

Apply genomics to precision medicine

Apply Genomics to Precision Medicine

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Genetics Branch*

*Center for Cancer Research
National Cancer Institute*

*TRACO
November 6, 2023*

Outline

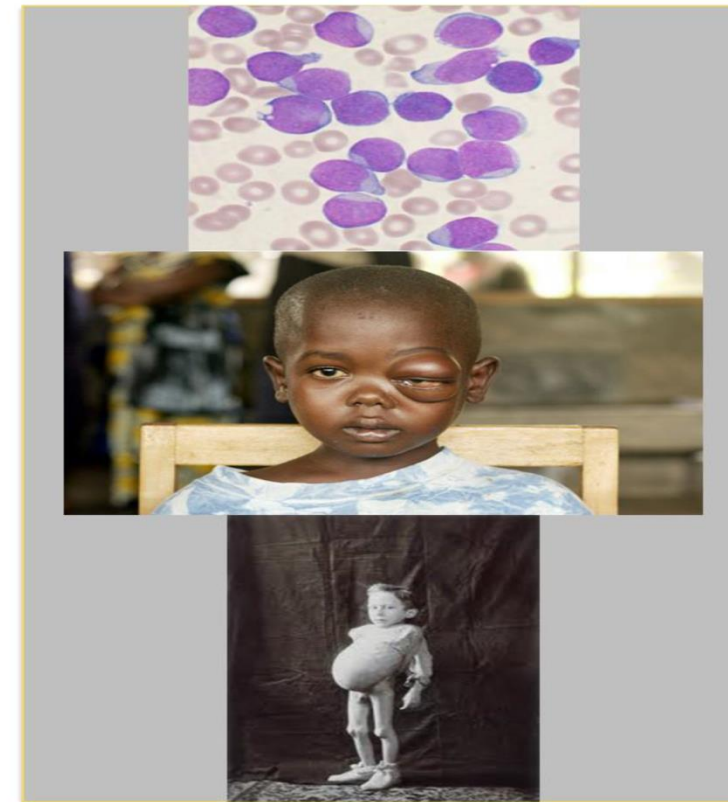
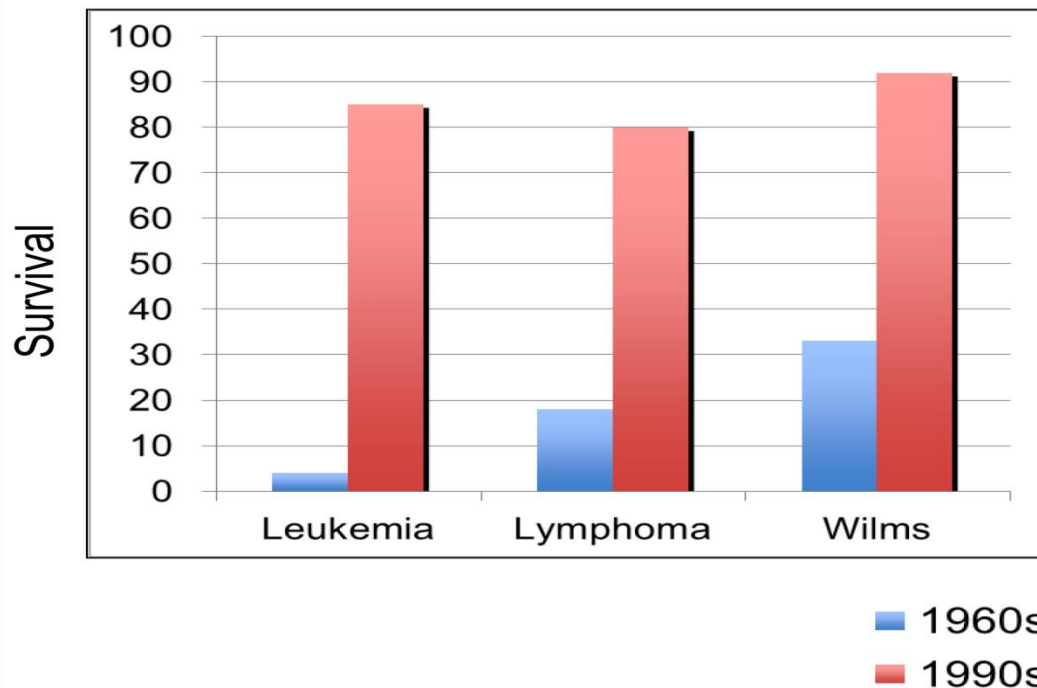
Outline

- **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

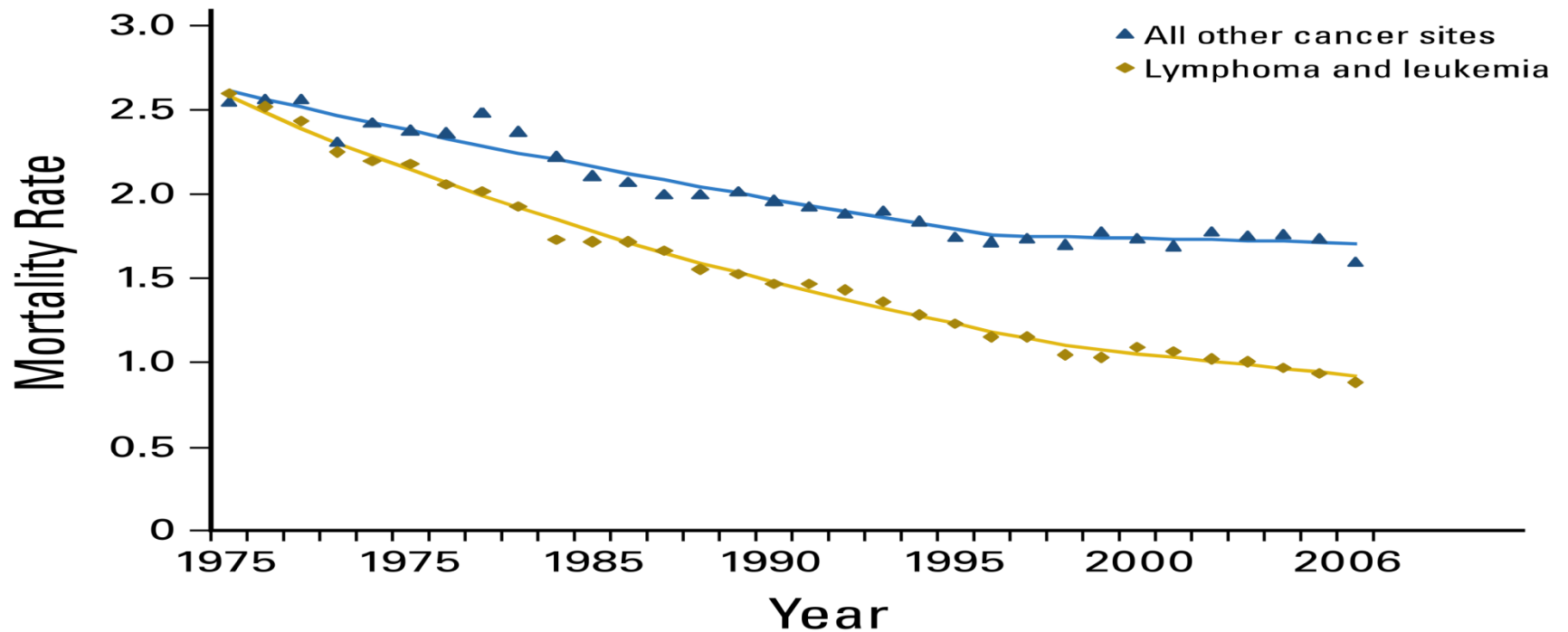


Courtesy: John Maris

Mortality rates

National Cancer Institute

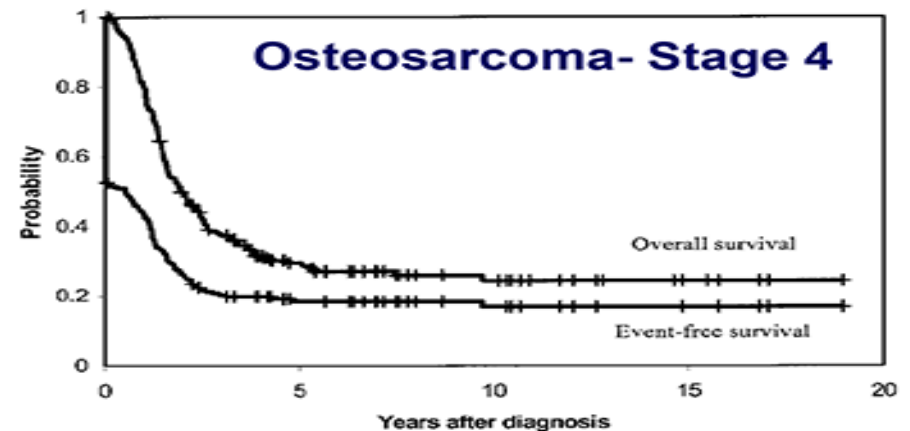
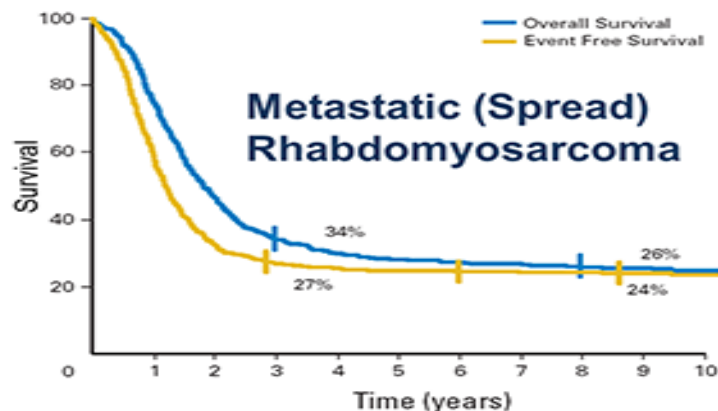
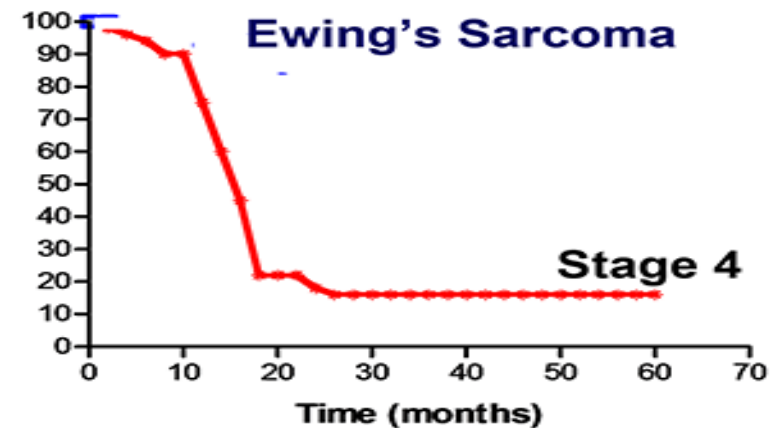
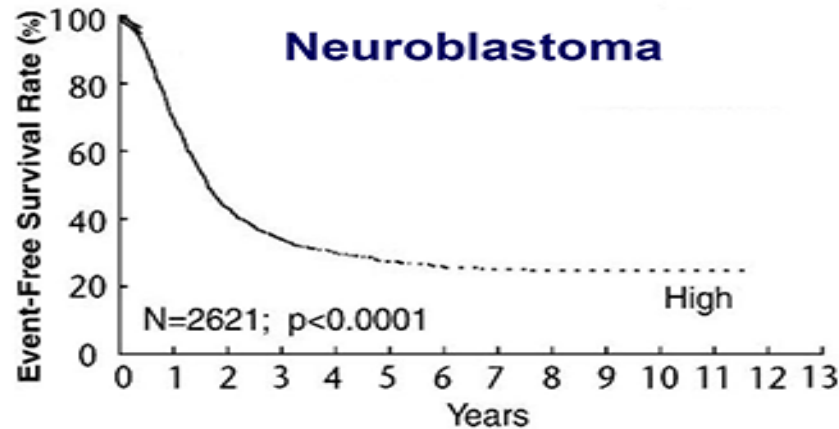
However in the past 16 years no improvement in mortality rates despite increased intensity of treatment



