

Genomics

Apply Genomics to Precision Medicine

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National Cancer Institute*

*TRACO
October 31, 2022*

Outline

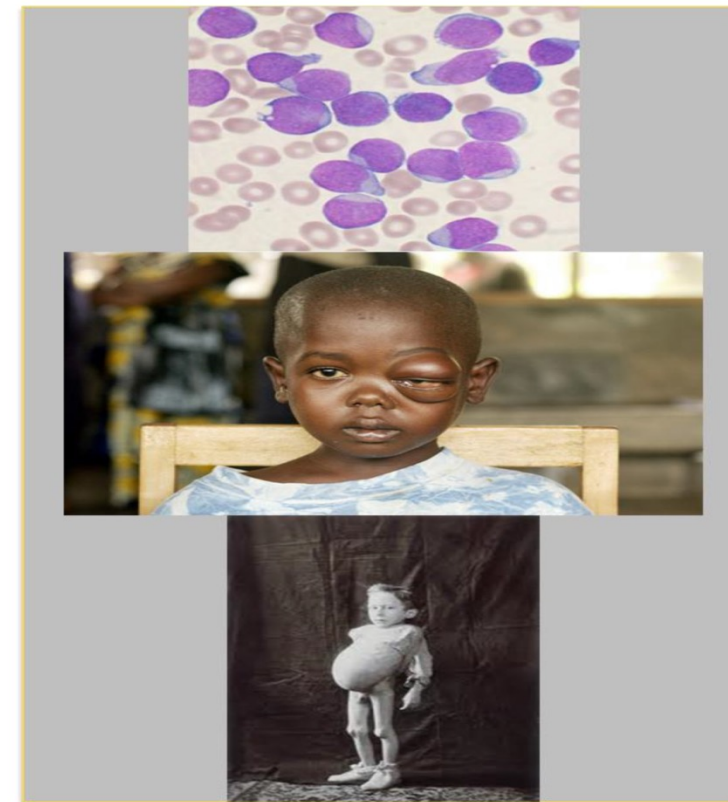
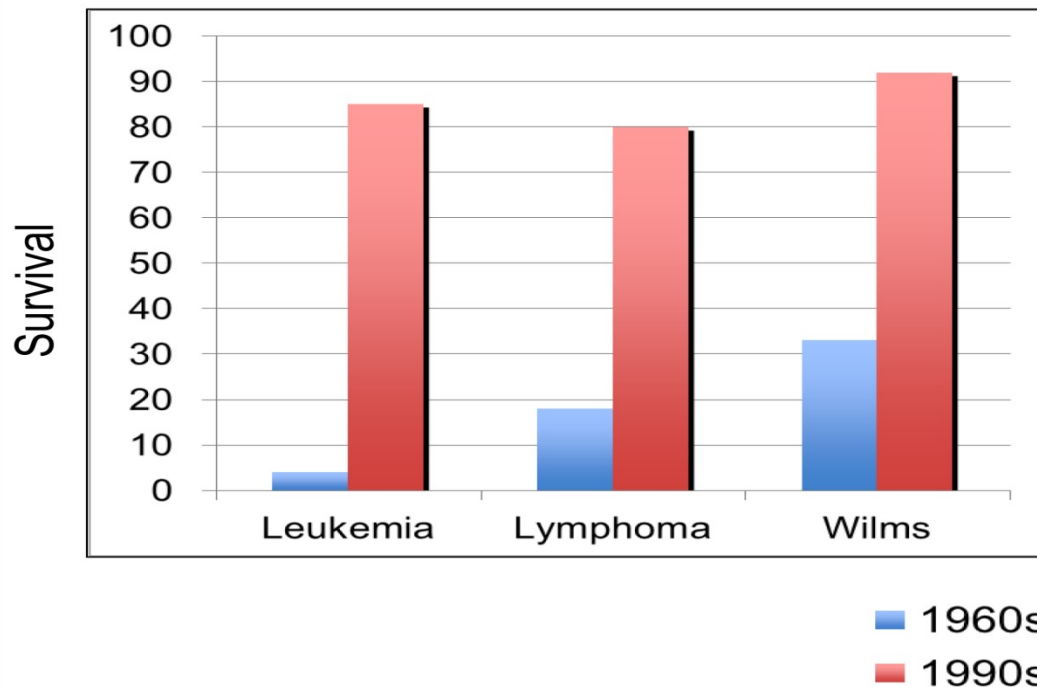
Outline

- **Success and Challenges of Treating Pediatric Cancers**
- **Genomics**
- **Tool to study genomics: Next-generation Sequencing**
- **Precision medicine – an application of genomics**

Childhood cancer

National Cancer Institute

Childhood cancer: The beginning of a modern medical success story

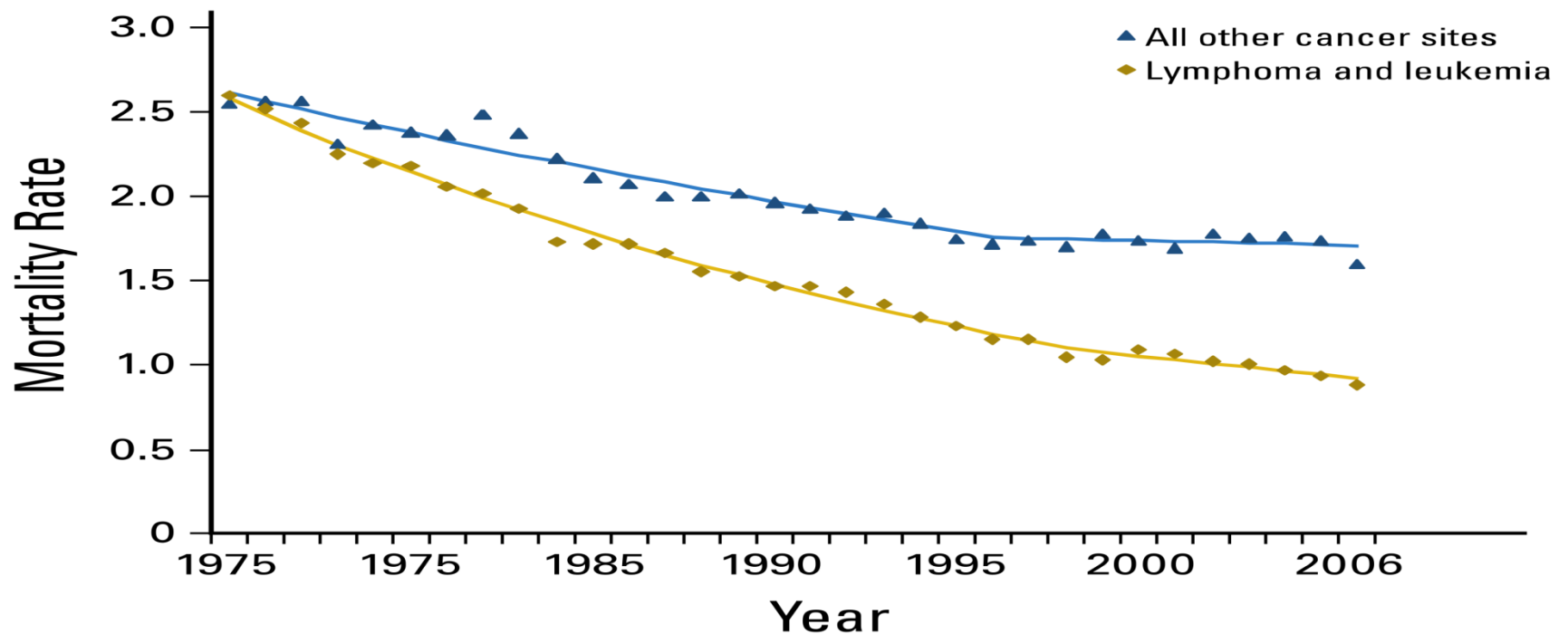


Courtesy: John Maris

Mortality rates

National Cancer Institute

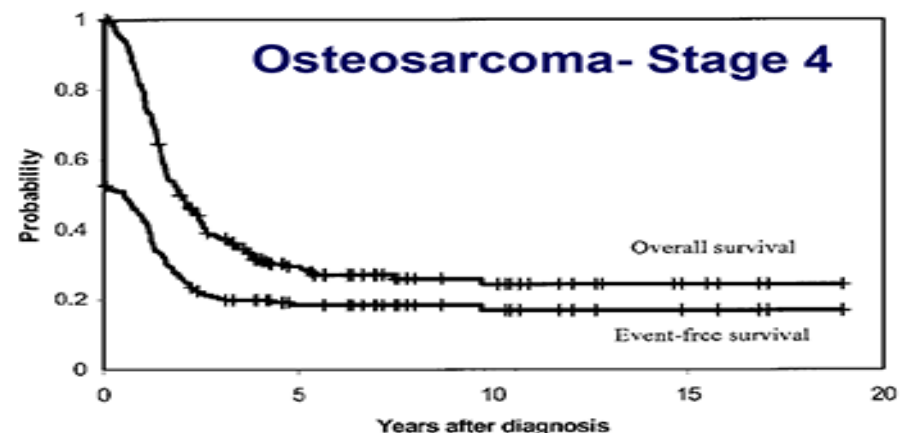
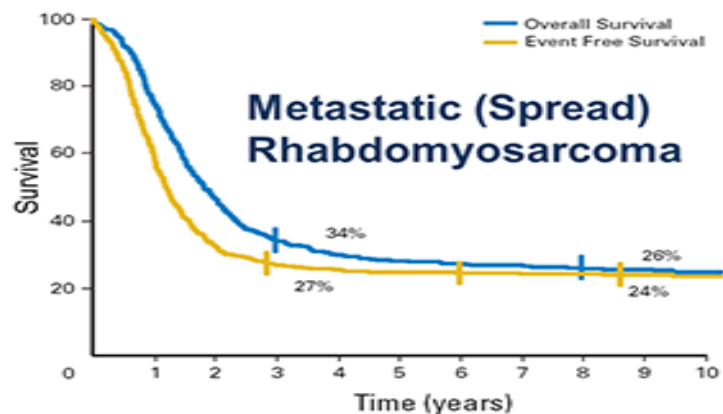
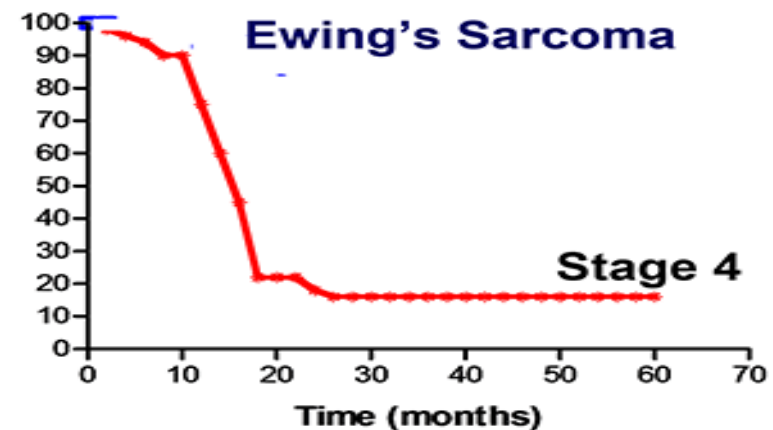
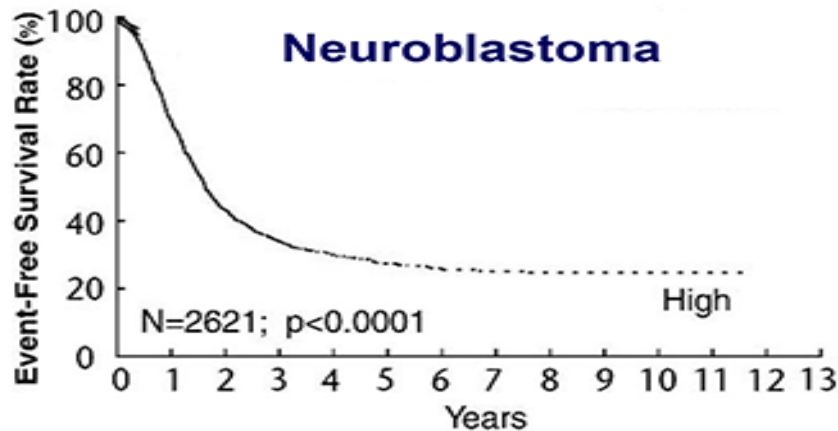
However in the past 16 years no improvement in mortality rates despite increased intensity of treatment



Courtesy: Malcolm Smith

Pediatric cancers

Metastatic, Recurrent, & Refractory Disease Remains Incurable



Gene expression

The dramatic consequences of gene expression in biology



Anise swallowtail, *Papilio zelicaon*

Same genome →
Different expression pattern
Different proteome
Different tissues
Different physiology

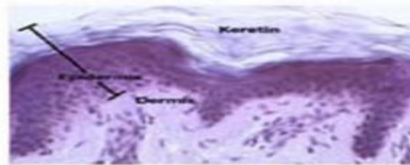


Gene expression

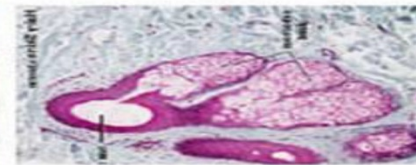
...but the complexity and diversity

Same genome or DNA →

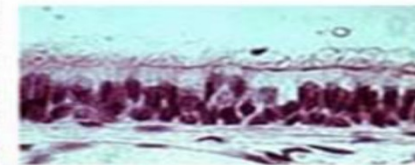
- Different expression pattern
- Different proteome
- Different tissues
- Different physiology



