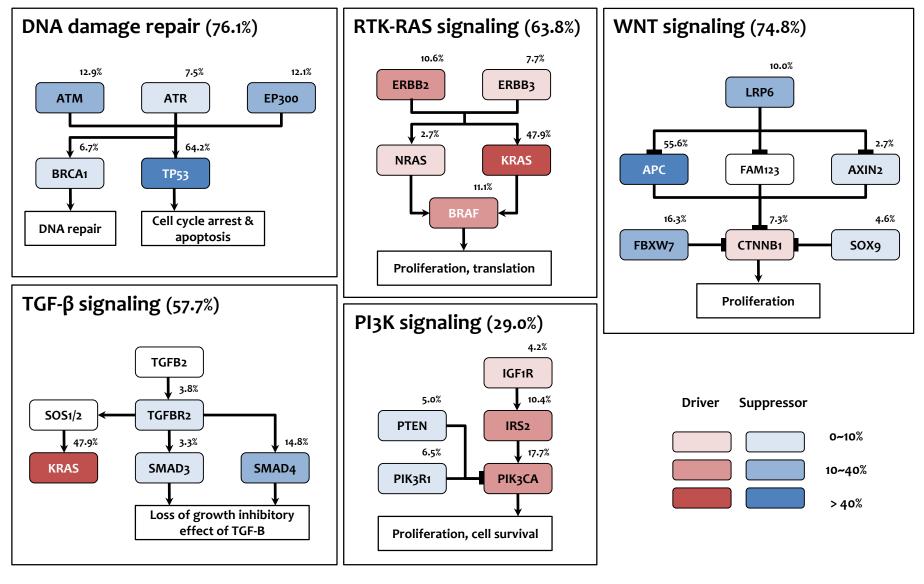


Han KY et al. manuscript in review

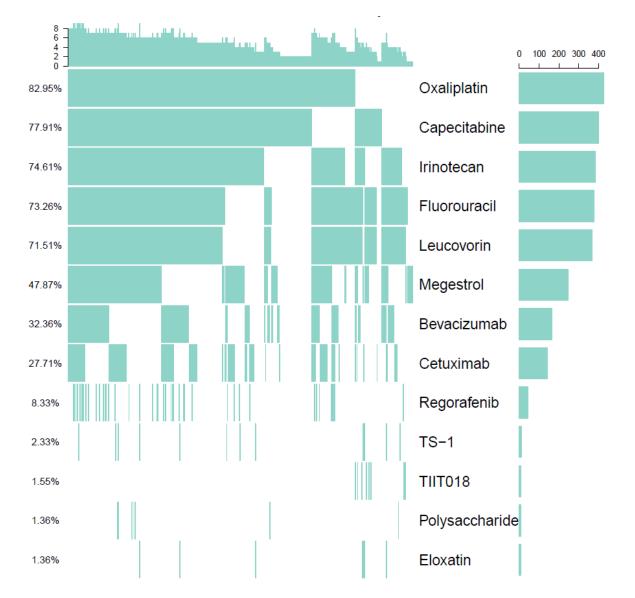
Mutational landscape of colorectal cancer



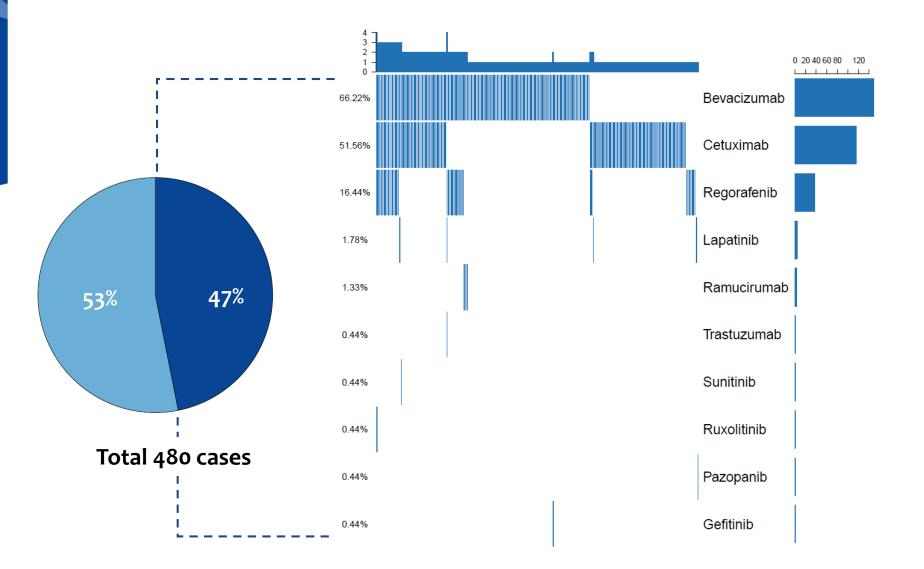
Recurrent mutations in oncogenic pathways