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

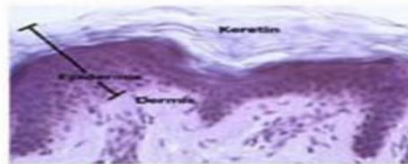


Gene expression

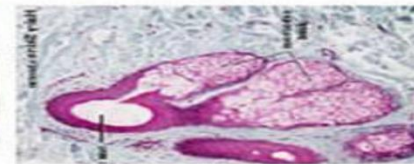
...but the complexity and diversity

Same genome or DNA →

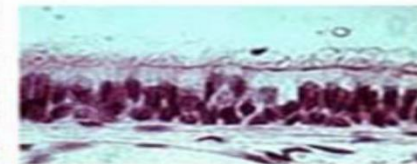
- Different expression pattern
- Different proteome
- Different tissues
- Different physiology



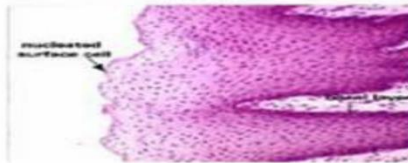
skin



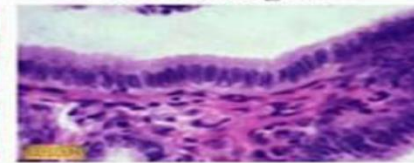
sebaceous gland



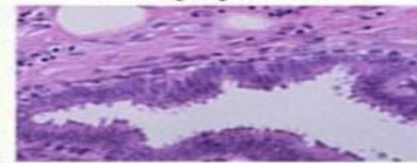
airway epithelium



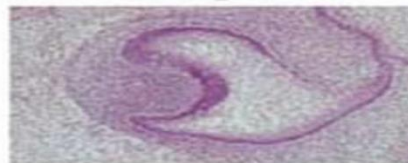
tongue



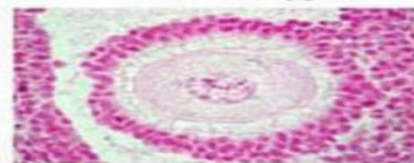
intestinal crypt



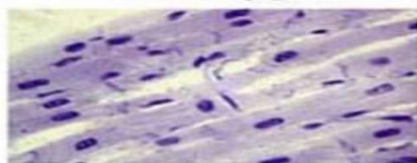
mammary gland



developing tooth



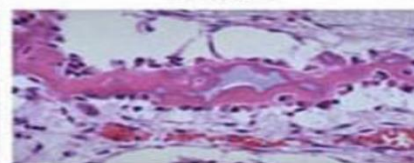
follicle



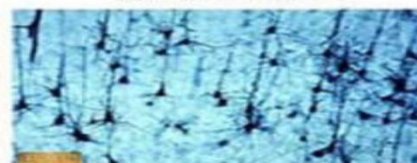
skeletal muscle



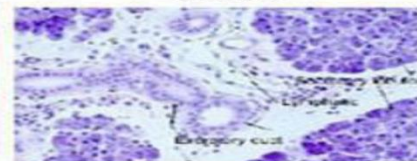
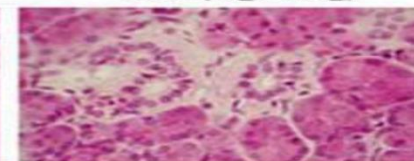
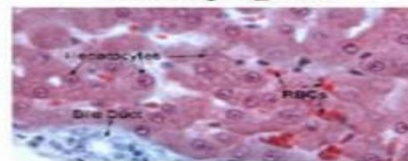
developing bone



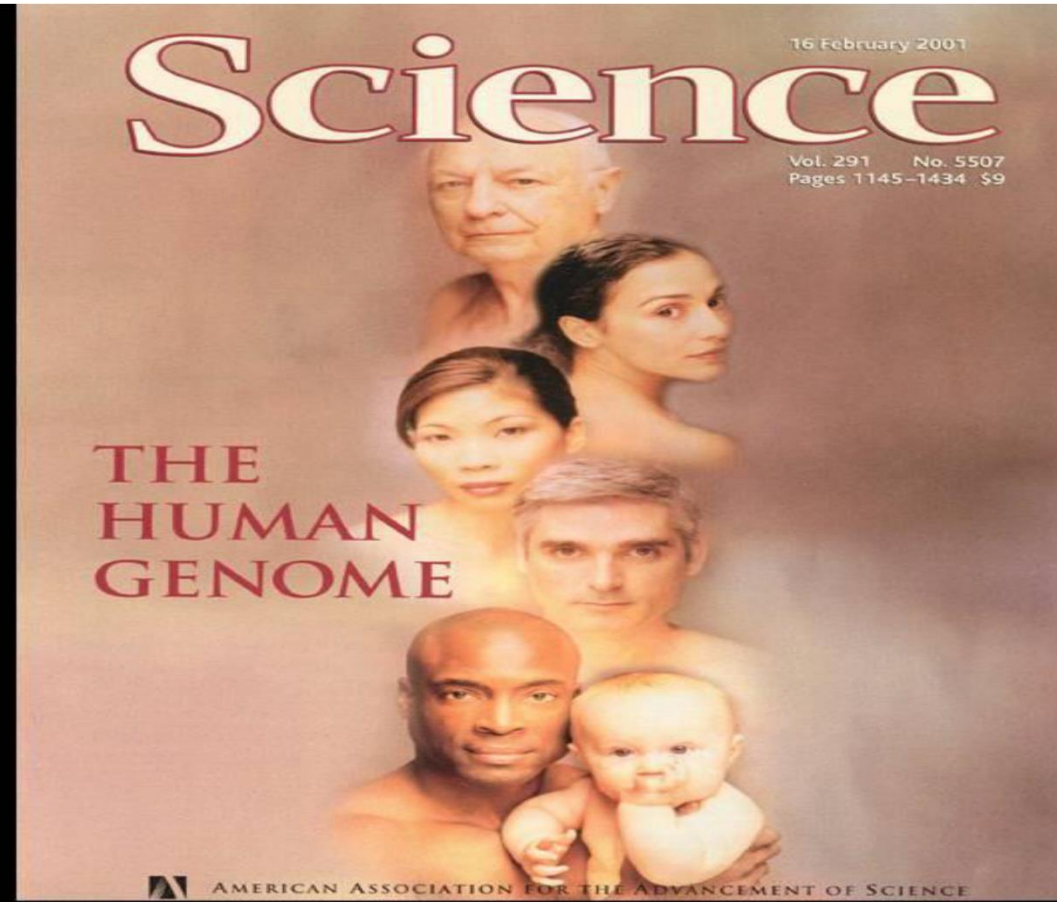
bone (high mag)