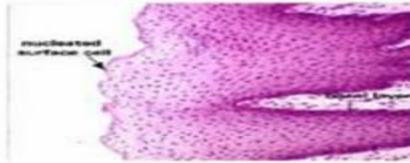
skin



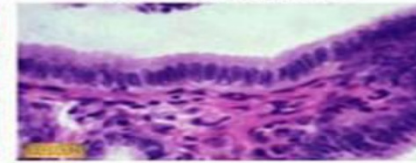
sebaceous gland



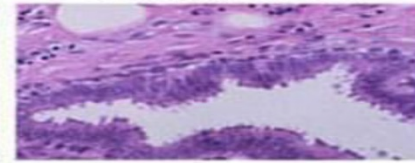
airway epithelium



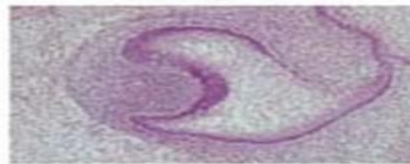
tongue



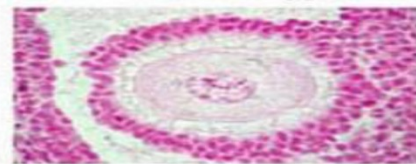
intestinal crypt



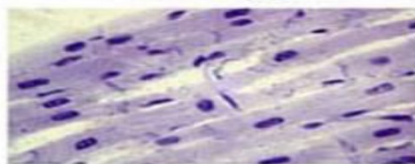
mammary gland



developing tooth



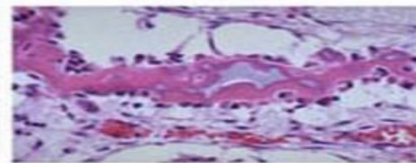
follicle



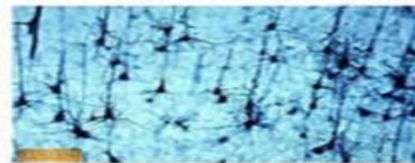
skeletal muscle



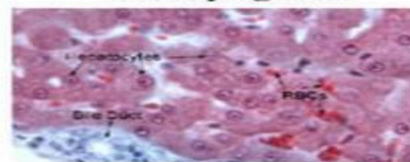
developing bone



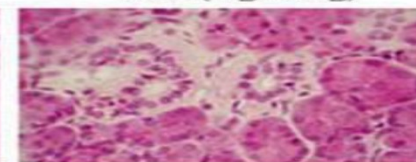
bone (high mag)



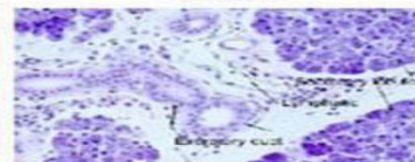
neuron



liver



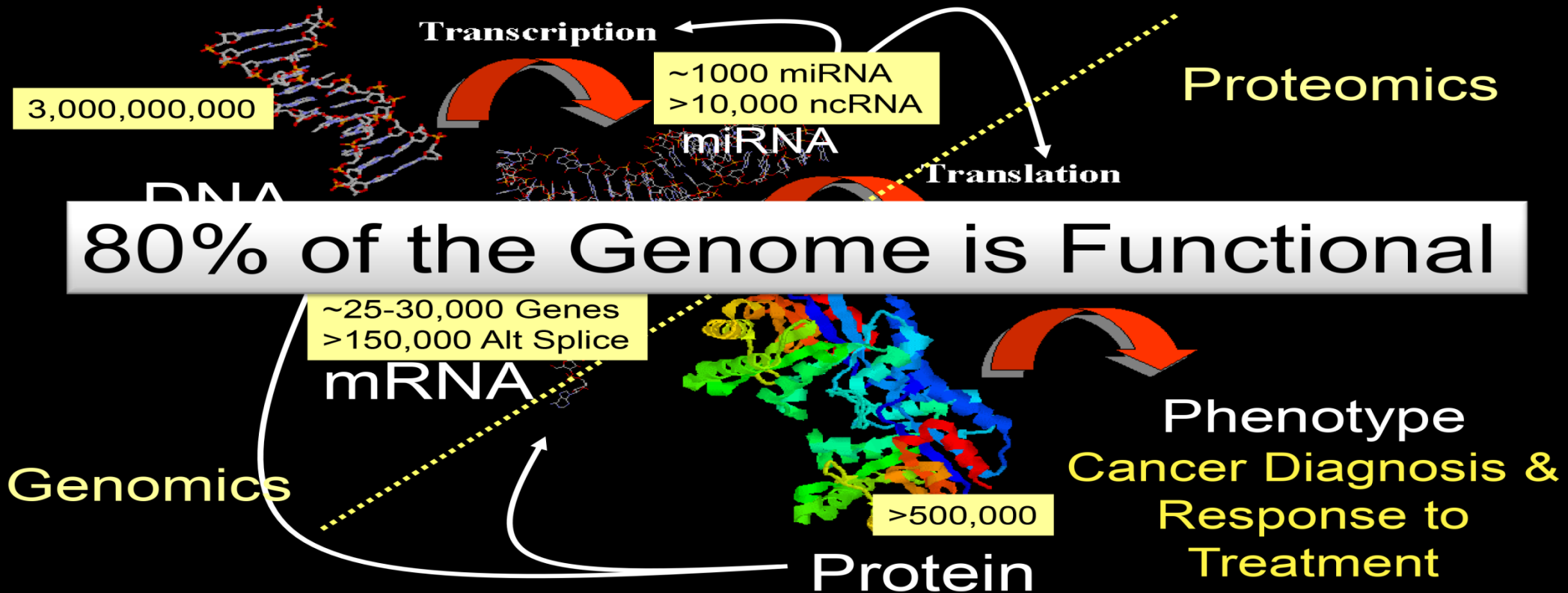
pancreas



parathyroid gland

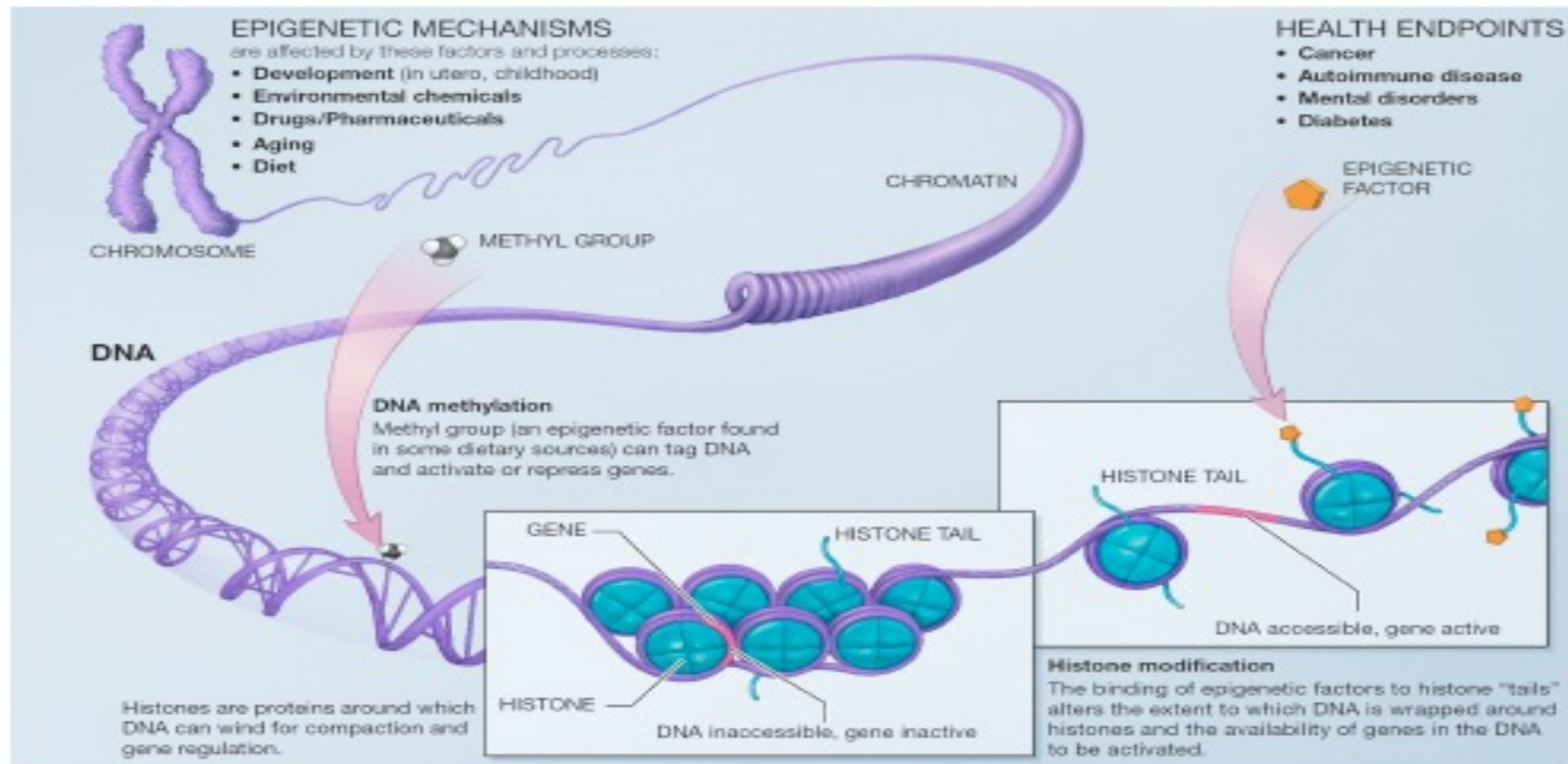
Gene expression

Biology is driven by the simultaneous expression of large numbers of genes acting in concert

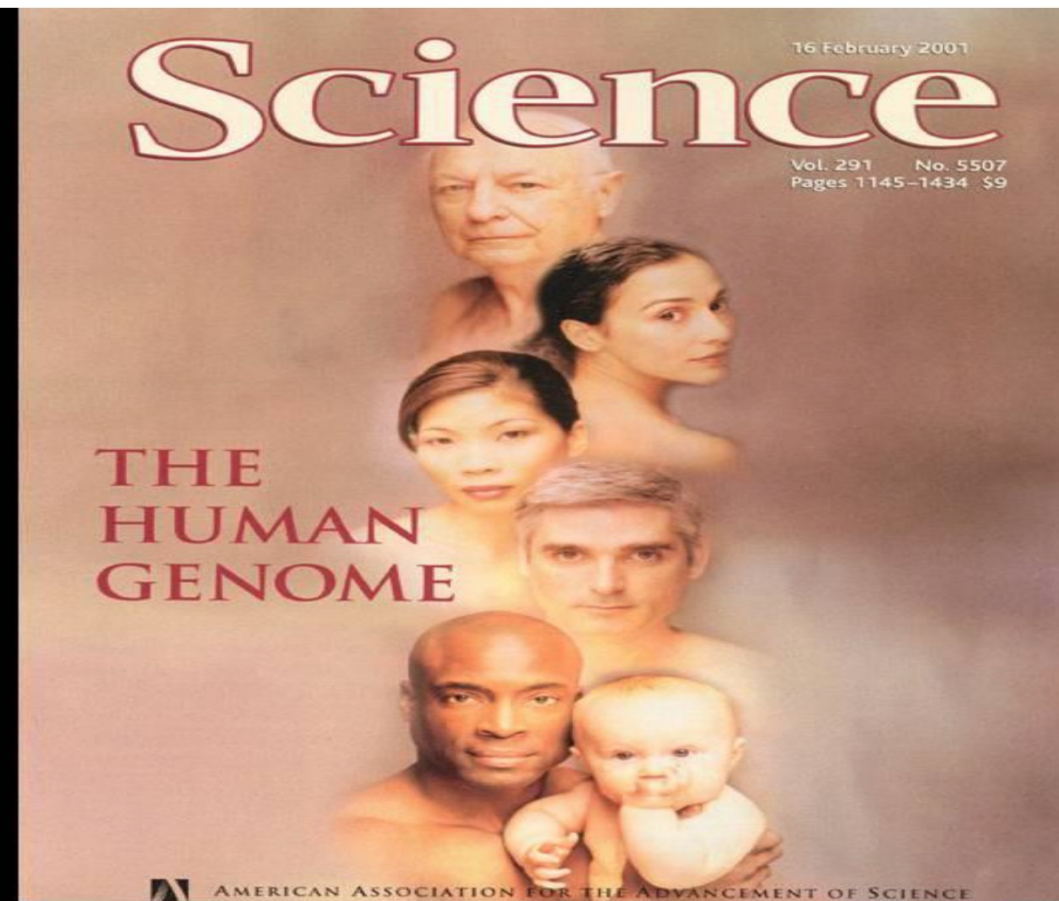


Epigenetics

Epigenetics controls gene expression



Human genome



Challenge

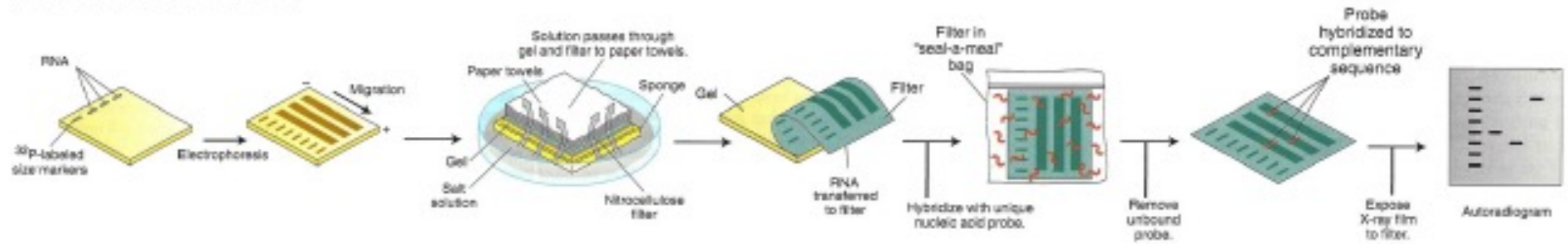
Challenge: how to measure/detect genes and their products in a massively parallel way?