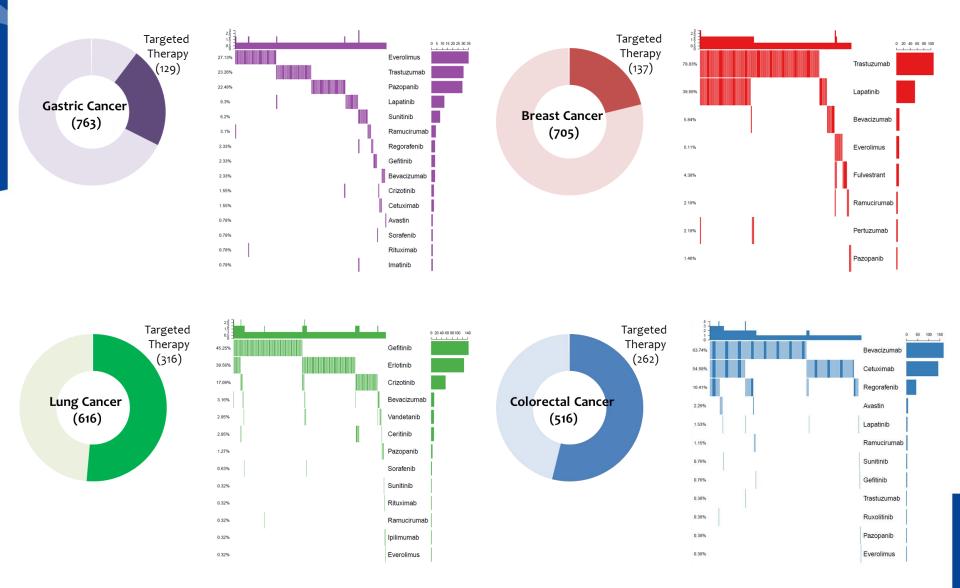
Treatment history of colorectal patients



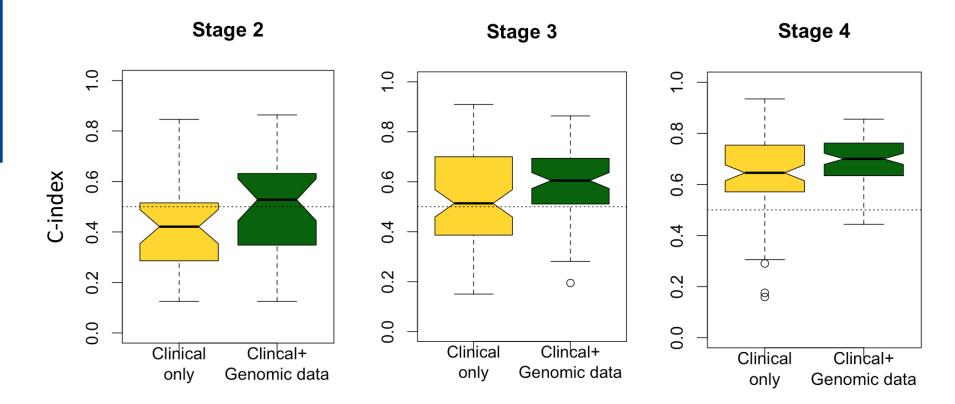
Colorectal cancer targeted therapy



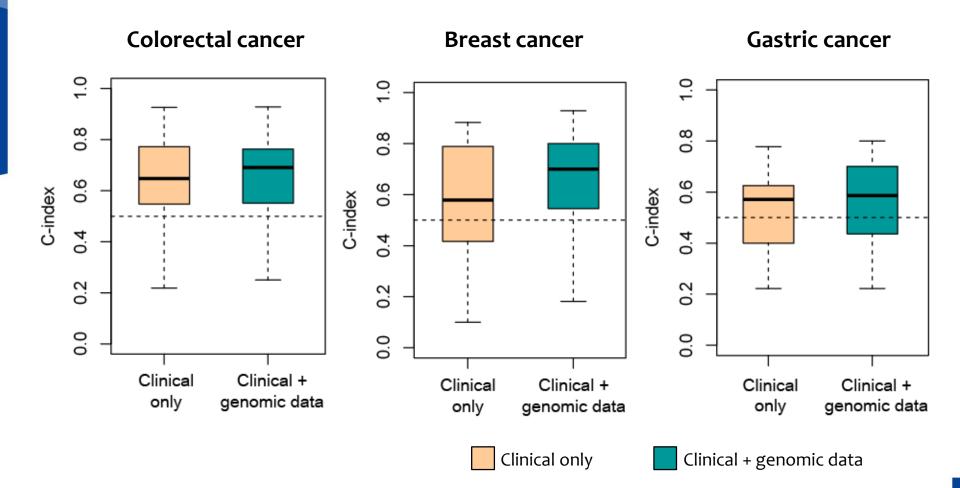
Targeted therapy in personalized medicine clinic



Combined prognostic markers (stage)



Combined prognostic markers (cancer types)



Network for integrated genomic and clinical data

Genome Data Bank

- Clinical grade sequencing data
- Structured clinical information
- Matched samples in biobank
- Global data sharing

Providing open platform for

Diagnostics development and service CDSS modeling for precision medicine

Biomarker discovery for diagnostics

Drug development on new targets

Acknowledgement

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