neuron

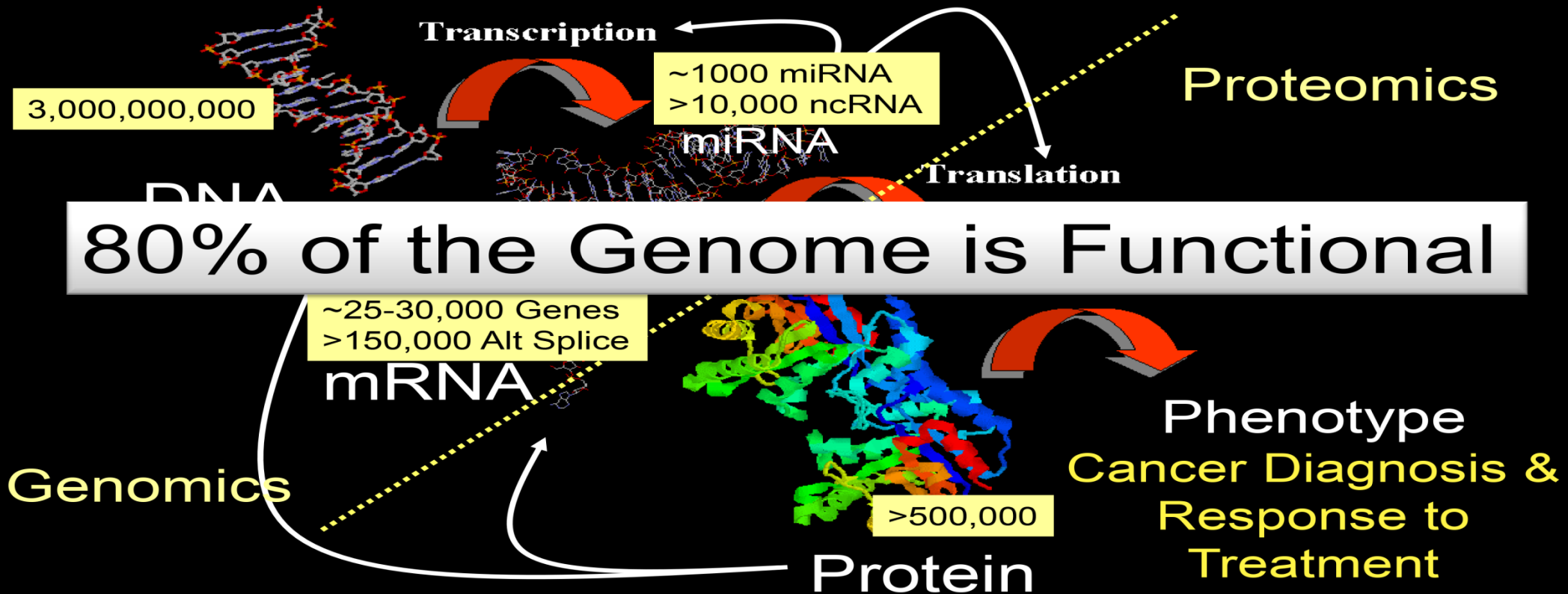


Human genome



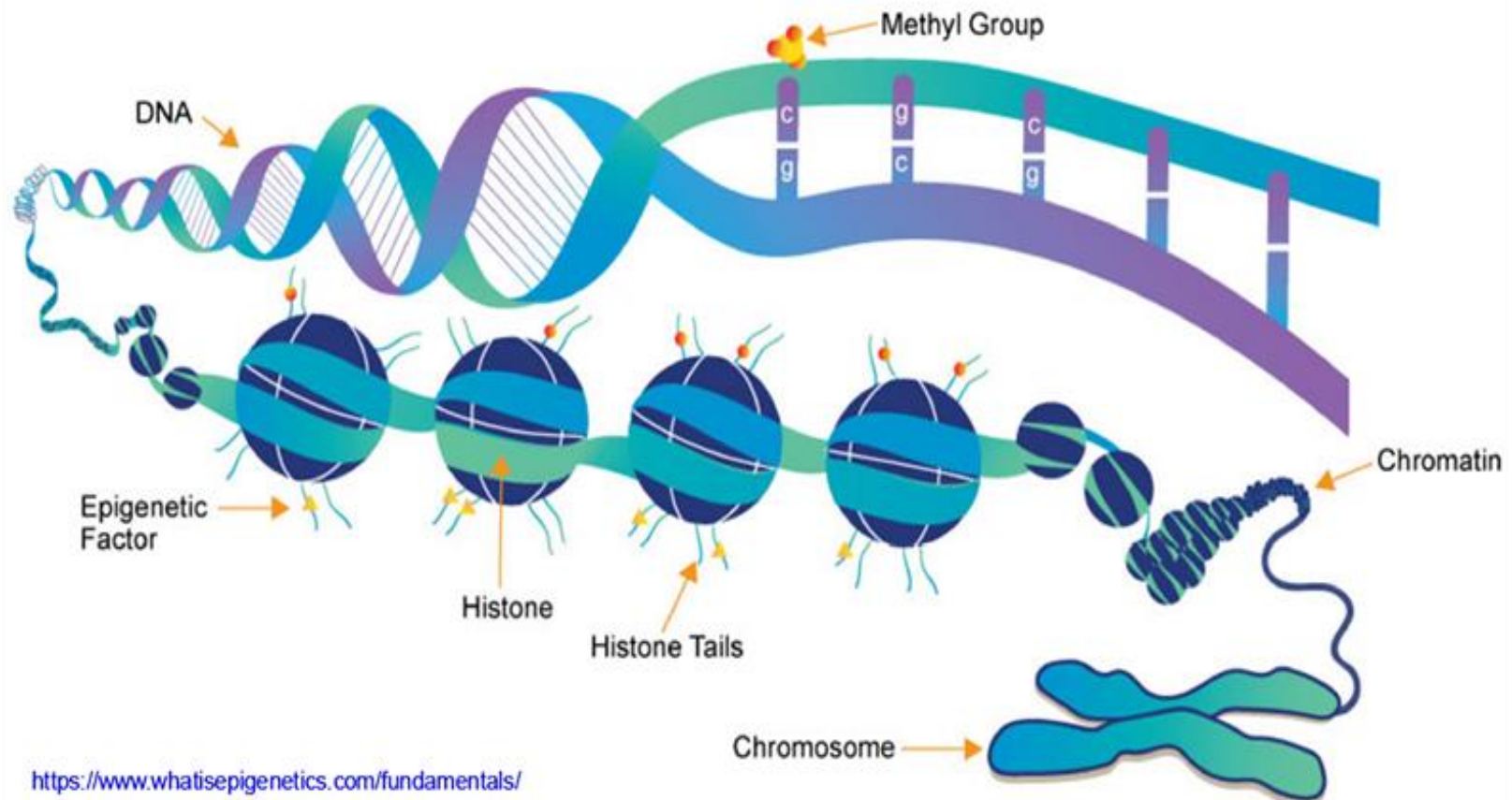
Gene expression

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



Epigenetics

Epigenetics controls the genetic information flow



Challenge

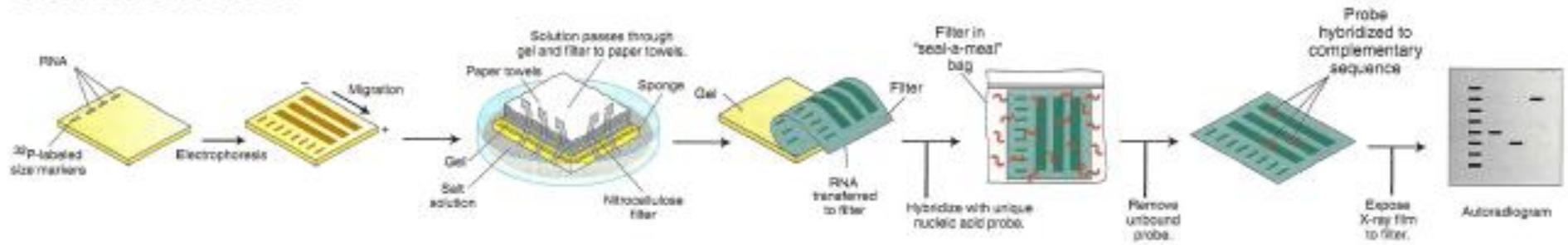
Challenge: how to measure/detect genes and their products in a massively parallel way?