- **High-throughput technologies**
- **Computational power**

Gene expression

How to measure the expression of genes

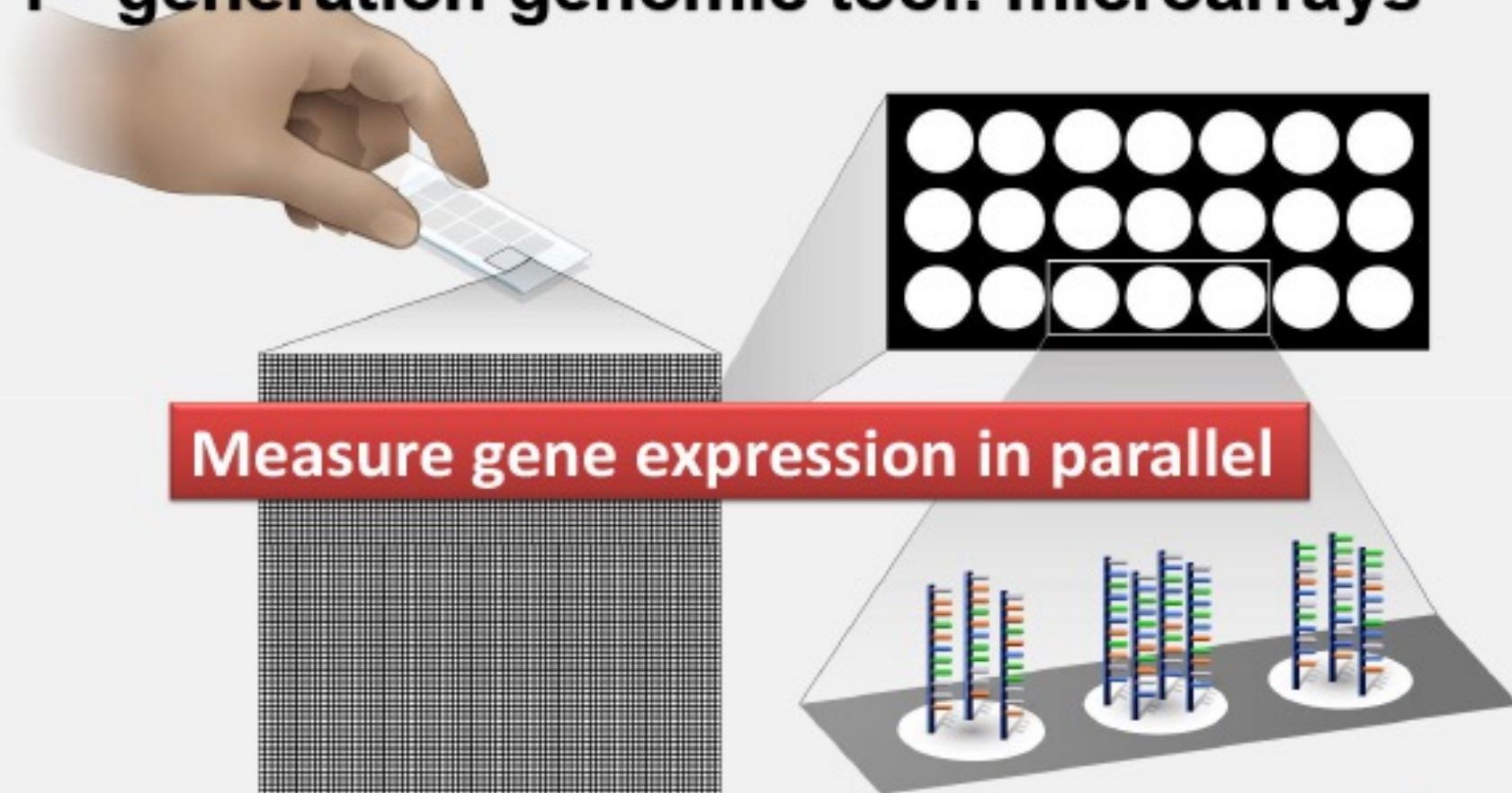
Northern blot



laborious and low throughput

Microarrays

1st generation genomic tool: microarrays



First generation tools

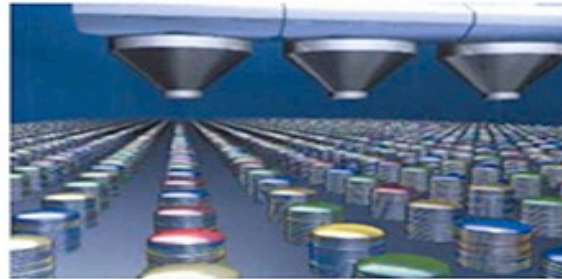
1st generation genomic tool: microarrays

Printing microarrays

Mechanical

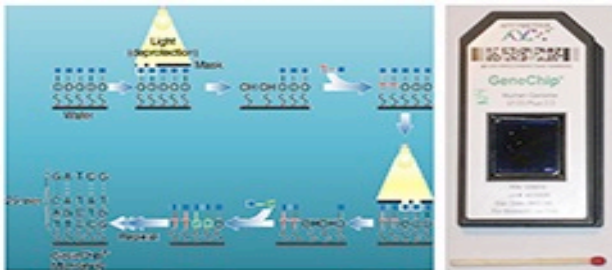


Electronic Piezo

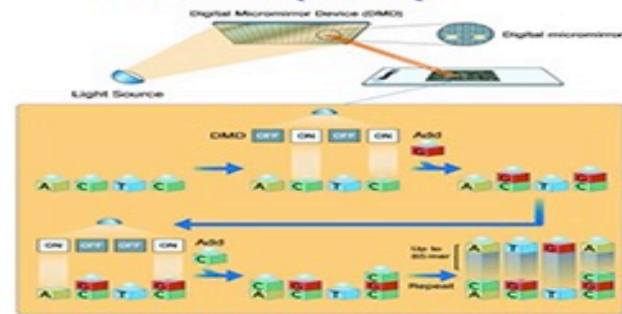


In-situ synthesis microarrays

Lithographic masks
and de-protection
through illumination

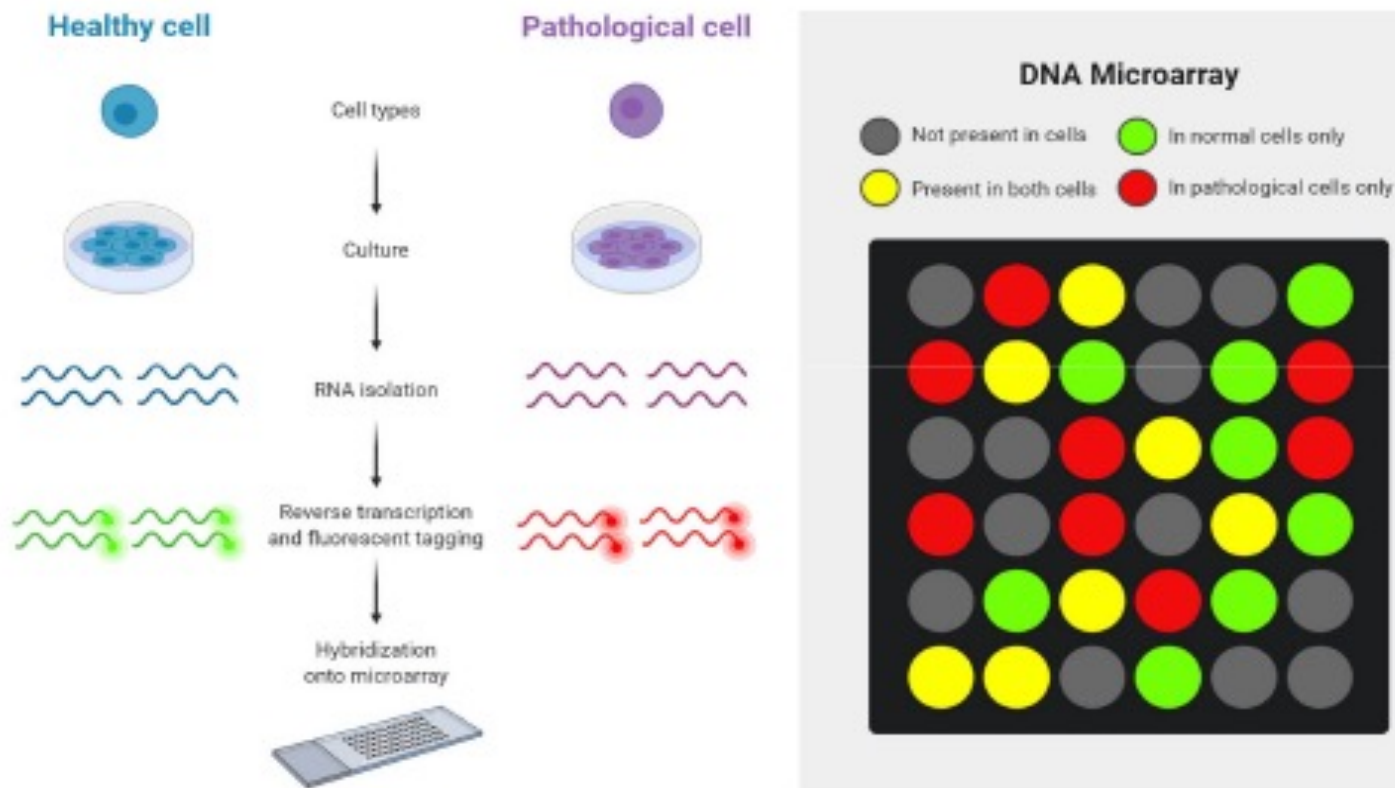


Digital micromirror
device (DMD)



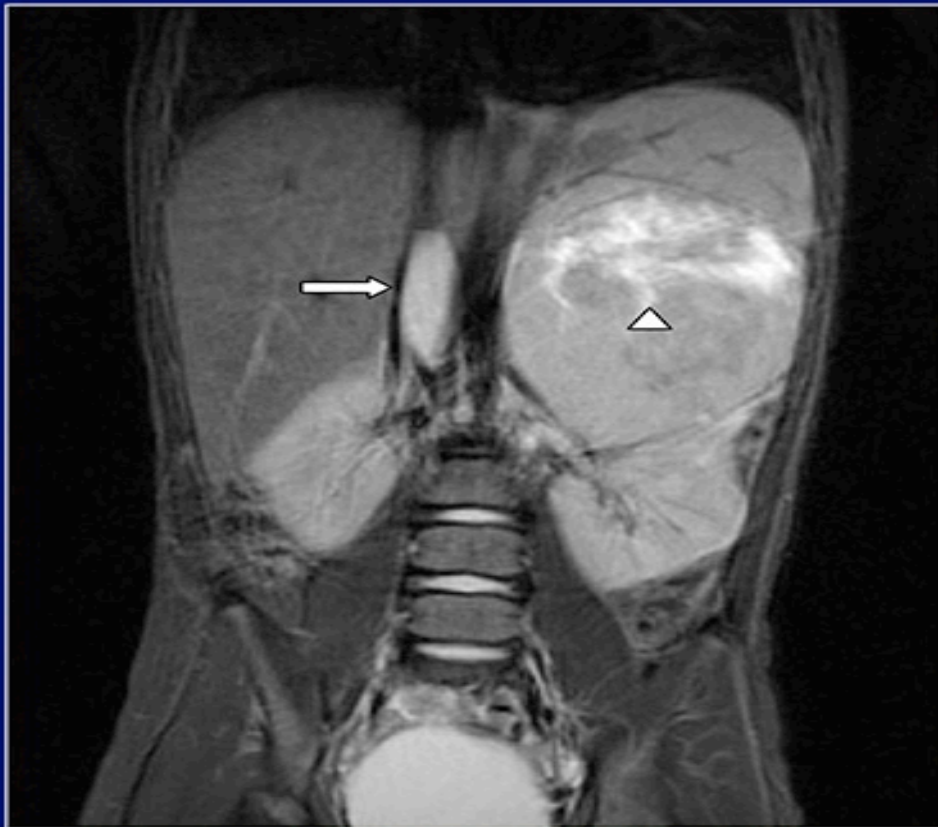
Microarrays

Microarrays – technologies of hybridization



Wilms tumor

MRI: 9 x 8 x 9 cm mass in upper pole left kidney, tumor in Left renal vein and inferior vena cava