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

Gene expression

How to measure the expression of genes

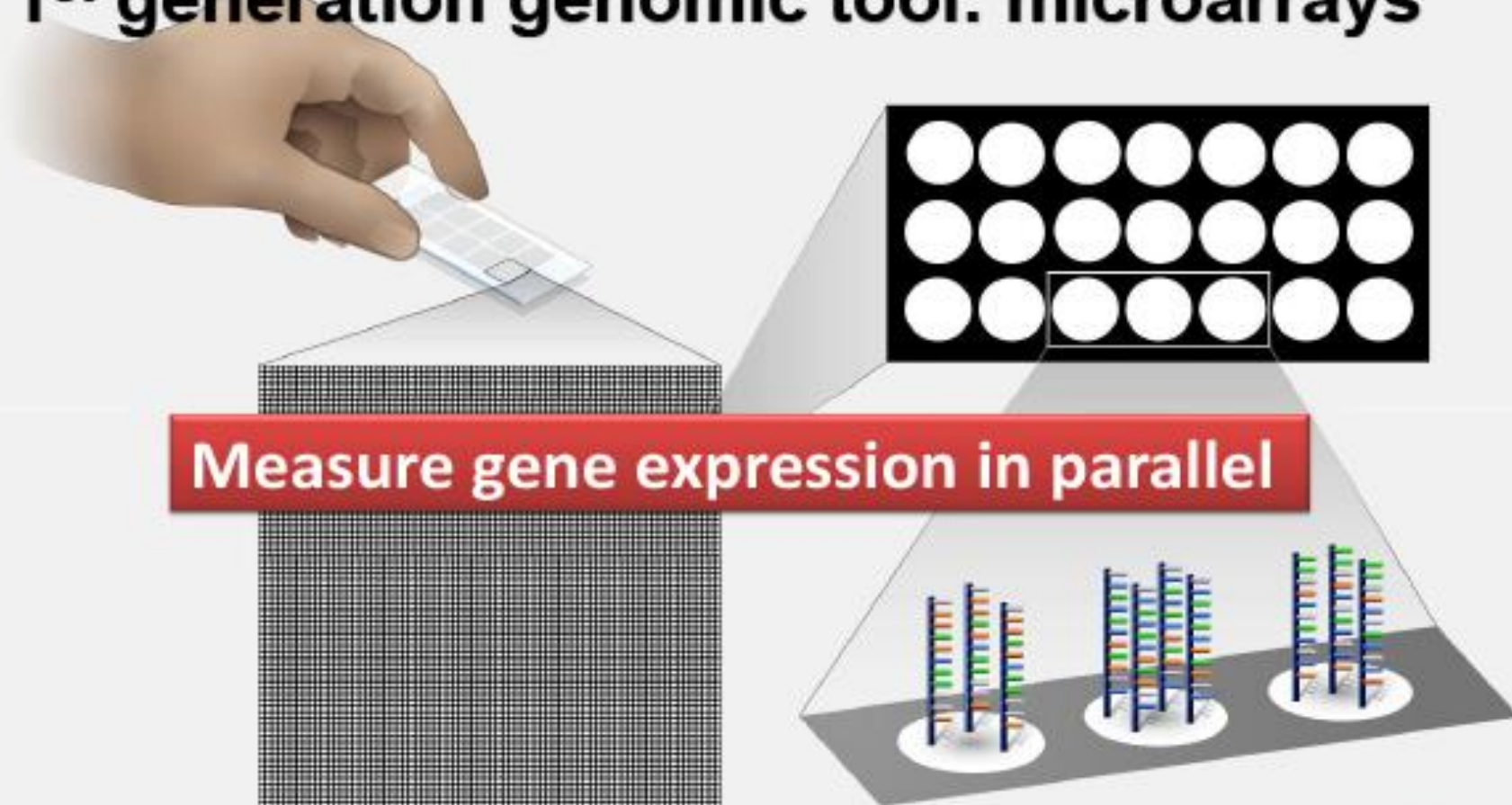
Northern blot



laborious and low throughput

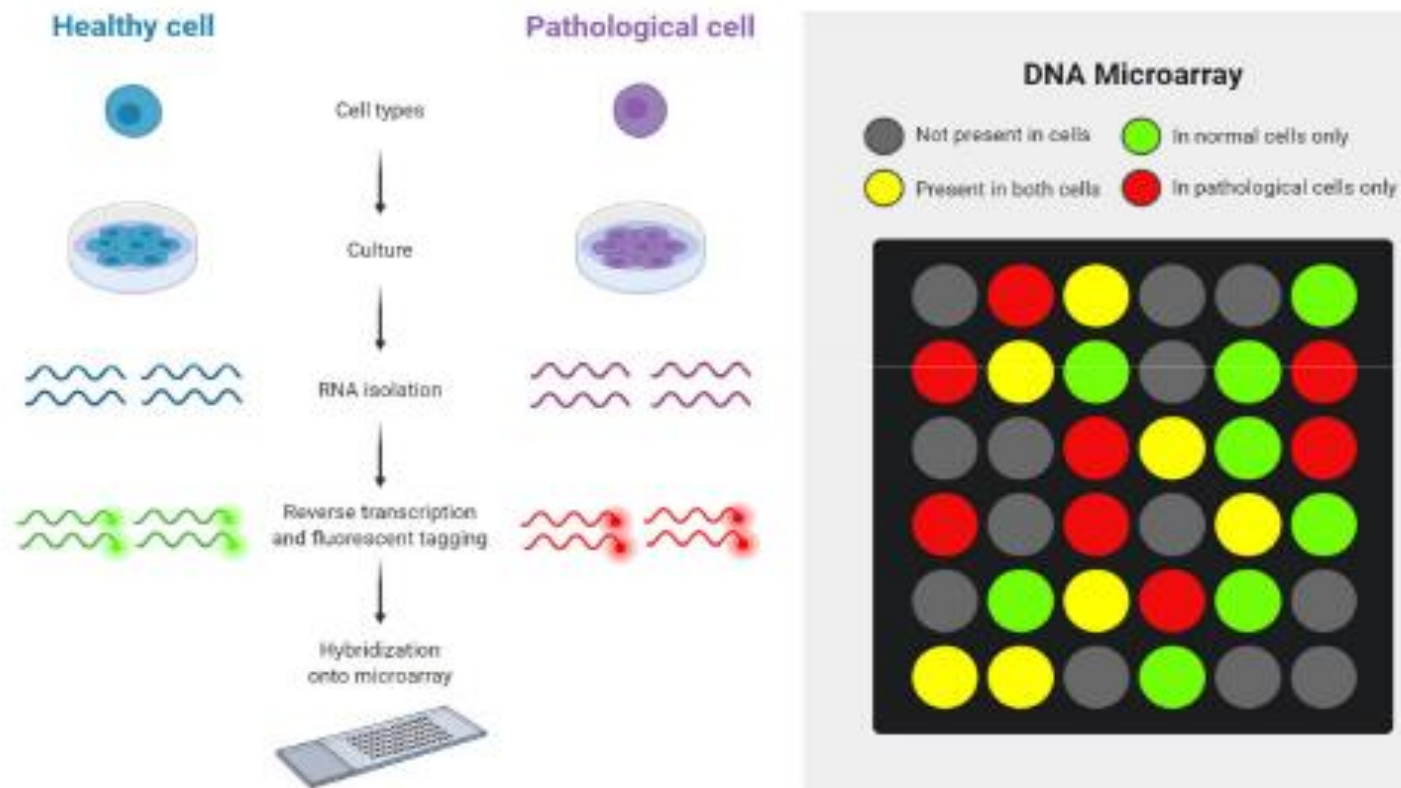
Microarrays

1st generation genomic tool: microarrays



Microarrays

Microarrays – technologies of hybridization

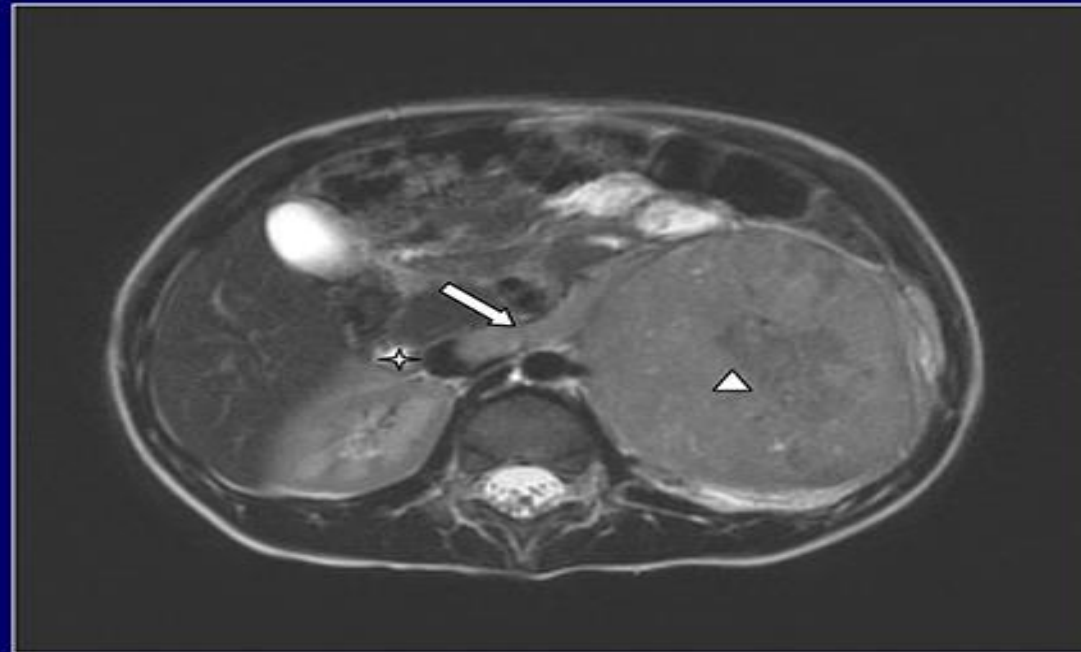


Wilms tumor

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

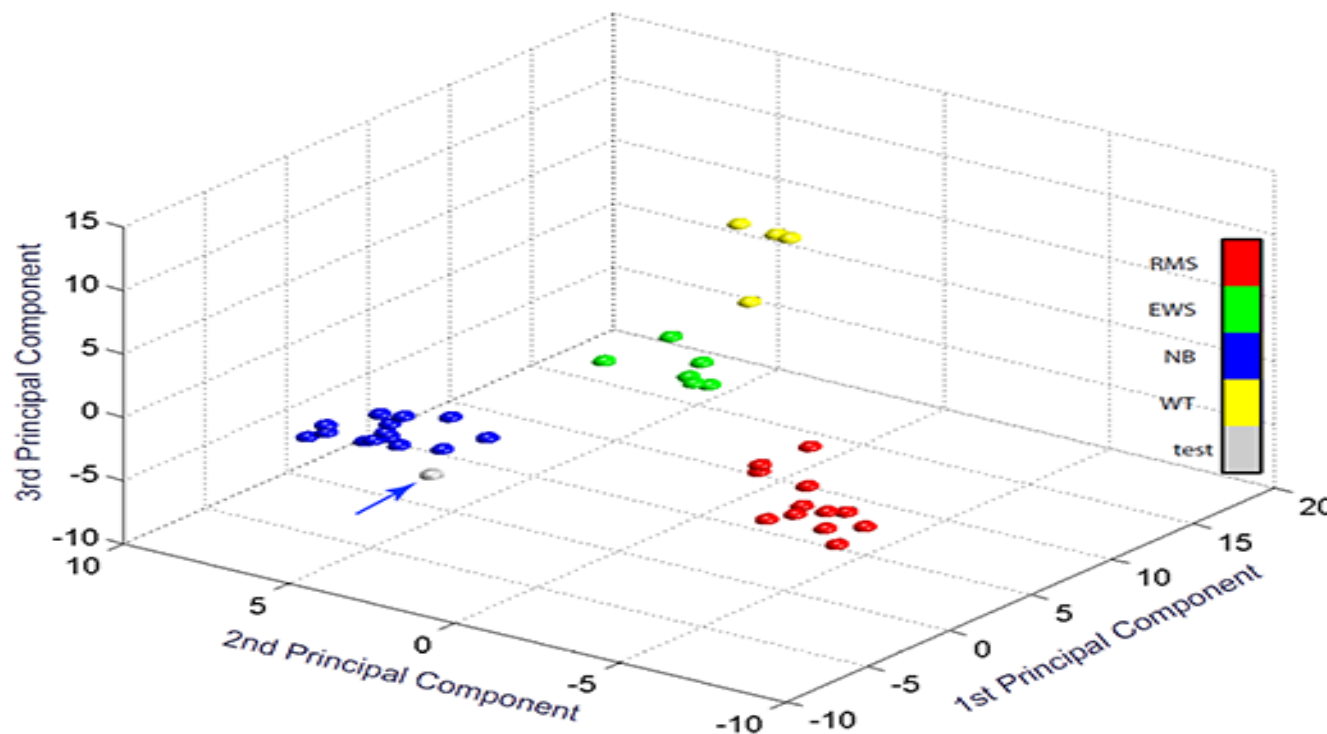


Initial diagnosis: Wilm's tumor



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

Sequencing

Modern Sequencing Technologies

First generation

Second generation
(next generation sequencing)

Third generation



Sanger Sequencing
Maxam and Gilbert
Sanger chain termination

500-1,000 bp

454, Solexa
Ion Torrent
Illumina

~50-600 bp

PacBio
Oxford Nanopore
Illumina Novaseq Series

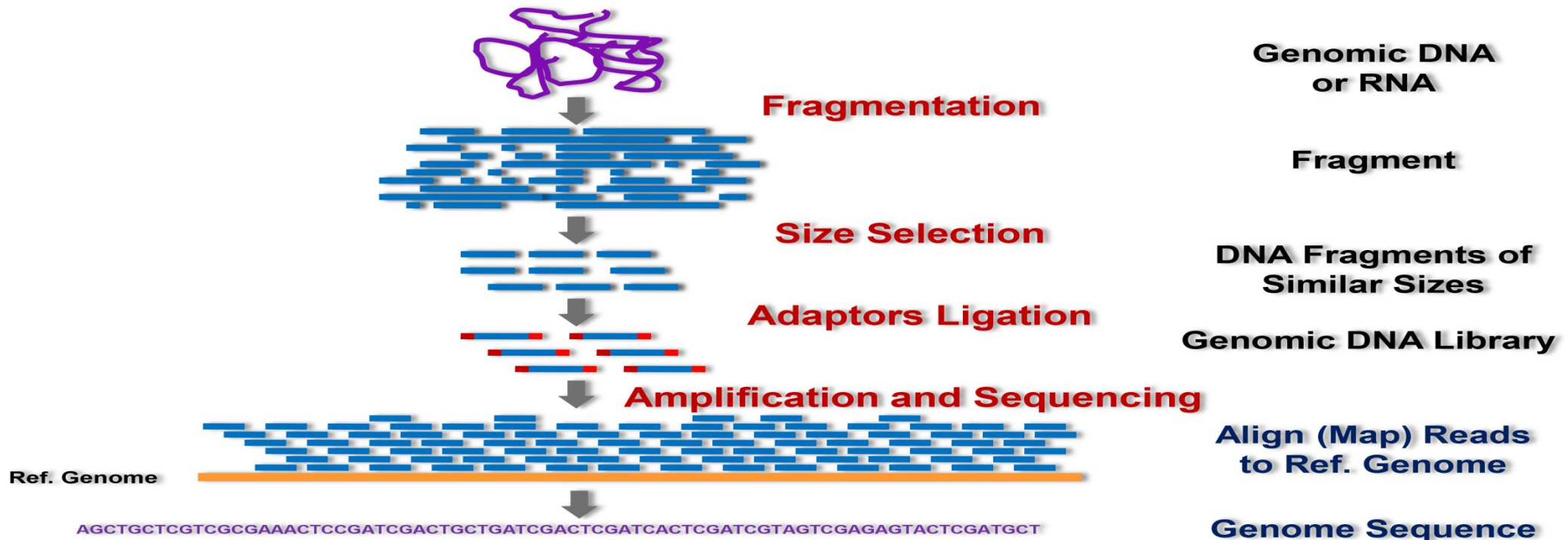
>10,000 bp

Short-read sequencing

Long-read sequencing

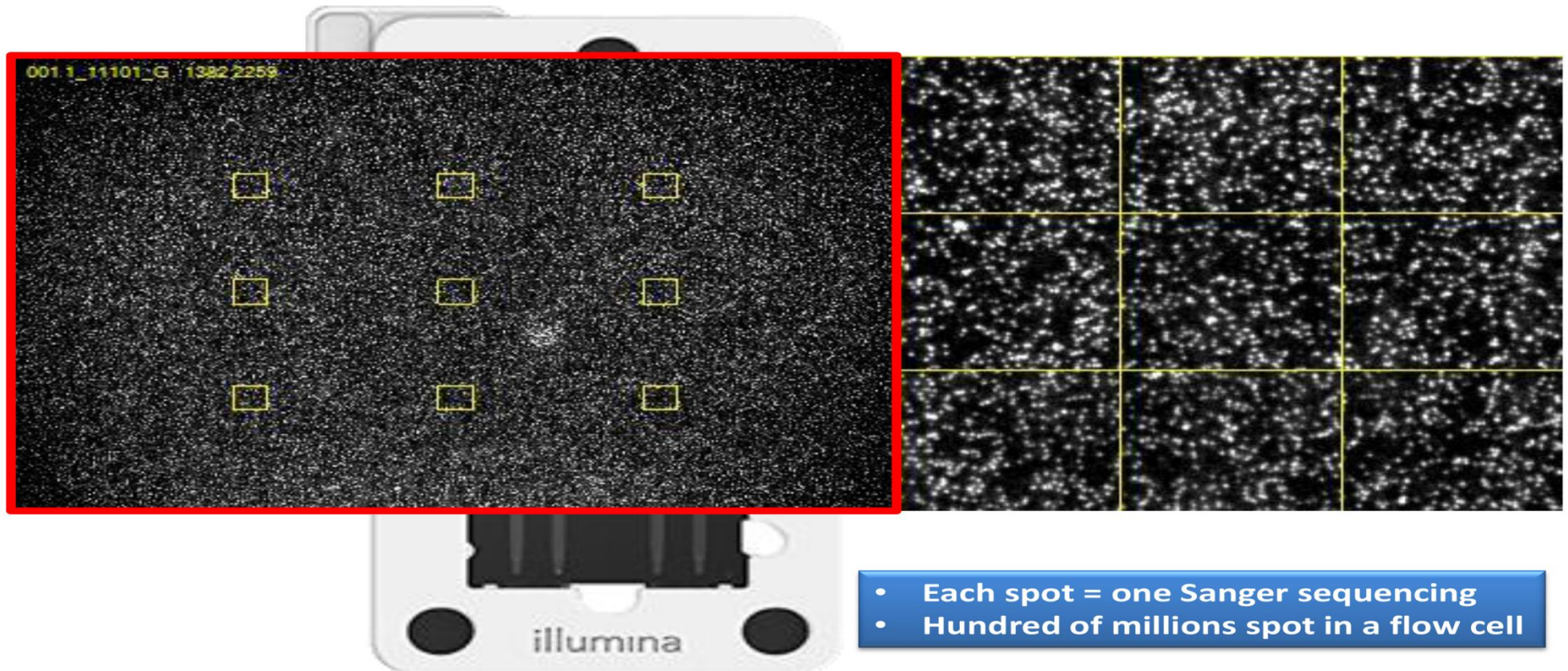
Next-generation sequencing

Next-Generation Sequencing



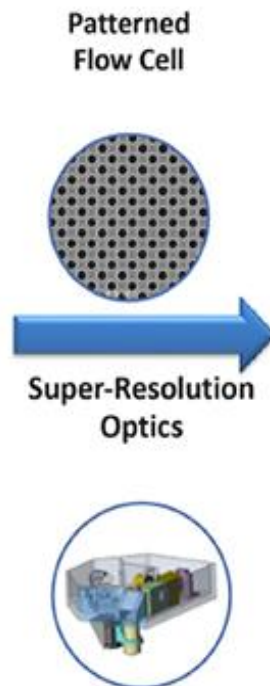
Massively Parallel Sequencing

Massively Parallel Sequencing



Desktop sequencers

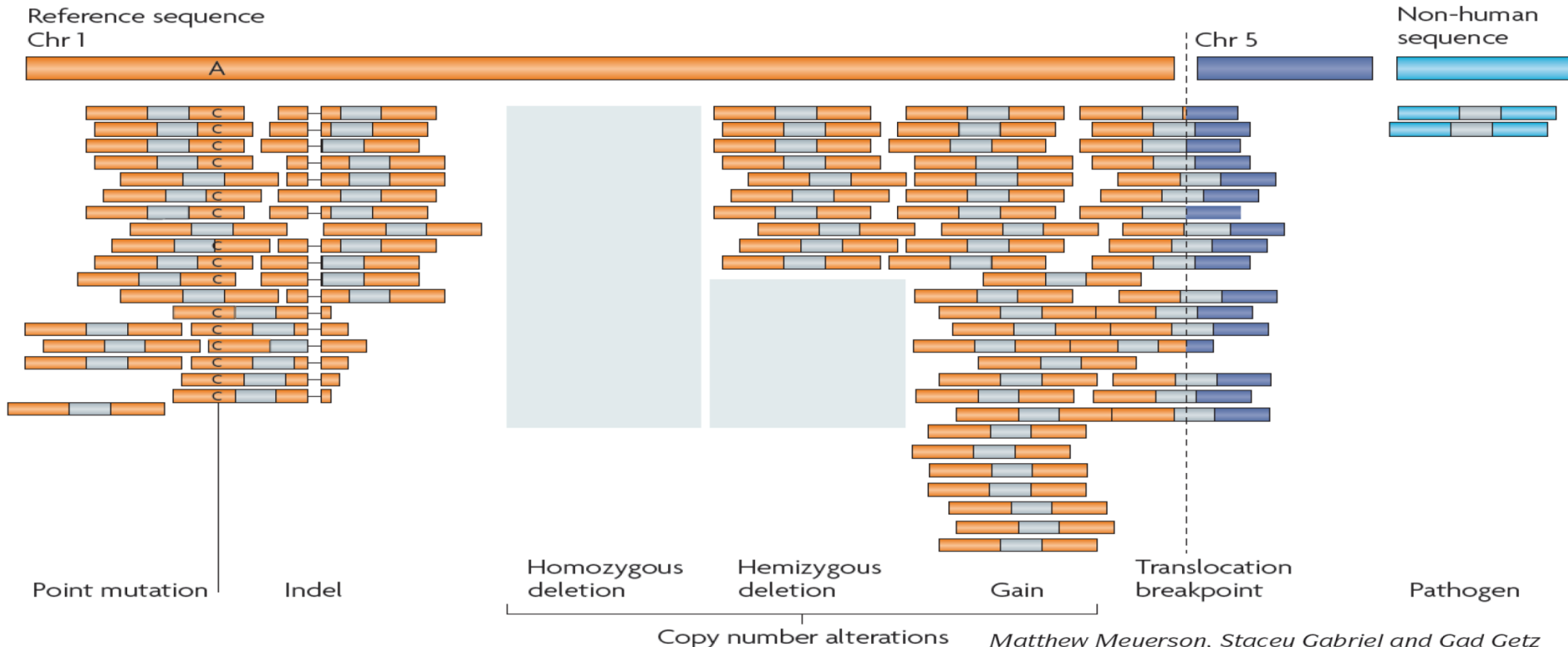
Modern desktop sequencers