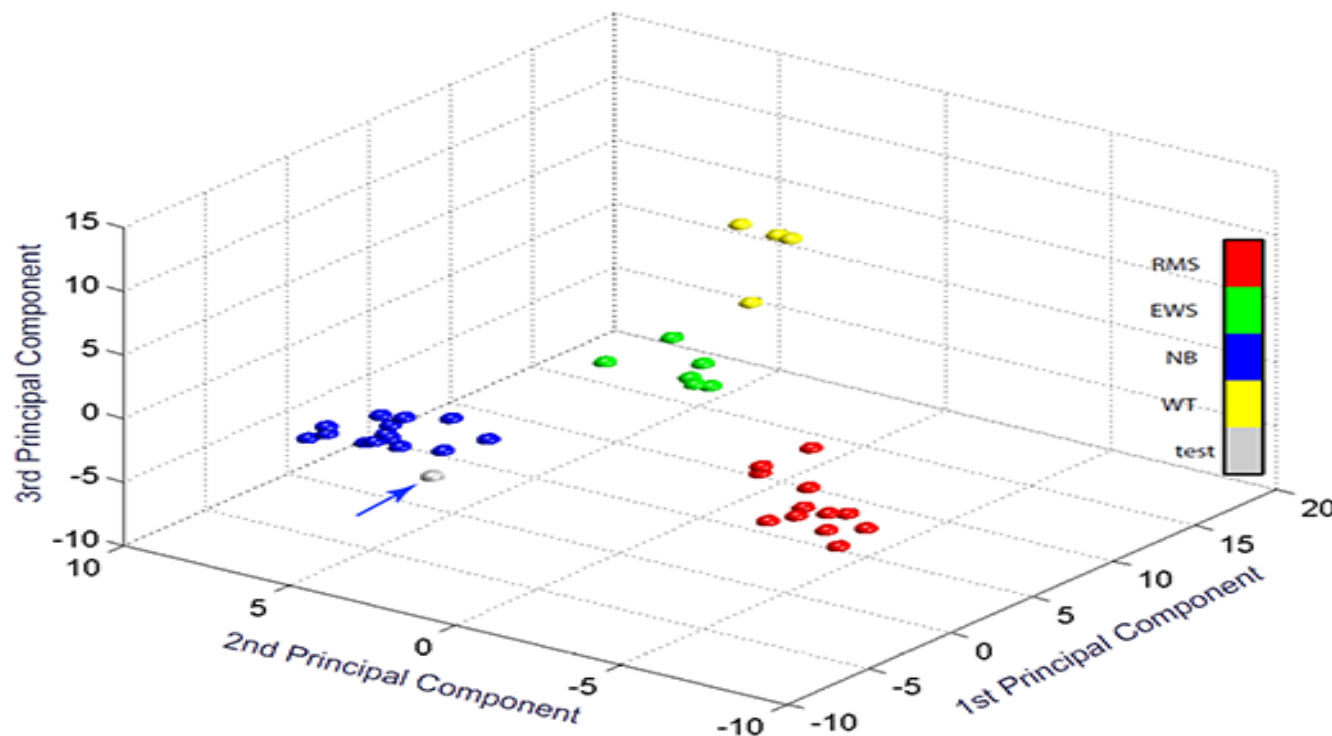


Initial diagnosis: Wilm's tumor



Cancer diagnosis

Diagnosis of cancers using gene expression profiles



Wilm's tumor

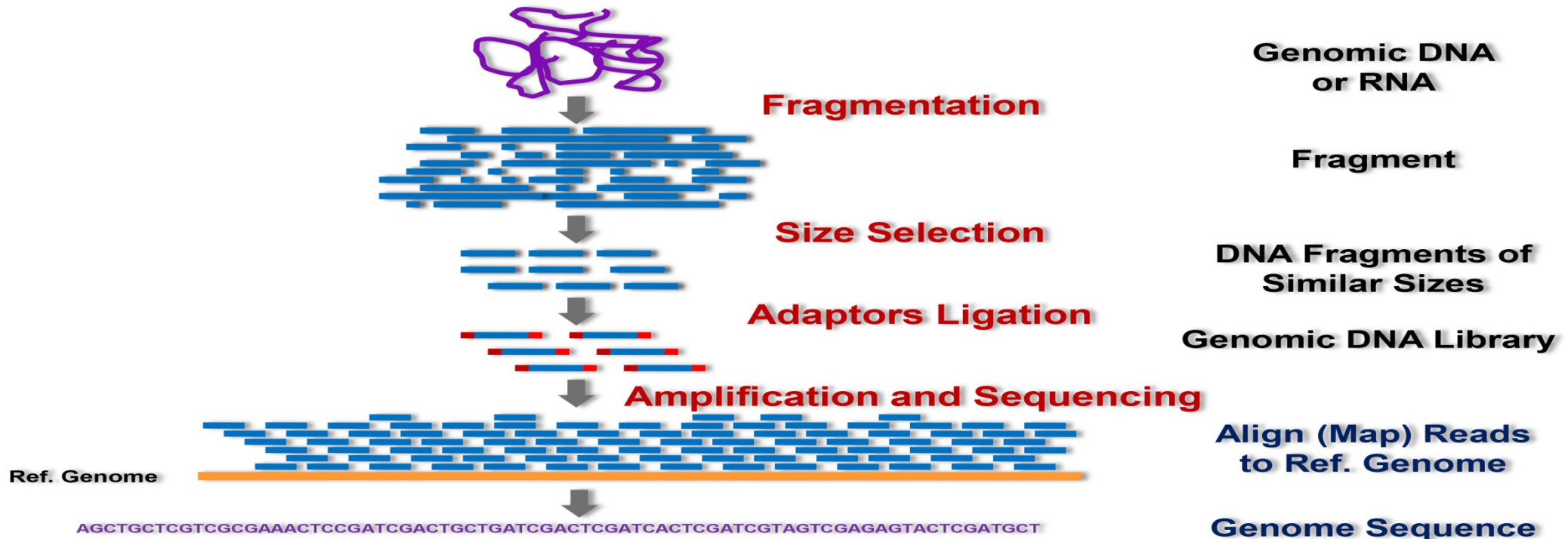


Neuroblastoma

- Patient was switched to high risk neuroblastoma treatment included stem cell transplant
- Doing well 1 yr after diagnosis

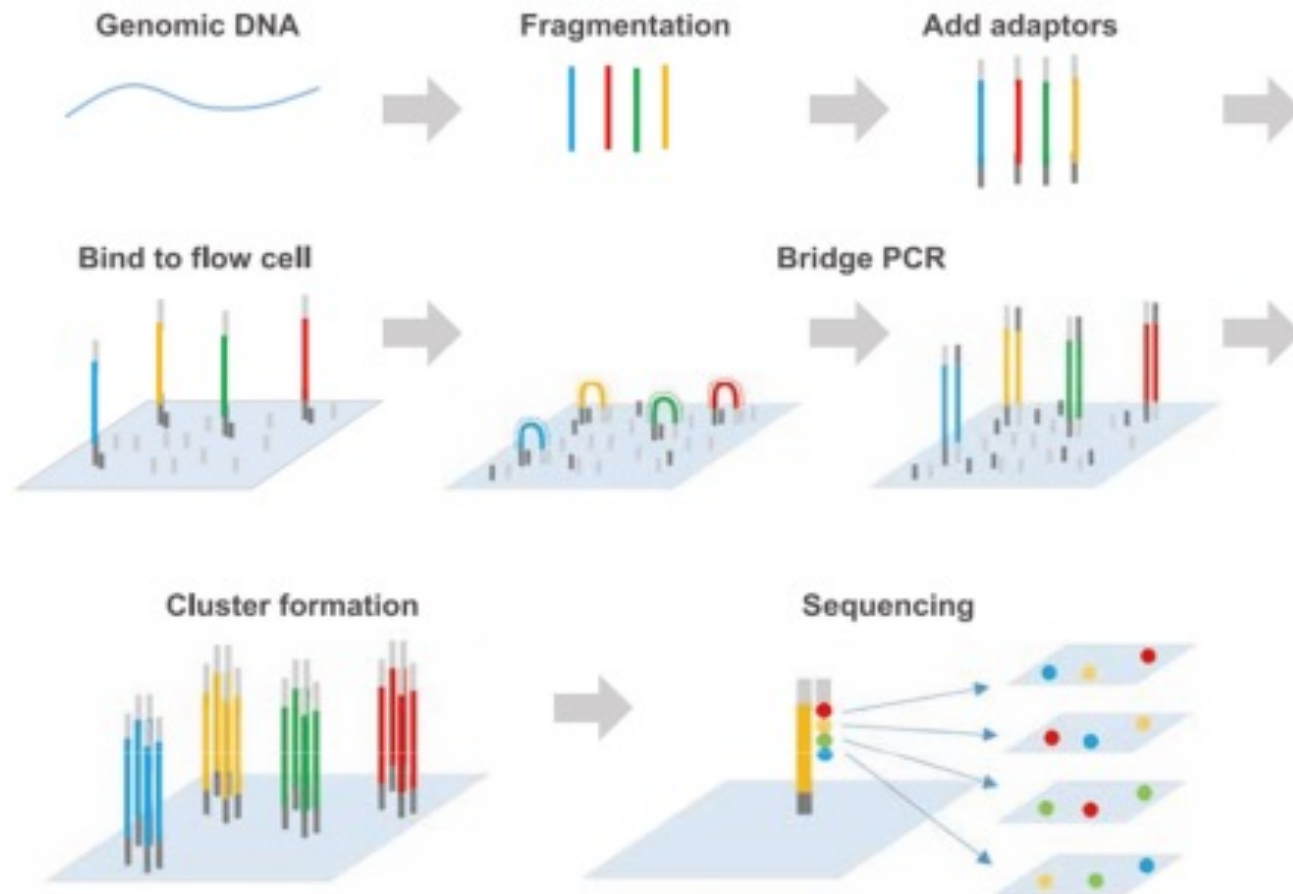
Next-generation sequencing

Next-Generation Sequencing



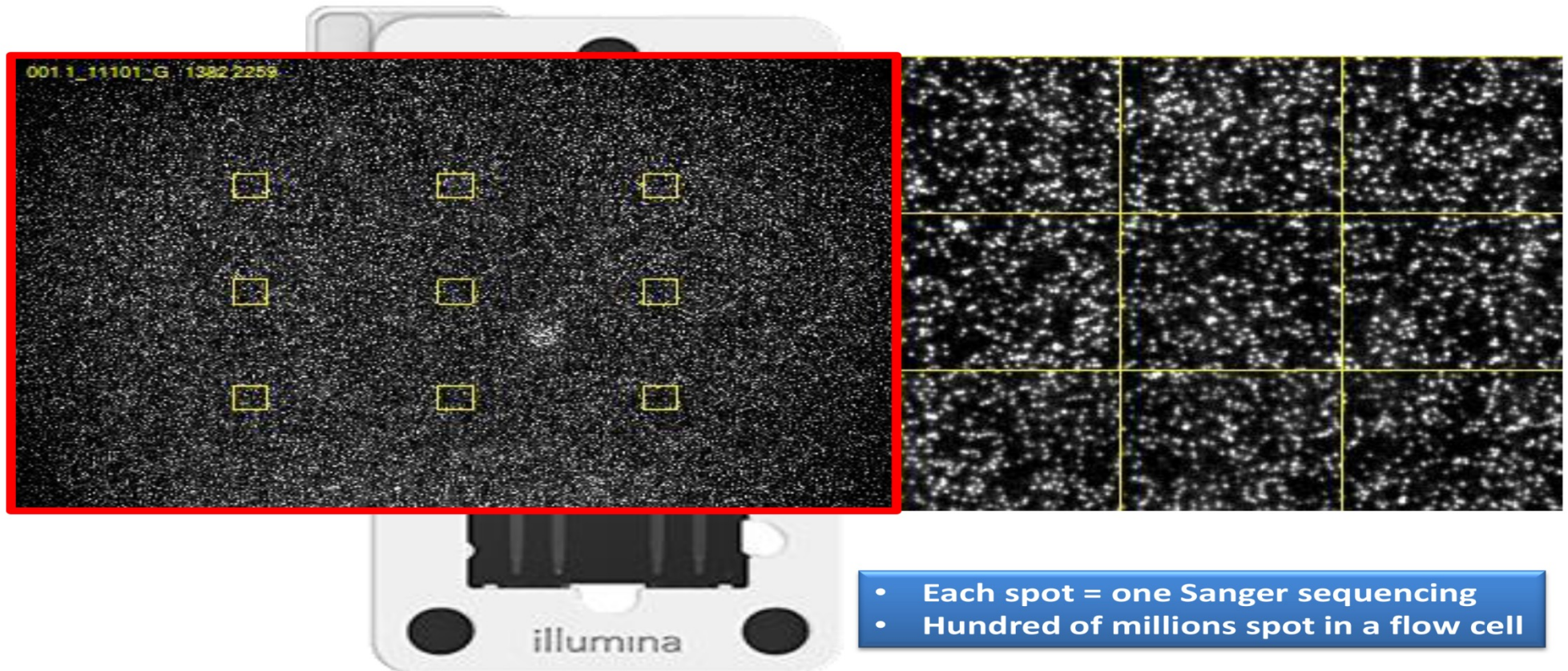
Sequencing by synthesis

Illumina Sequencers: sequencing by synthesis (SBS)



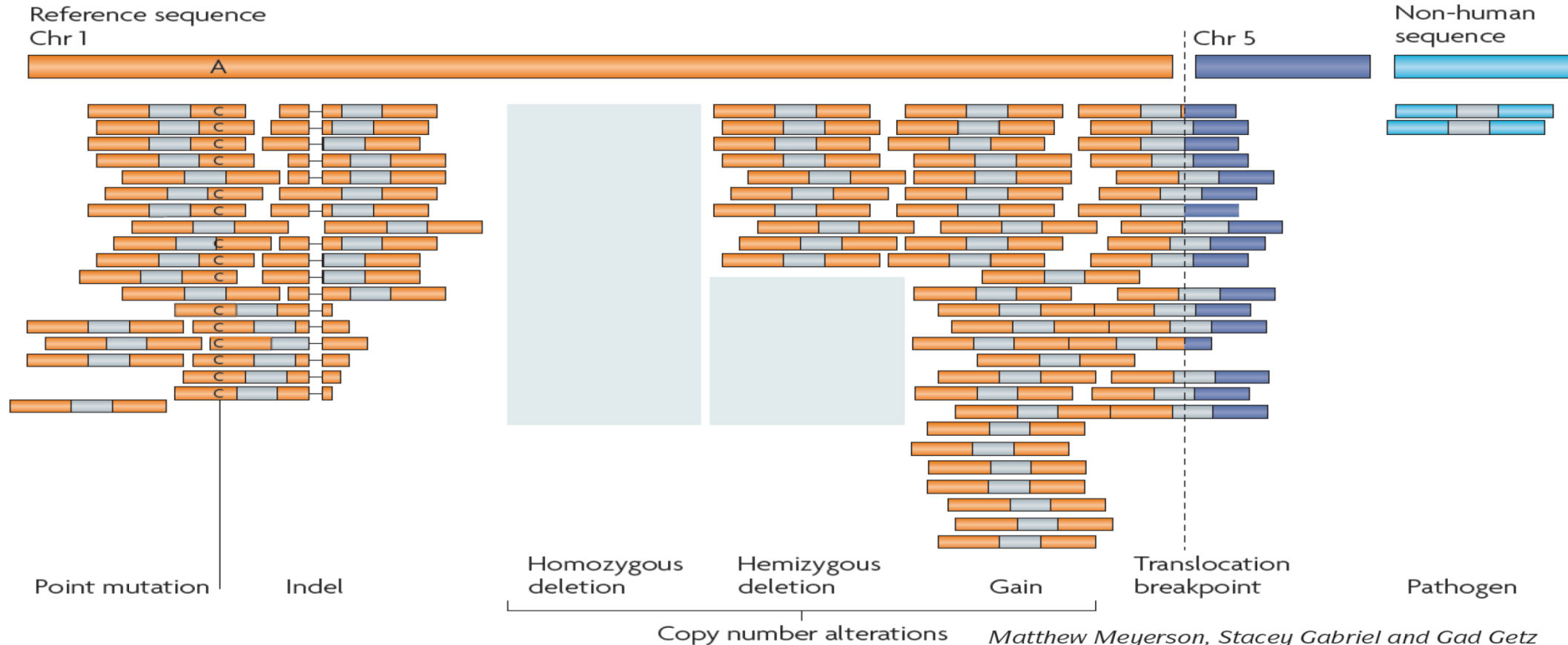
Massively Parallel Sequencing

Massively Parallel Sequencing



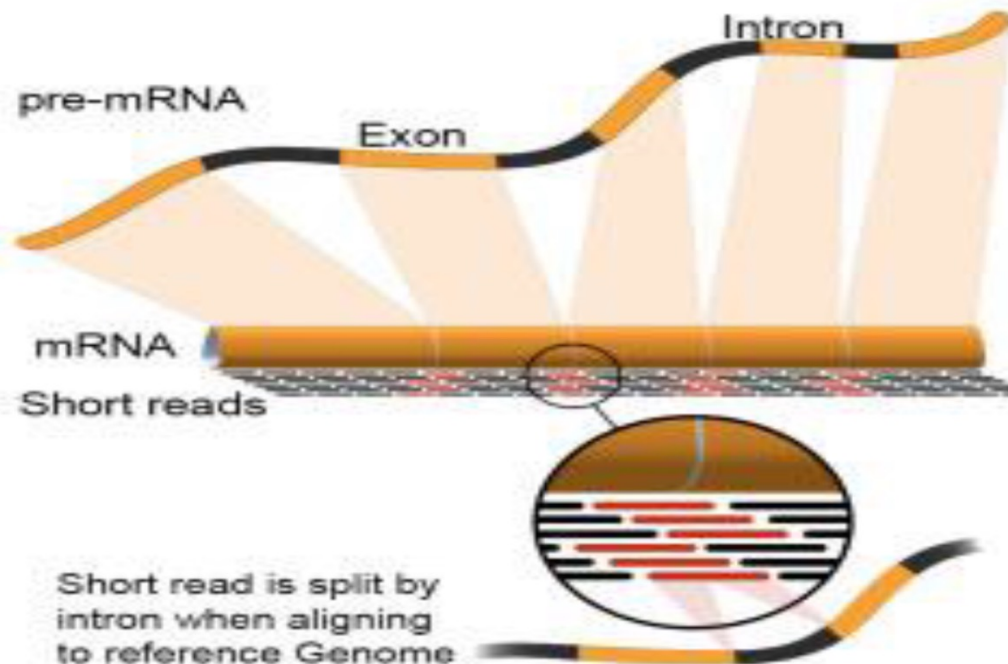
Genomic Alterations

Genomic alterations detected by DNA sequencing



Genomic Alterations

Genomic Alterations Detected by RNA Transcriptome Sequencing



- Digital Gene Expression
- Expressed Mutations
- Alternative Splicing Events
- Expressed Fusion Transcripts
- RNA editing
- Novel Transcripts
- Non-coding RNAs