- 1.2 billion reads
- 400 Gb (~133 human genomes)
- <40 hours

Genomic Alterations

Genomic alterations detected by DNA sequencing



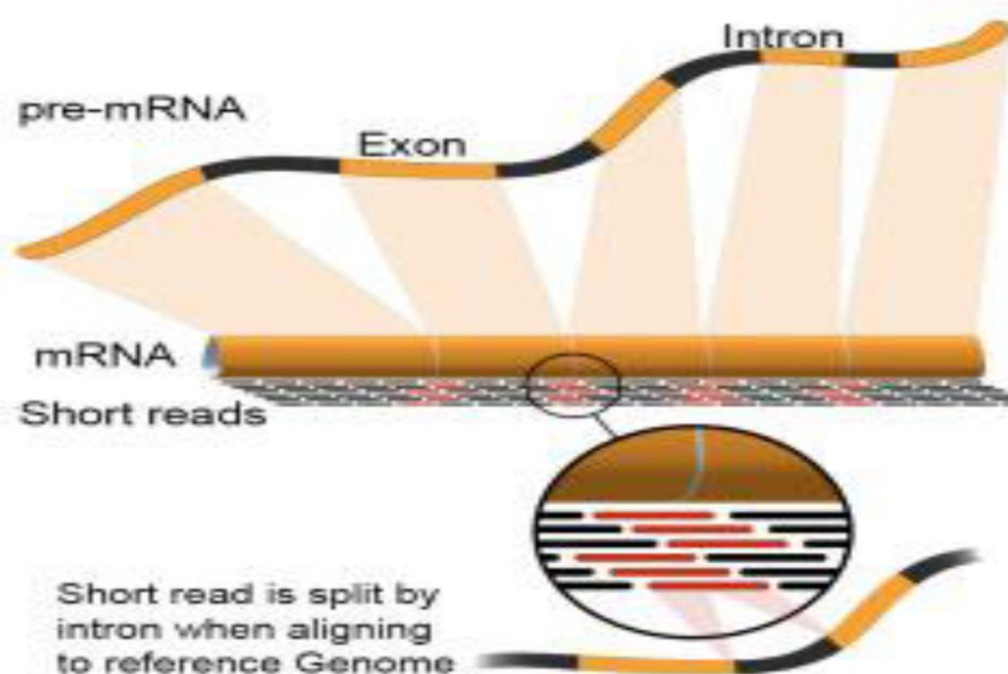
Sequencing

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

- **No prior knowledge is needed for probe design as in microarrays**
- **Massive capacity at a base-pair resolution**
 - 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 types of genomic and epigenomic information**

Genomic Alterations

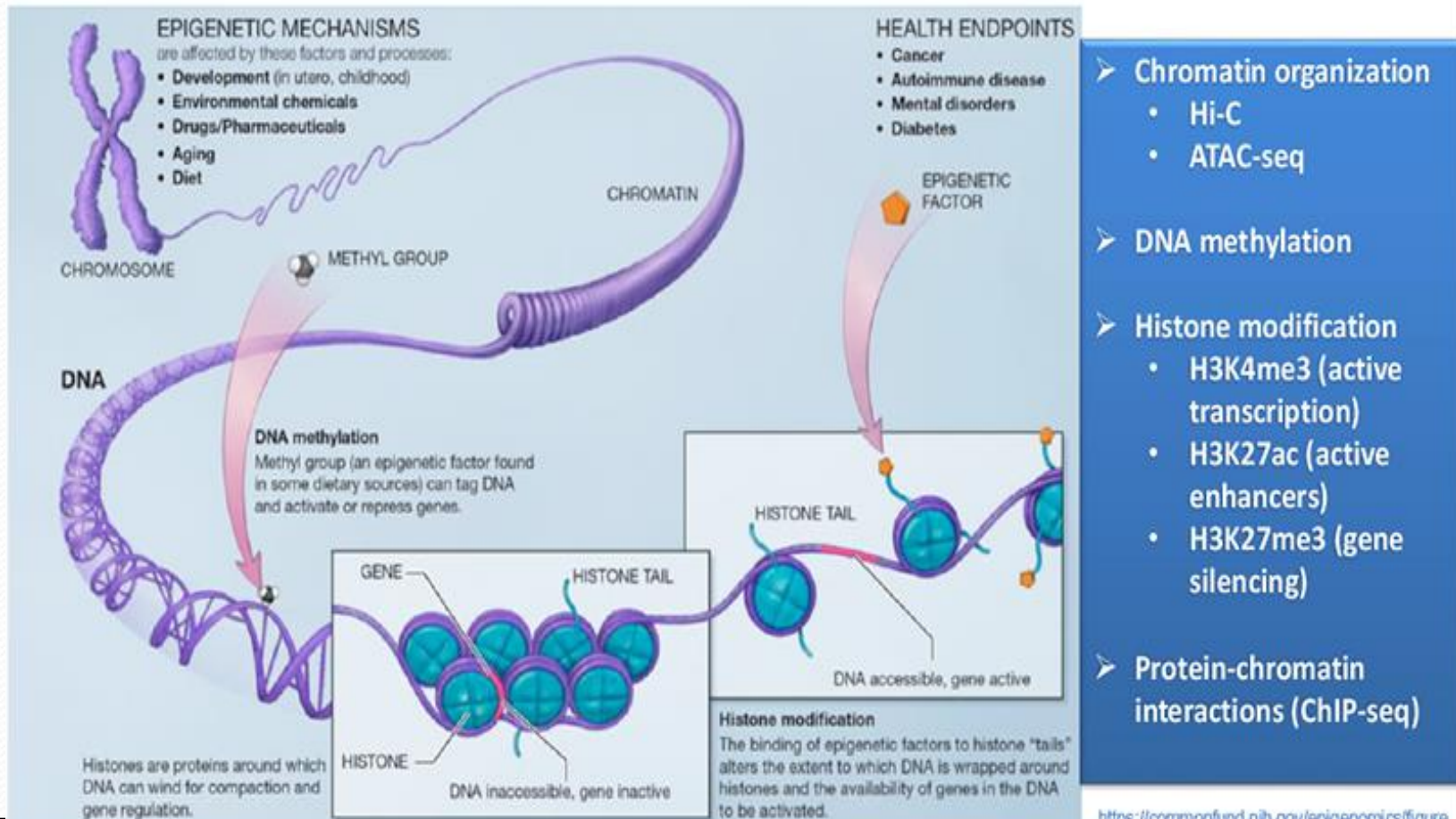
Genomic Alterations Detected by RNA Transcriptome Sequencing



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

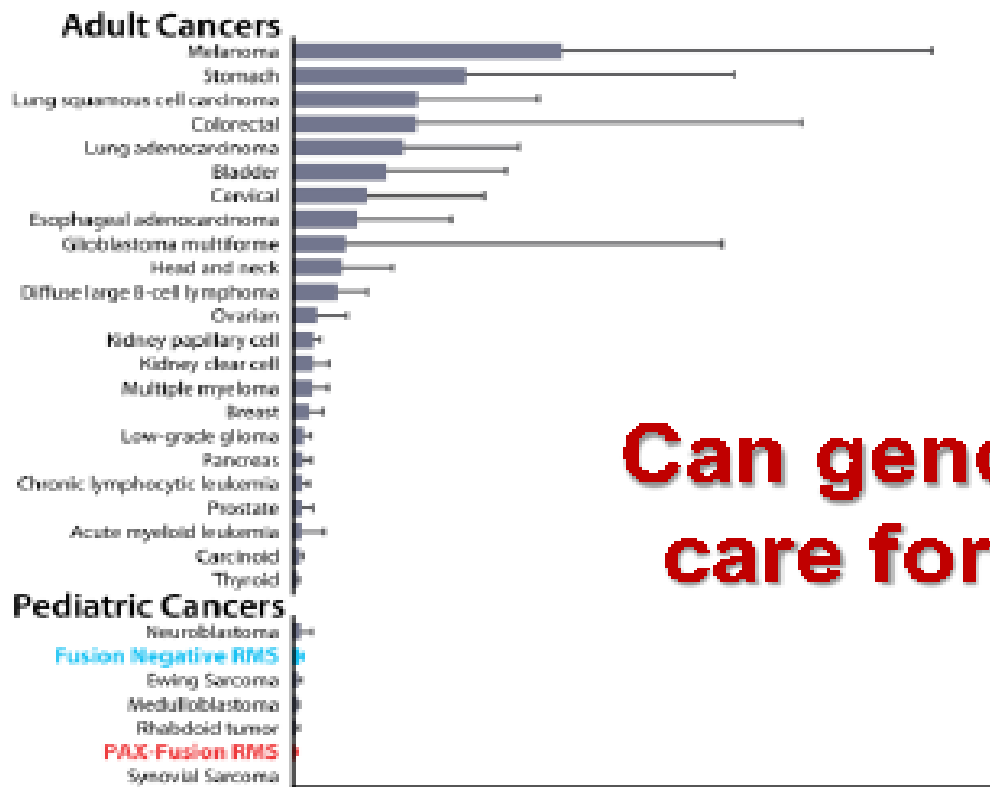
Epigenetics

Study epigenetics, the control of gene expression



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

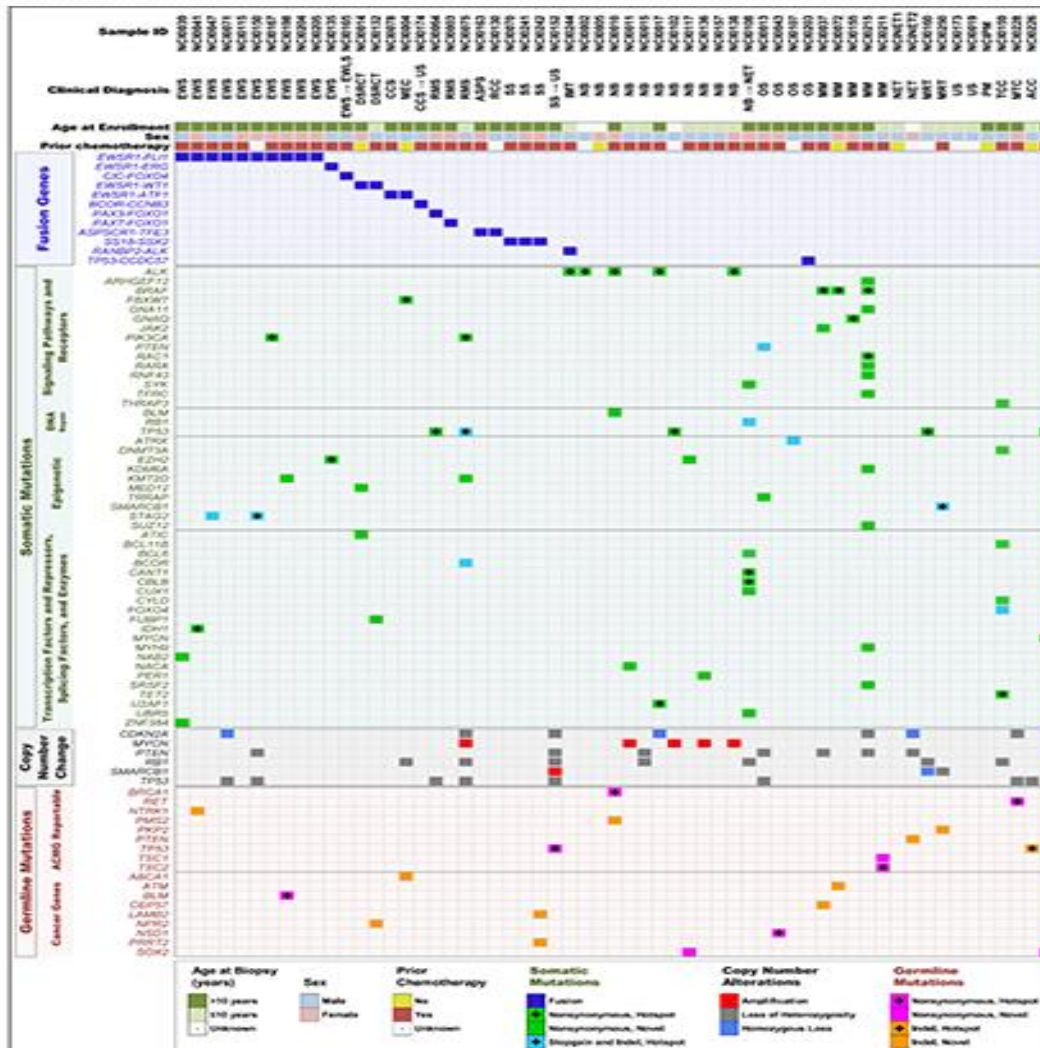
Title: “Comprehensive Omics Analysis of Pediatric Solid Tumors and Establishment of a Repository for Related Biological Studies” or Omics protocol

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 Fusion genes



Multi-Omics Integrated Landscape

RNAseq
Diagnostic, Driver, Actionable

DNAseq and RNAseq
Somatic: Driver, Actionable

DNA copy number & RNAseq
Somatic: Driver, Actionable

DNAseq
Germ line: Disease causing, Actionable

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

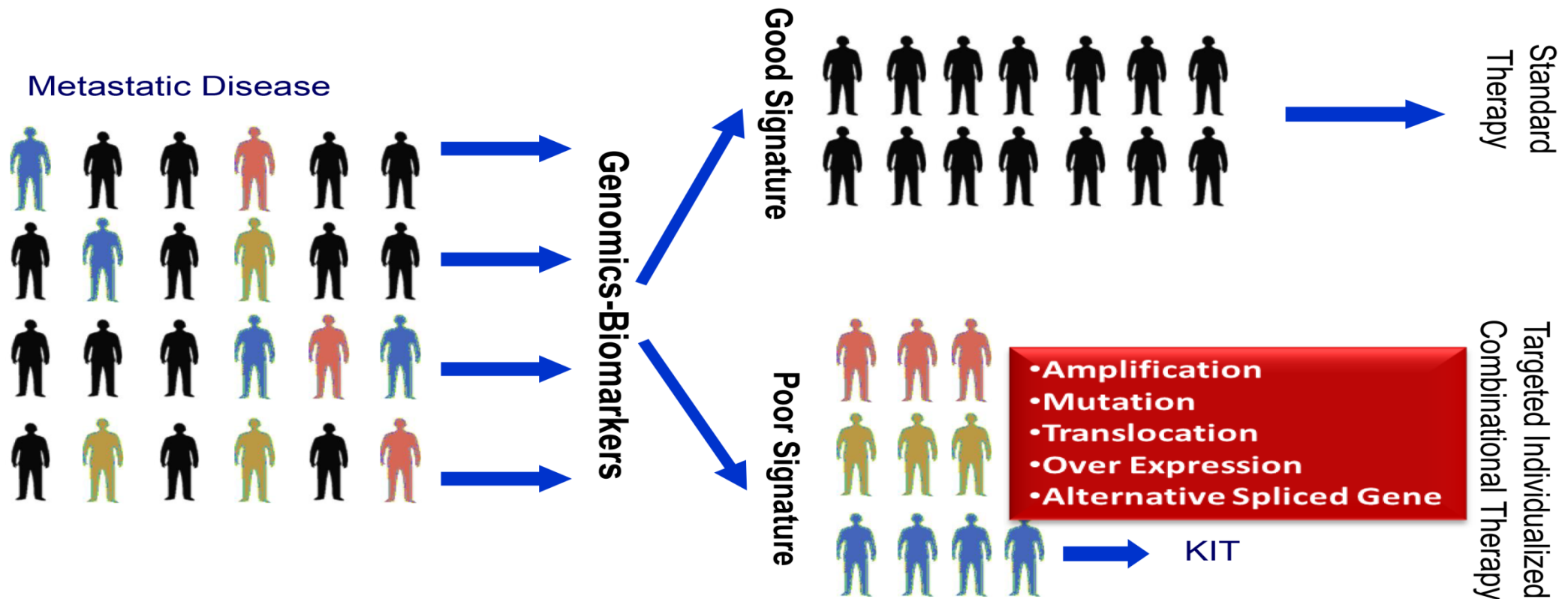
Sample	Diagnosis	Gene	Stage	Morbidity	Mutation	AA Change	Level	Drug	Clinical trial: Pediatric	PDA-Approval in adults	Exact mutation vs. hotspot	Reference preclinical data for level 3
NCI0037	HM	BR4F	Relapsed	WES/WT	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0073	HM	BR4F	Diagnostic	WES/WT	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0215	HM	BR4F	Relapsed	WES/WT	NS SNV	p.V600E	1	Vemurafenib, dabrafenib	Yes	Yes	Exact	—
NCI0155	HM	GR4G	Relapsed	WES/WT	NS SNV	p.Q209L	1	Temsirolimus, trametinib, vemurafenib	No	Yes	Exact	—
NCI0002	NB	ALK	—	WES/WT	NS SNV	p.R1275Q	2a	Crizotinib	Yes	Yes	Exact	—
NCI0010	NB	ALK	Relapsed	WES/WT	NS SNV	p.F1174V	2a	Crizotinib	Yes	Yes	Exact	—
NCI0017	NB	ALK	Relapsed	WES/WT	NS SNV	p.F1174L	2a	Crizotinib	Yes	Yes	Exact	—
NCI0138	NB	ALK	Relapsed	WES/WT	NS SNV	p.Y1298S	2a	Crizotinib	Yes	Yes	Exact	—
NCI0244	IMT	ALK	Relapsed	WT	AAANBP2-ALK fusion	—	2a	Crizotinib	No	Yes	Exact	—
NCI0244	IMT	ALK	Relapsed	WES/WT	NS SNV	p.Y1177T	2a	Crizotinib	No	Yes	Exact	—
NCI0216	HM	BR4F	Relapsed	WES/WT	NS SNV	p.S248P	2a	Trametinib	No	Yes	—	—
NCI0041	EWS	DNF	Relapsed	WES/WT	NS SNV	p.R102C	2a	IDH1 inhibitors	No	No	Exact	—
NCI0075	RMS	PR3C4	Relapsed	WES/WT	NS SNV	p.P104Q	2a	PI3K/AKT/mTOR inhibitors	Yes	Yes	Exact	—
NCI0167	EWS	PR3C4	Refractory	WES/WT	NS SNV	p.D907G	2a	PI3K/AKT/mTOR inhibitors	Yes	Yes	Exact	—
NCI0013	OS	PTEN	Relapsed	WES/WT	Frameshift deletion	p.R80fs	2a	PI3K/AKT/mTOR inhibitors	Yes	No	—	—
NCI0122	NET	PTEN	—	WES/WT	Germline frameshift deletion/somatic LOH	p.R14fs	2a	PI3K/AKT/mTOR inhibitors	Yes	No	—	—
NCI0220	MTC	RET	Relapsed	WES/WT	Germline SNV	p.M918T	2a	Vandetanib	Yes	Yes	Exact	—
NCI0017	NB	CDKN24	Relapsed	SNP Array/WT	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	38
NCI0071	EWS	CDKN24	Relapsed	SNP Array/WT	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	36
NCI0112	NET	CDKN24	—	SNP Array/WT	Homozygous loss	—	3	CDK4/6 inhibitor	No	No	—	38
NCI0011	NB	MYCN	Relapsed	SNP Array/WT	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0175	RMS	MYCN	Relapsed	SNP Array/WT	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0102	NB	MYCN	—	SNP Array/WT	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0136	NB	MYCN	Relapsed	SNP Array/WT	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0138	NB	MYCN	Relapsed	SNP Array/WT	Amplification	—	3	Bromodomain inhibitors	No	No	—	37
NCI0238	WT	MYCN	Relapsed	WES/WT	NS SNV	p.P44L	3	Bromodomain inhibitors	No	No	—	37, 38
NCI0160	HRT	SMARCB1	—	SNP Array/WT	Homozygous loss	—	3	CDK2 inhibitors	No	No	—	39, 40
NCI0250	HRT	SMARCB1	Refractory	WES/WT	NS SNV	p.R400C	3	CDK2 inhibitors	No	No	—	39, 40
NCI0047	EWS	ST4G2	Relapsed	WES/WT	NS SNV	p.E904K	3	PARP inhibitors	Yes	No	—	41
NCI0180	EWS	ST4G2	—	WES/WT	NS SNV	p.R286C	3	PARP inhibitors	Yes	No	Hotspot	41
NCI0231	HM	TSC1	Relapsed	WES/WT	NS SNV	p.S826R	3	Everolimus	No	Yes	—	42
NCI0231	HM	TSC2	Relapsed	WES/WT	NS SNV	p.T248A	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.