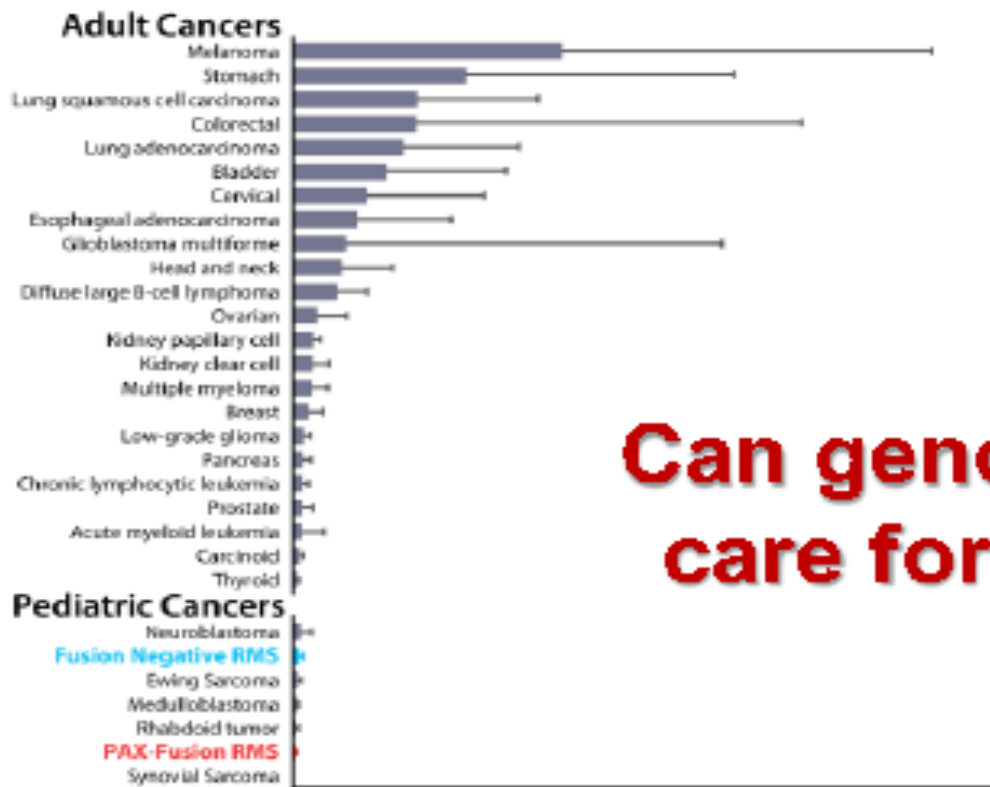
Next-generation sequencing

Next-generation sequencing: a platform for many applications to study genome and epigenome

- No need of prior knowledge for probe design as in microarrays
- Parallel sequencing at basepair resolution– massive-throughput
 - Then: *~13 years for the 1st human genome* using Sanger sequencing by 20 centers in 7 countries
 - Now: *multiple human genomes in 2 days* using a NGS sequencer
- A single platform for different kinds of genomic and epigenomic information
 - DNA and RNA sequencing
 - Genome modification, e.g. methylation
 - Chromatin accessibility, e.g. ATAC-seq
 - Chromatin 3D organization, e.g. Hi-C
 - Protein-DNA interaction, e.g. ChIP-seq

Pediatric cancer mutations

Pediatric Cancers Have A Low Number of Somatic and Actionable Mutations At Initial Diagnosis



Can genomics help clinical care for cancer patients?

Clinomics for precision medicine

Personalized Medicine and Imaging

Clinical
Cancer
Research

MultiDimensional ClinOmics for Precision Therapy of Children and Adolescent Young Adults with Relapsed and Refractory Cancer: A Report from the Center for Cancer Research

Wendy Chang^{1,2,3}, Andrew S. Brohl^{1,4}, Rajesh Patidar¹, Sivasish Sindiri¹, Jack F. Shern^{1,2}, Jun S. Wei¹, Young K. Song¹, Marielle E. Yohe^{1,2}, Berkley Gryder¹, Shile Zhang¹, Kathleen A. Calzone⁵, Nityashree Shivaprasad¹, Xinyu Wen¹, Thomas C. Badgett^{1,6}, Markku Miettinen⁷, Kip R. Hartman^{8,9}, James C. League-Pascual^{2,8}, Toby N. Trahair¹⁰, Brigitte C. Widemann², Melinda S. Merchant², Rosandra N. Kaplan², Jimmy C. Lin¹, and Javed Khan¹

Clin Cancer Res. May 2016

Protocol Number: 10-C-0086

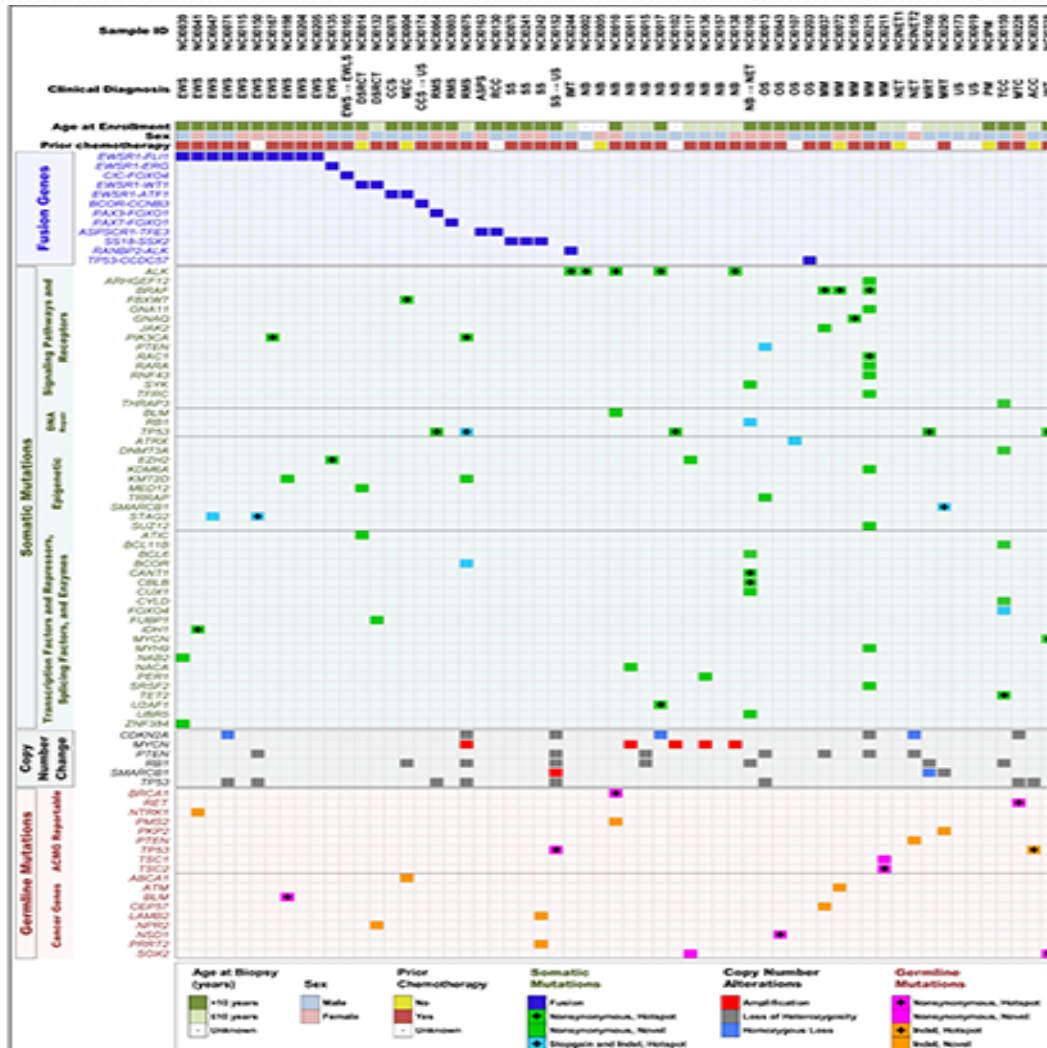
Title: “Comprehensive Omics Analysis of Pediatric Solid Tumors and Establishment of a Repository for Related Biological Studies” or Omics protocol

Study design

Study Design

- Pilot study to determine the utility and feasibility of performing comprehensive genomic analyses to identify clinically actionable mutations in pediatric and young adult patients with metastatic, refractory or relapsed solid tumors
- 59 patients enrolled to the pediatric oncology branch, Center for Cancer Research (CCR), NCI (2010-2014)
- Age 7 months-25 years
- 20 diagnostic categories (non-CNS, solid tumors)
- Comprehensive multi-omics exome germline & tumor, RNAseq tumor & Illumina Omni SNP arrays of tumor

Multi-omics integrated landscape



Multi-Omics Integrated Landscape

RNAseq
Diagnostic, Driver, Actionable

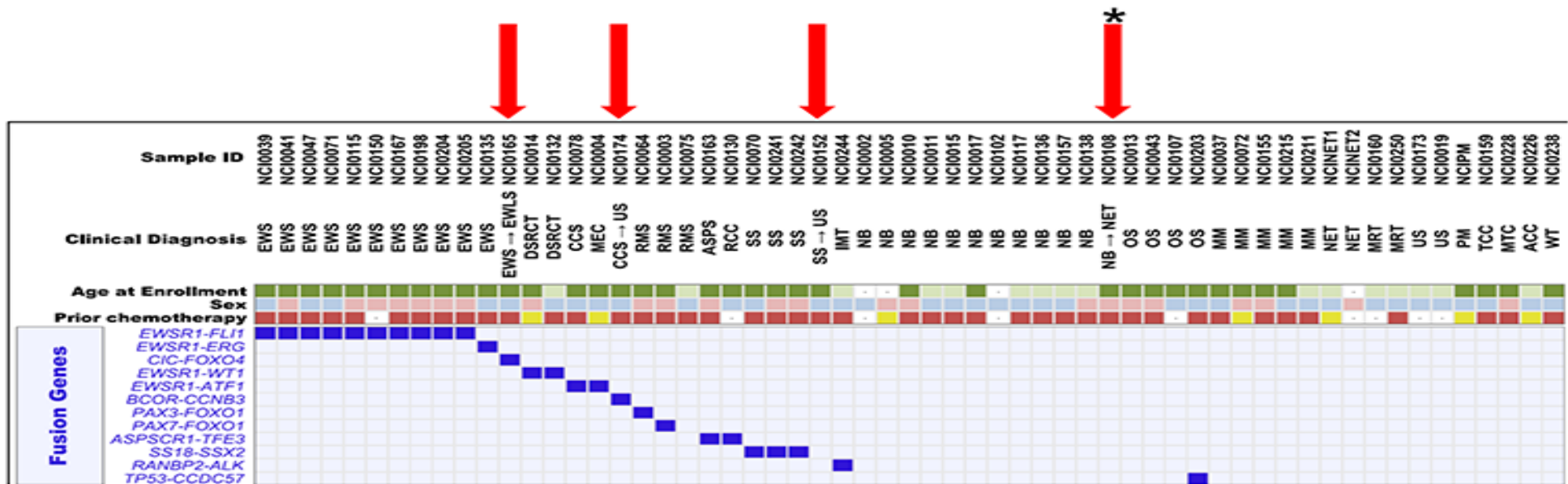
DNaseq and RNAseq

DNA copy number & RNAseq
Somatic: Driver, Actionable

DNaseq
Germ line: Disease causing,
Actionable

Fusion genes

Presence or absence of fusion genes and/or expression profiles confirms diagnosis or leads to revision of diagnosis



Germline mutations

**~10% of Pediatric and Adolescent Young Adults with Cancers
have Actionable Germline Mutations**

Table 1. Germline mutations in American College of Medical Genetics (ACMG) reportable genes and tumor suppressor genes identified in 7 patients

Sample	Diagnosis	Gene	Mutation	Disease	Hotspot	Notes	Reportable by Strict ACMG Criteria
NCI0072	MM	<i>ATM</i>	p.Y380fs	Ataxia-Telangiectasia and cancer predisposition syndrome	No	Frameshift insertion of tumor suppressor gene	Yes
NCI0010	NB	<i>BRCA1</i>	Q131X	Hereditary breast and ovarian cancer syndrome	Yes	Pathogenic, reportable	Yes
NCI0010	NB	<i>PMS2</i>	p.K356fs	Lynch syndrome and mismatch repair cancer syndrome	No	Frameshift deletion of tumor suppressor gene	Yes
NCINET2	NET	<i>PTEN</i>	p.R14fs	PTEN Hamartoma tumor syndrome	No	Frameshift deletion of tumor suppressor gene	Yes
NCI0228	MTC	<i>RET</i>	M918T	Multiple endocrine neoplasia 2B	Yes	Pathogenic, reportable	Yes
NCI0152	SS → US	<i>TP53</i>	R175H	Li-Fraumeni syndrome	Yes	Patient tumor has LOH of wild-type tp53 on other allele	No
NCI0226	ACC	<i>TP53</i>	A159K	Li-Fraumeni syndrome	Yes	Tumor has LOH of wild-type tp53 on other allele, novel, 2 base non-frameshift substitution, c.358_359delGinsTT	No
NCI0211	MM	<i>TSC1</i>	p.S828R	Tuberous sclerosis type 1, lymphangioleiomyomatosis, focal cortical dysplasia, and everolimus sensitivity	No	Nonsynonymous SNV, autosomal dominant, patient also has a germline TSC2 mutation	No
NCI0211	MM	<i>TSC2</i>	p.T246A	Tuberous sclerosis type 2, and lymphangioleiomyomatosis	Yes	Nonsynonymous SNV, autosomal dominant, patient also has a germline TSC1 mutation	No

NOTE: Mutations were confirmed by direct visualization on an IGV viewer, and by Sanger sequencing.

Abbreviations: ACC, adrenocortical carcinoma; MM, malignant melanoma; MTC, medullary thyroid carcinoma; NET, neuroendocrine tumor; RMS, rhabdomyosarcoma; SS, synovial sarcoma; US, undifferentiated sarcoma; horizontal arrow indicates change in diagnosis.

Somatic mutations

Approximately 50% (30/59) of Pediatric and Adolescent Young Adults with Cancers Have Actionable Somatic Mutations

Table 2. Summary of actionable mutations in relapsed and refractory pediatric solid tumors

Sample	Diagnosis	Gene	Stage	Modality	Mutation	AA Change	Level	Drug	Clinical trial: Pediatric	PDA-Approval in adults	Exact mutation vs. hotspot	Reference preclinical data for level 3
NCI0037	HM	BRAF	Relapsed	WES/WTS	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0072	HM	BRAF	Diagnostic	WES/WTS	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0215	HM	BRAF	Relapsed	WES/WTS	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0155	HM	GNAS	Relapsed	WES/WTS	NS SNV	p.Q209L	1	Tamoxifen, trametinib, vemurafenib	No	Yes	Exact	—
NCI0002	NB	ALK	—	WES/WTS	NS SNV	p.R1275Q	2a	Crizotinib	Yes	Yes	Exact	—
NCI0010	NB	ALK	Relapsed	WES/WTS	NS SNV	p.P1174V	2a	Crizotinib	Yes	Yes	Exact	—
NCI0017	NB	ALK	Relapsed	WES/WTS	NS SNV	p.F1174L	2a	Crizotinib	Yes	Yes	Exact	—
NCI0138	NB	ALK	Relapsed	WES/WTS	NS SNV	p.Y1278S	2a	Crizotinib	Yes	Yes	Exact	—
NCI0244	IMT	ALK	Relapsed	WTS	AA/NBQ2-ALK fusion	—	2a	Crizotinib	No	Yes	Exact	—
NCI0244	IMT	ALK	Relapsed	WES/WTS	NS SNV	p.I117T	2a	Crizotinib	No	Yes	Exact	—
NCI0215	HM	GNAS	Relapsed	WES/WTS	NS SNV	p.S248P	2a	Trametinib	No	Yes	—	—
NCI0041	EWS	DNM	Relapsed	WES/WTS	NS SNV	p.R32C	2a	IDH1 inhibitors	No	No	Exact	—
NCI0075	RMS	PKC4	Relapsed	WES/WTS	NS SNV	p.P104G	2a	PI3K/AKT/mTOR inhibitors	Yes	Yes	Exact	—
NCI0167	EWS	PKC4	Refractory	WES/WTS	NS SNV	p.D907G	2a	PI3K/AKT/mTOR inhibitors	Yes	Yes	Exact	—
NCI0013	OS	PTEN	Relapsed	WES/WTS	Frameshift deletion	p.R80fs	2a	PI3K/AKT/mTOR inhibitors	Yes	No	—	—
NCI0122	NET	PTEN	—	WES/WTS	Germline frameshift deletion/somatic LOH	p.R94fs	2a	PI3K/AKT/mTOR inhibitors	Yes	No	—	—
NCI0220	HTC	RET	Relapsed	WES/WTS	Germline SNV	p.H98T	2a	Vandetanib	Yes	Yes	Exact	—
NCI0017	NB	CDKN2A	Relapsed	SNP Array/WTS	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	36
NCI0071	EWS	CDKN2A	Relapsed	SNP Array/WTS	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	36
NCI0122	NET	CDKN2A	—	SNP Array/WTS	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	36
NCI0011	NB	MYCN	Relapsed	SNP Array/WTS	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0075	RMS	MYCN	Relapsed	SNP Array/WTS	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0102	NB	MYCN	—	SNP Array/WTS	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0136	NB	MYCN	Relapsed	SNP Array/WTS	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0138	NB	MYCN	Relapsed	SNP Array/WTS	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0238	WT	MYCN	Relapsed	WES/WTS	NS SNV	p.P44L	3	Bromodomain inhibitors	No	No	—	37, 38
NCI0160	HRT	SMARCB1	—	SNP Array/WTS	Homozygous loss	—	3	EZH2 inhibitors	No	No	—	39, 40
NCI0250	HRT	SMARCB1	Refractory	WES/WTS	NS SNV	p.R40X	3	EZH2 inhibitors	No	No	—	39, 40
NCI0047	EWS	STAG2	Relapsed	WES/WTS	NS SNV	p.E984X	3	PARP inhibitors	Yes	No	—	41
NCI0180	EWS	STAG2	—	WES/WTS	NS SNV	p.R276X	3	PARP inhibitors	Yes	No	Hotspot	41
NCI0231	HM	TSC1	Relapsed	WES/WTS	NS SNV	p.S826R	3	Everolimus	No	Yes	—	42
NCI0231	HM	TSC2	Relapsed	WES/WTS	NS SNV	p.T246A	3	Everolimus	No	Yes	—	42

NOTE: SNVs were confirmed by direct visualization on an IGV viewer, and validation by Sanger sequencing or confirmation CLIA-certified laboratories.

Abbreviations: EWS, Ewing sarcoma; IMT, epithelioid inflammatory myofibroblastic sarcoma; HM, malignant melanoma; HRT, malignant rhabdoid tumor; MTC, medullary thyroid carcinoma; NB, neuroblastoma; NET, neuroendocrine tumor; OS, osteosarcoma; RMS, rhabdomyosarcoma; WT, Wilms tumor.

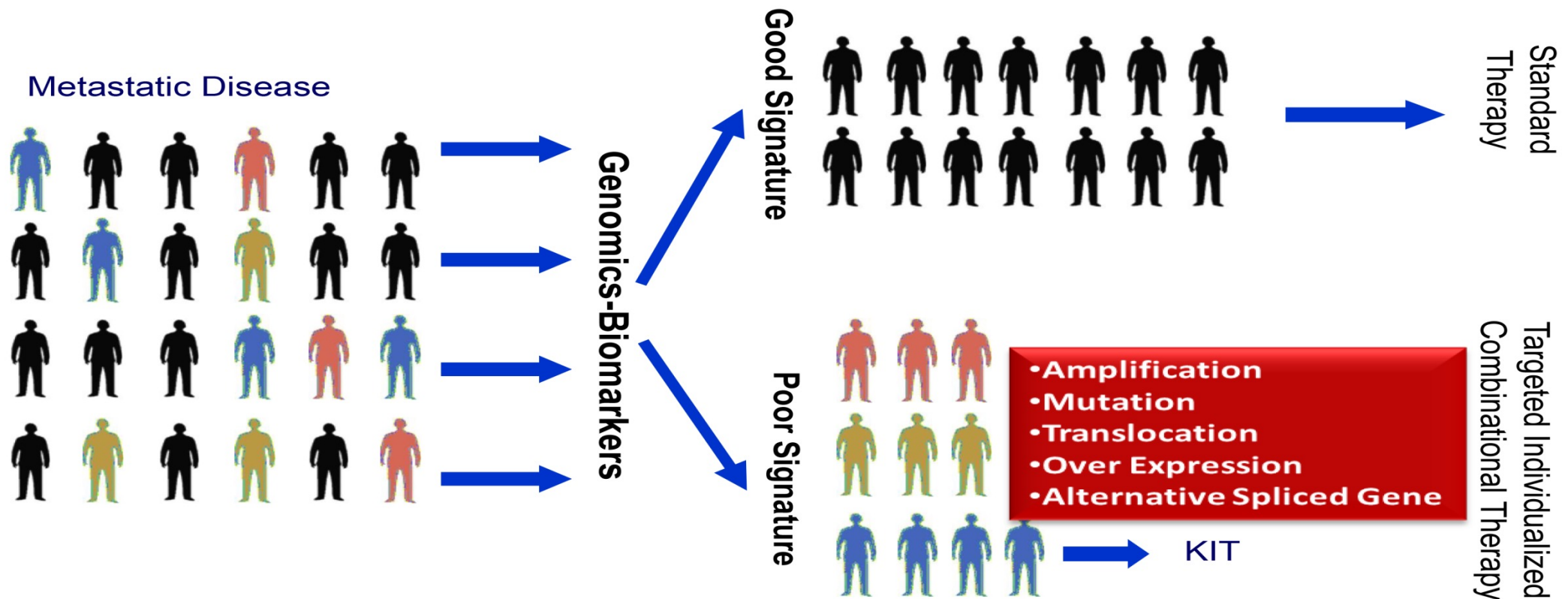
Summary

Summary

- Demonstrated the importance and feasibility of performing multi-dimensional ClinOmics in the clinical setting in real time
- ~50% of children with pediatric or AYA patients with relapsed or refractory cancers have actionable somatic mutations
- ~ 10% have actionable germline mutations
- Importance of performing parallel germline sequencing; some therapeutically actionable (e.g. DNA repair, PTEN, TSC1, TSC2, HRAS, RET, ALK)
- Increased tumor burden in relapsed tumors; implications for immunotherapy
- Single agent pediatric MATCH like trials are planned by COG-NCI

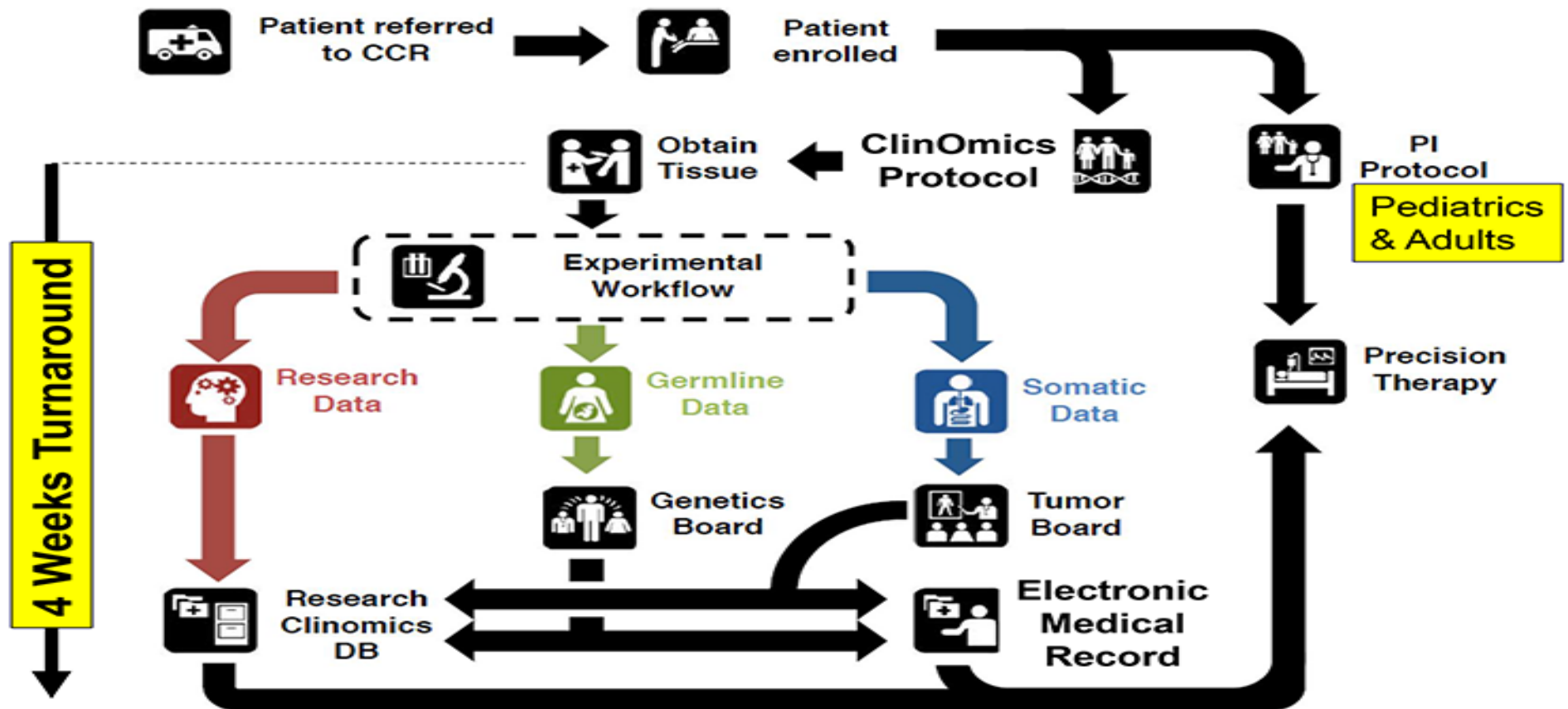
Future Trials

Genomics Enabling Precision Therapy-The Future for Pediatric Trials



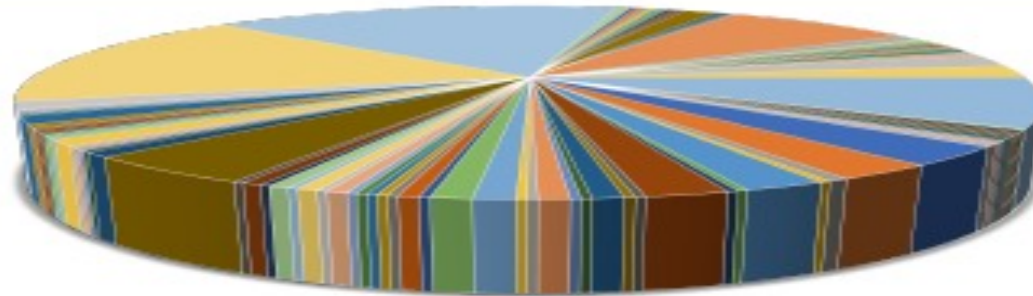
ClinOmics program

CCR ClinOmics Program-CLIA



Patient diagnoses

396 Patients of 93 diagnoses



BRAC

- (1) Anaplastic Astrocytoma
- (2) Anaplastic Piloc
- (3) Bladder cancer
- (4) Cholangiocarcinoma
- (5) Dermatofibrosarcoma protuberans
- (6) Diffuse intrinsic pontine glioma
- (7) Ependymoma
- (8) Glioblastoma
- (9) Glioblastoma
- (10) Grade II Oligodendroglioma
- (11) Invasive well differentiated squamous cell carcinoma
- (12) Lymphocytosis
- (13) Melanoma
- (14) Mesothelioma Pleural
- (15) Metastatic Pancreatic Neuroendocrine Carcinoma
- (16) Multiple Retic Tumors
- (17) Neuroblastoma (I)
- (18) Osteosarcoma
- (19) Papillary tumor of the pineal region
- (20) Poorly differentiated carcinoma (lung vs. thyroid)
- (21) Renal cell carcinoma
- (22) Small Cell Cancer of rectum
- (23) Temporal high grade glioma
- (24) Uveal melanoma

- (25) Acute lymphoblastic leukemia
- (26) Anaplastic Ependymoma
- (27) Anaplastic Fibrous Histiocytoma
- (28) Breast cancer
- (29) Chondroma
- (30) Desmoid Fibrosarcoma
- (31) Endometrial cancer
- (32) Ewing's sarcoma
- (33) Glioblastoma
- (34) Hepatic Angiosarcoma
- (35) Keratoacanthoma
- (36) Melanocytosis
- (37) Merkel Cell Carcinoma
- (38) Mesothelioma Thoracic
- (39) MPR
- (40) Myxopapillary Ependymoma
- (41) Neuronal tumor
- (42) Ovarian Serous Carcinoma
- (43) Pilocytic Astrocytoma
- (44) Prostate cancer
- (45) Pseudopapilloma
- (46) Small cell carcinoma of the ovary hypercalcemic type (OCHT)
- (47) Teratoma

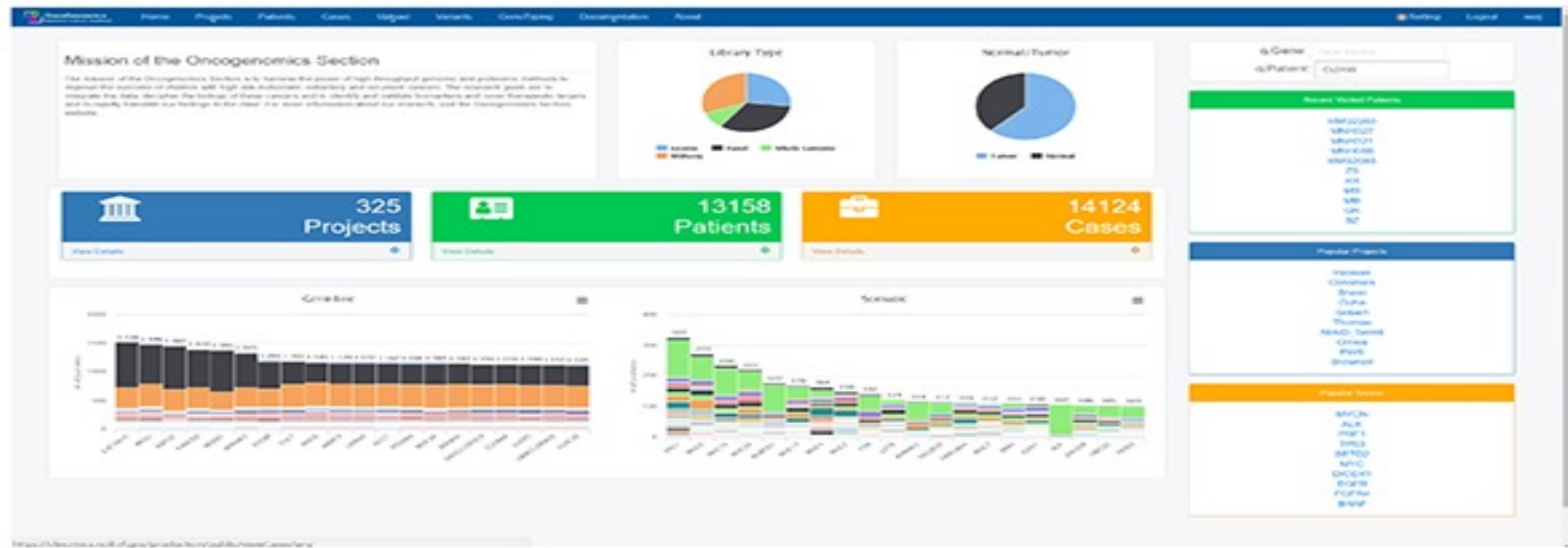
- (48) Acute myeloid leukemia
- (49) Anaplastic meningioma
- (50) Astrocytoma
- (51) Carcinoid, BRCA1 positive
- (52) Clear cell sarcoma
- (53) Desmoplastic small round cell tumor
- (54) Endometrial Stromal Sarcoma
- (55) Extracranial small cell cancer
- (56) Glioma
- (57) Hepatocellular cancer
- (58) Left Cerebellar Sarcoma
- (59) Medullary Thyroid Cancer metastatic
- (60) Mesothelioma
- (61) Metastatic Anal Carcinoma
- (62) Multinodular and Vasculating Neuronal Tumor
- (63) Neuroendocrine carcinoma
- (64) Neuroendocrine giant cell tumor
- (65) Ovarian Teratoma
- (66) Pleomorphic Xanthoastrocytoma
- (67) Pleomorphic gliosarcoma
- (68) RSC
- (69) Small cell endometrium
- (70) Thyroid

- (71) Ampullary cancer
- (72) Anaplastic Oligodendroglioma
- (73) Atypical Central Neurocytoma
- (74) Carcinoma of the Pelvis
- (75) Colon cancer
- (76) Diffuse Astrocytoma, Grade II
- (77) Endometrioid
- (78) Gallbladder cancer
- (79) Gliosarcoma
- (80) Hepatocellular carcinoma
- (81) Lung Adenocarcinoma
- (82) Medulloblastoma
- (83) Mesothelioma Peritoneal
- (84) Metastatic NET
- (85) Multiple carcinoma
- (86) Neuroendocrine Tumor
- (87) NSCLC
- (88) Pancreatic cancer
- (89) Pleomorphic xanthoastrocytoma
- (90) Recurrent Medulloblastoma
- (91) Small cell bladder
- (92) Synovial sarcoma
- (93) Undifferentiated sarcoma

ClinOmics Data Portal

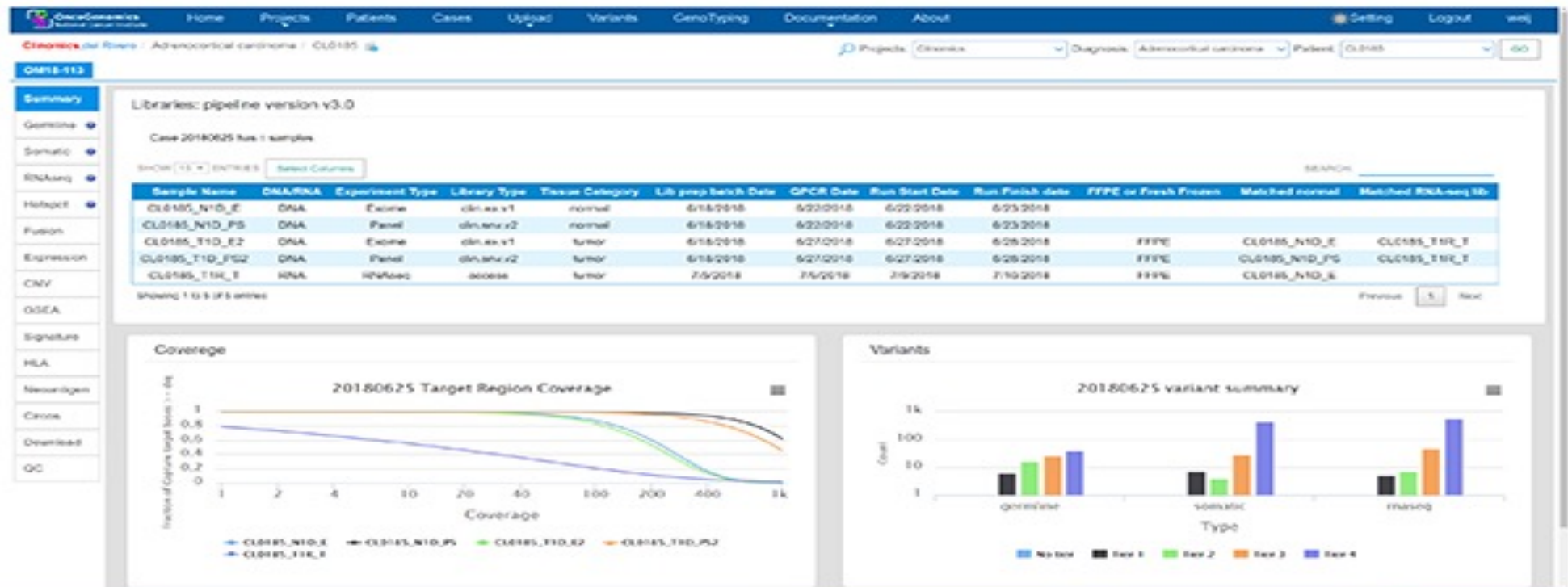
ClinOmics Data Portal

<https://clinomics.ncifcrf.gov/production/public/>



Patient Summary

Patient Summary Page



QC report

QC Report: Sequencing Statistics & Genotyping

Run Statistics

Summary | Clones | Coverage | Transcript Coverage | Hotspot | Contours | Compare | **DNA QC** | RNA QC | RNA QC v2 | FASTQC | Genotyping | Versions

Genome ☐ Show 15 entries Search:

Sample_ID	MEAN BAIT COVERAGE	MEAN TARGET COVERAGE	Total reads	Mapped reads	Percent mapped	On-target reads	Percent on-target	Unique on-target reads	Percent unique on-target	Hq unique on-target reads	Percent Hq unique on-target	Percent Hq unique positions at 20x	Percent Hq unique positions at 30x	Percent Hq unique positions at 50x	Percent Hq unique positions at 100x	Percent Hq unique positions at 200x	Percent Hq unique positions at 400x
CL0185_N1D_E_HJWNCBGK7	190	210	250645548	207511346	82.55	108950939	52.06	137432996	88.81	132687067	88.55	96.41	85.53	92.74	79.74	43.42	5.53
CL0185_N1D_PS_HJWNCBGK7	888	781	61689380	61218679	99.80	41885021	68.43	26381444	82.86	28877230	97.81	88.38	88.30	88.18	87.75	86.80	86.75
CL0185_T1D_E2_HJYOBGK7	170	182	230619044	237360954	98.48	153950821	64.87	124328705	86.74	120344271	88.72	96.06	84.78	90.70	74.07	35.34	3.91
CL0185_T1D_PS2_HJYOBGK7	876	833	56426879	60183182	98.88	34227908	67.84	21781328	83.88	21288182	97.78	88.33	88.25	88.04	86.88	81.71	72.70

Showing 1 to 4 of 4 entries

☒ QC threshold

Previous 1 Next

Genotyping

Summary | Clones | Coverage | Transcript Coverage | Hotspot | Contours | Compare | **DNA QC** | RNA QC | RNA QC v2 | FASTQC | **Genotyping** | Versions

Genome ☐ Comment...

☒ Pass ☐ Fail

☒ History

Show 15 entries Search:

Sample	CL0185_N1D_E	CL0185_N1D_PS	CL0185_T1D_E2	CL0185_T1D_PS2	CL0185_T1D_T
CL0185_N1D_E	100%	100%	100%	99%	88%
CL0185_N1D_PS	100%	100%	100%	98%	88%
CL0185_T1D_E2	100%	100%	100%	100%	88%

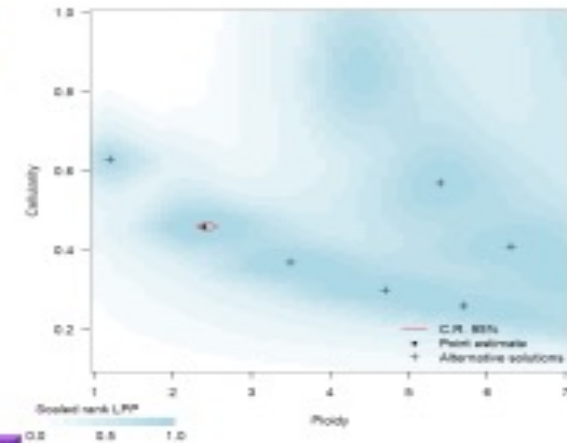
QC Report: Coverage

QC Report: Coverage

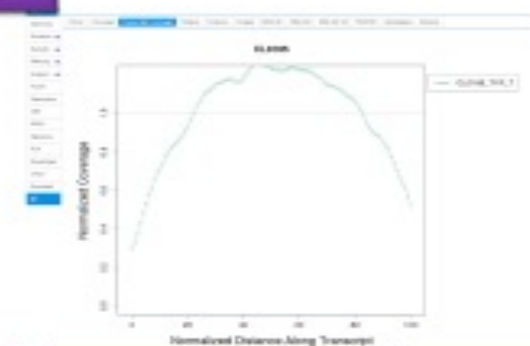
Circos



Tumor Content



RNA Coverage



Hotspot Coverage



Germline and somatic mutations

Germline and Somatic Mutations

The screenshot displays the UCSC Genome Browser interface. At the top, there's a navigation bar with various tools and links. Below it, a search bar and a list of tracks are visible. The main track shows a genomic region with various annotations. The ClinVar track is highlighted, showing a list of variants. The interface includes a search bar, navigation tools, and a detailed view of the selected variant.

EGFR mutations

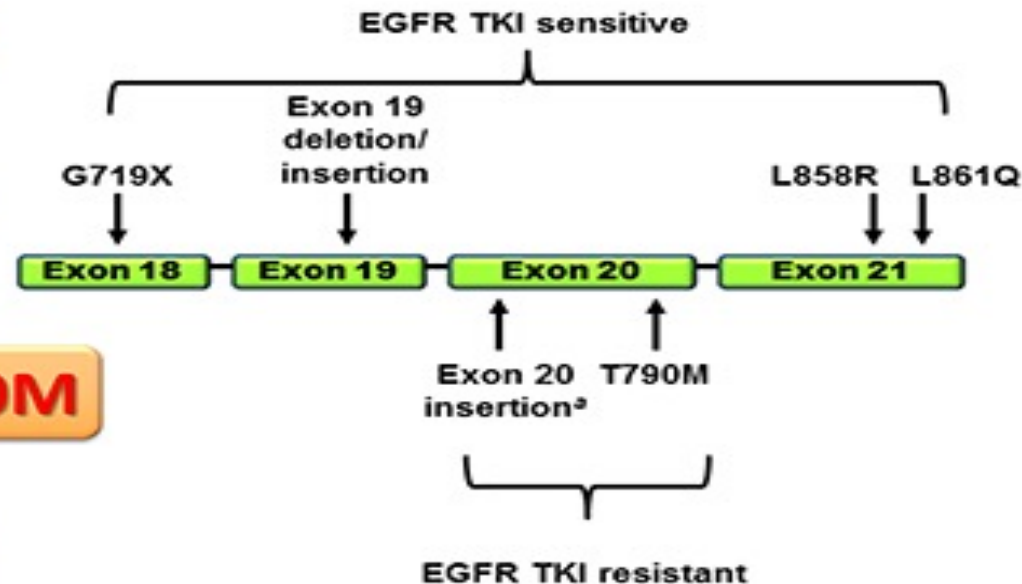
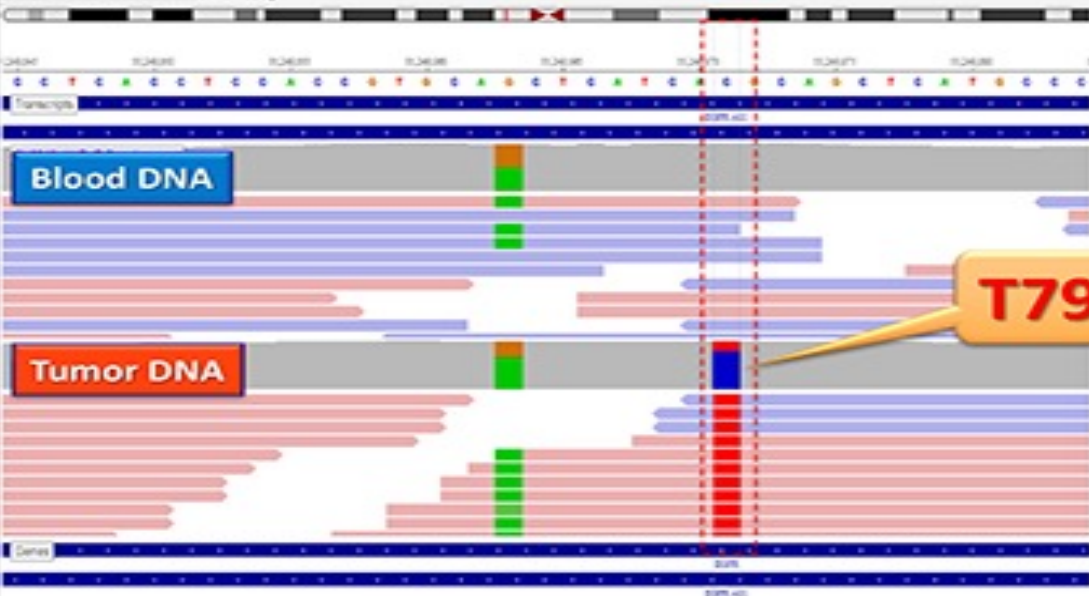
EGFR mutations in NSCLC

GV view of patient: CL0040 case: OM16-007 Total 4 sample(s)

ic: (check sample to load)

CL0040_ND_P Panel, normal (Panel, normal) CL0040_T1D_P Panel, tumor (Panel, tumor)

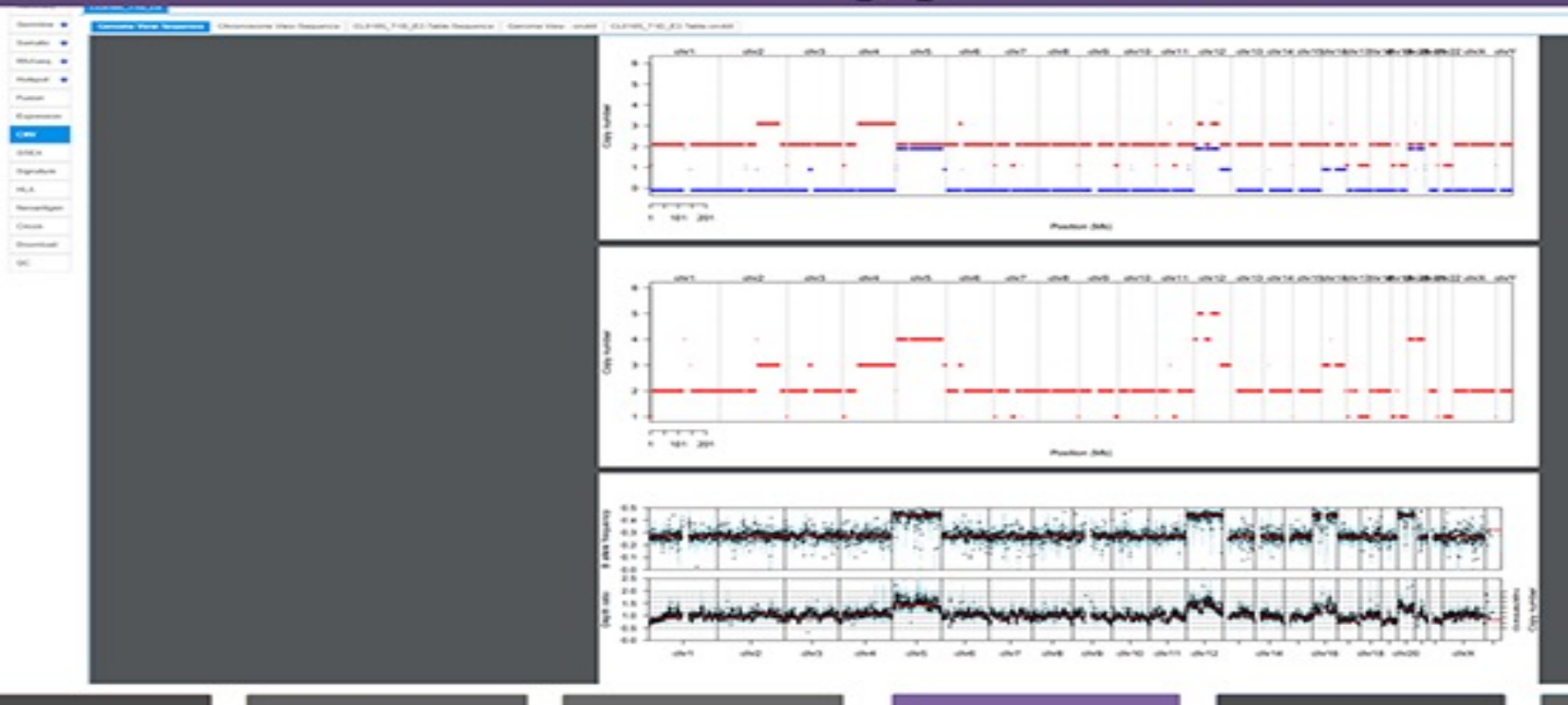
chr7:55,243,244-55,249,267 53 bp



<https://www.mycancergenome.org/content/disease/lung-cancer/egfr/>

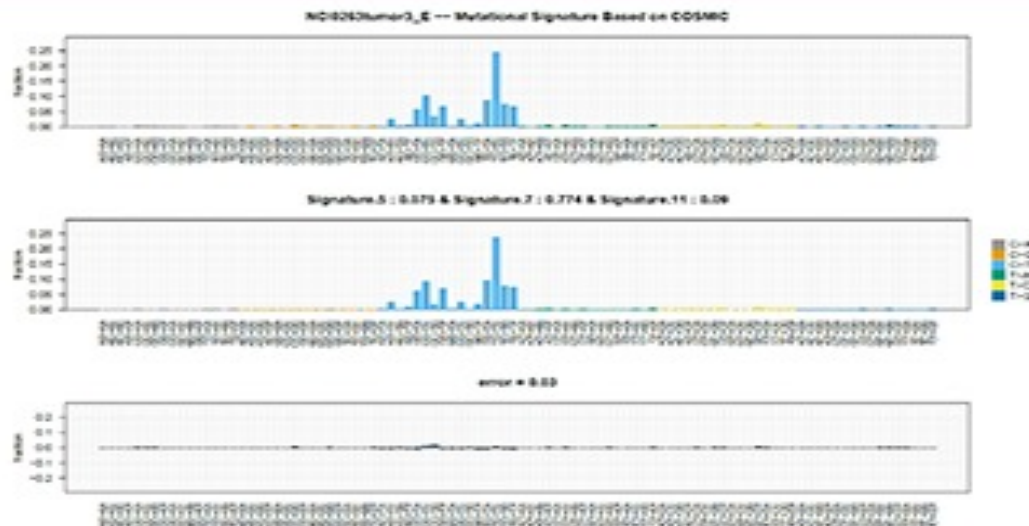
Tumor Copy Number

Tumor Copy Number

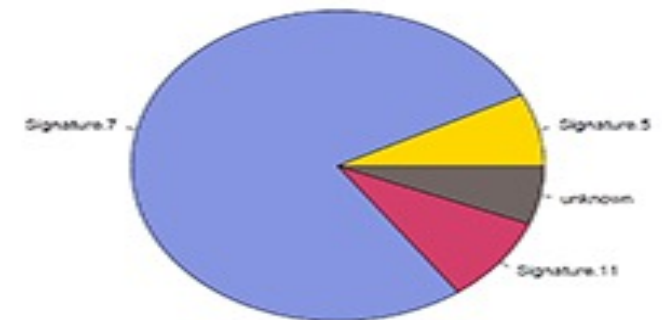


Mutation Signatures

Mutation Signatures for Tumor

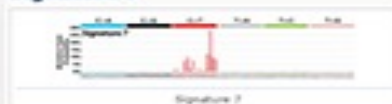


NCI0263: Melanoma



COSMIC (<https://cancer.sanger.ac.uk/cosmic/signatures>)

Signature 7



Cancer types: Signature 7 has been found predominantly in skin cancers and in cancers of the lip categorized as head and neck or oral squamous cancers.

Proposed aetiology: Based on its prevalence in ultraviolet exposed areas and the similarity of the mutational pattern to that observed in experimental systems exposed to ultraviolet light Signature 7 is likely due to ultraviolet light exposure.

Additional mutational features: Signature 7 is associated with large numbers of CC>TT dinucleotide mutations at dipyrimidines. Additionally, Signature 7 exhibits a strong transcriptional strand bias indicating that mutations occur at pyrimidines (via, e.g. by formation of pyrimidine-pyrimidine photoproducts) and these mutations are being repaired by transcription-coupled nucleotide excision repair.

Comments: N/A

Signature 7: UV signature

Mutation Burden

Mutation Burden

The screenshot displays the OncoGenomics National Cancer Institute web application interface. The top navigation bar includes links for Home, Projects, Patients, Cases, Upload, Variants, GenoTyping, Documentation, and About. A user profile 'weij' is logged in. The breadcrumb trail shows 'Clinomics, del Rıvero / Adrenocortical carcinoma / CL0185'. Below this, filters for Projects (Clinomics), Diagnosis (Adrenocortical carcinoma), and Patient (CL0185) are visible, along with a 'GO' button. The left sidebar contains a list of analysis types: Summary, Germline, Somatic (selected), RNAseq, Hotspot, Fusion, Expression, CNV, GSEA, Signature, and HLA. The main content area shows the 'Mutation_Burden' tab selected. It includes a 'Callers' dropdown set to 'MuTect', a 'Select Columns' button, and a 'Show 15 entries' option. A table displays two entries for 'Adrenocortical carcinoma' with columns for Diagnosis, Sample Name, Experiment Type, Caller, Burden, Total bases, and Burden Per MB. The 'Burden Per MB' column is highlighted with a red box. The first entry has a burden of 612 and total bases of 45196537, resulting in a burden per MB of 13.54. The second entry has a burden of 36 and total bases of 2465827, resulting in a burden per MB of 14.6. A search bar is located above the table. At the bottom of the table, it indicates 'Showing 1 to 2 of 2 entries (filtered from 6 total entries)' and includes 'Previous' and 'Next' navigation buttons.

OncoGenomics National Cancer Institute

Home Projects Patients Cases Upload Variants GenoTyping Documentation About

Setting Logout weij

Clinomics, del Rıvero / Adrenocortical carcinoma / CL0185

Projects: Clinomics Diagnosis: Adrenocortical carcinoma Patient: CL0185 GO

OM18-113

Summary Germline Somatic RNAseq Hotspot Fusion Expression CNV GSEA Signature HLA

Somatic-All Somatic-CL0185_T1D_PS2-Panel Somatic-CL0185_T1D_E2-Exome Mutation_Burden

Callers: MuTect

Select Columns

Show 15 entries

Search:

Diagnosis	Sample Name	Experiment Type	Caller	Burden	Total bases	Burden Per MB
Adrenocortical carcinoma	CL0185_T1D_E2	Exome	MuTect	612	45196537	13.54
Adrenocortical carcinoma	CL0185_T1D_PS2	Panel	MuTect	36	2465827	14.6

Showing 1 to 2 of 2 entries (filtered from 6 total entries)

Previous 1 Next

Fusion Gene Detection

Fusion Gene Detection from RNA-seq experiments



Useful Genomic Information

Other Useful Genomic Information

- **HLA typing (Tissue typing)**
- **Neoantigen prediction**
- **Gene expression**
- **Gene Set Enrichment Analysis (GSEA)**
- **Survival analysis if outcome data is available**

Conclusions:

Next generation sequencing (including whole genome, exome and transcriptome) determines the complete genomic and epigenetic portrait of cancers at the base pair level.

Integrated analyses of the cancer can identify biologically relevant diagnostic, prognostic biomarkers and novel targets for precision medicine.

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