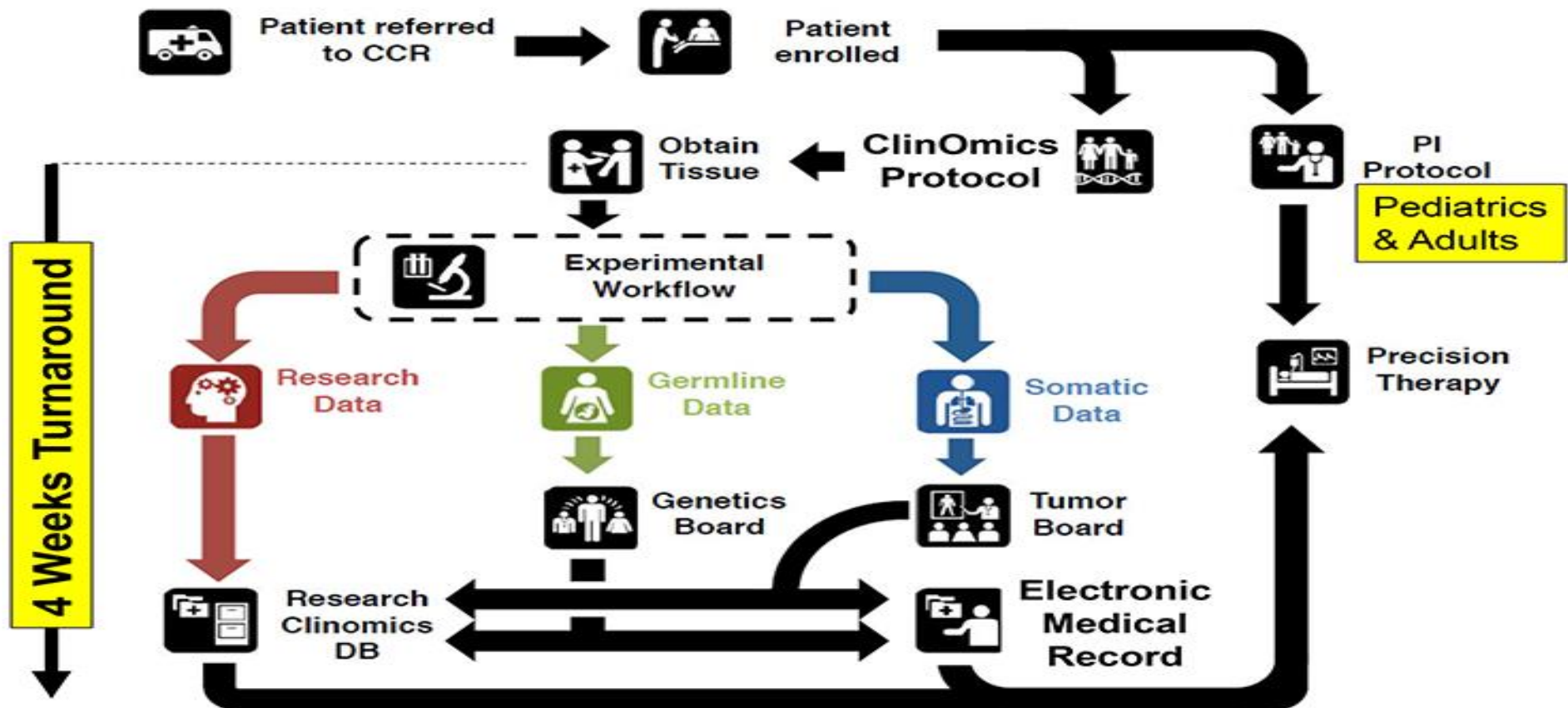
Future Trials

Genomics Enabling Precision Therapy-The Future for Pediatric Trials



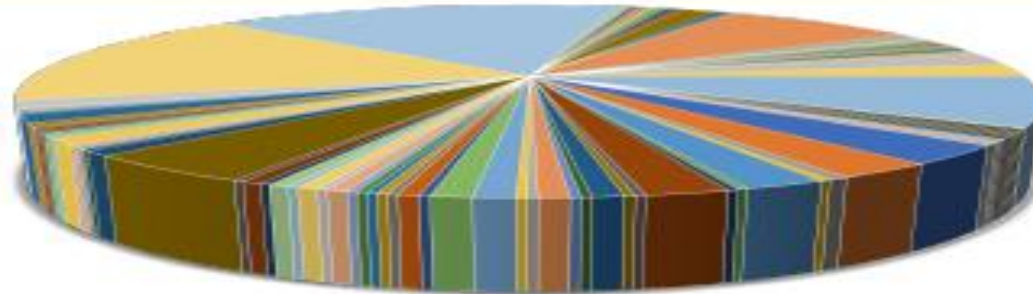
ClinOmics program

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 3 Oligodendroglioma
- (11) Invasive well differentiated squamous cell carcinoma
- (12) Lymphocytoma
- (13) Melanoma
- (14) Mesothelioma Pleural
- (15) Metastatic Pancreatic Neuroendocrine Carcinoma
- (16) Multiple Skin Tumors
- (17) Neuroblastoma I
- (18) Osteosarcoma
- (19) Papillary cancer of the pleural 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 Epithelioma
- (27) Anaplastic Fibrosarcoma
- (28) Breast cancer
- (29) Chondroma
- (30) Desmoplast Fibrosarcoma
- (31) Endometrial cancer
- (32) Ewing's sarcoma
- (33) Glioblastoma
- (34) Hepatic Angiosarcoma
- (35) Kaposi's sarcoma
- (36) Melanoma
- (37) Merkel Cell Carcinoma
- (38) Mesothelioma Thoracic
- (39) MPPH
- (40) Myxopapillary Ependymoma
- (41) Neuroblastoma
- (42) Ovarian Serous Carcinoma
- (43) Pilocytic Astrocytoma
- (44) Prostate cancer
- (45) Pseudopapillary
- (46) Small cell carcinoma of the ovary hypercalcemic type (OEDH)
- (47) Teratoma

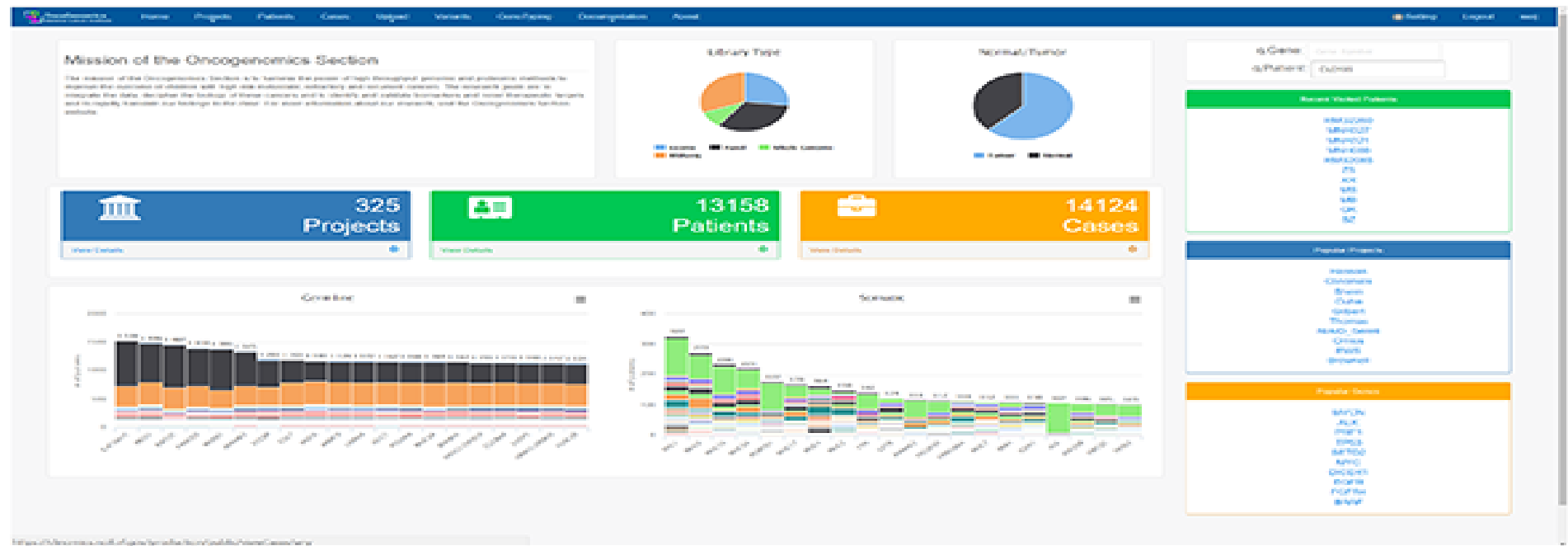
- (48) Acute myeloid leukemia
- (49) Anaplastic meningioma
- (50) Astrocytoma
- (51) Carcinoid, BRCA1 positive
- (52) Clear cell sarcoma
- (53) Desmoplastic small round cell tumor
- (54) Endometrial Stromal Sarcoma
- (55) Extracranial Small Cell Cancer
- (56) Glioma
- (57) Hepatocellular cancer
- (58)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

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

ClinOmics Data Portal

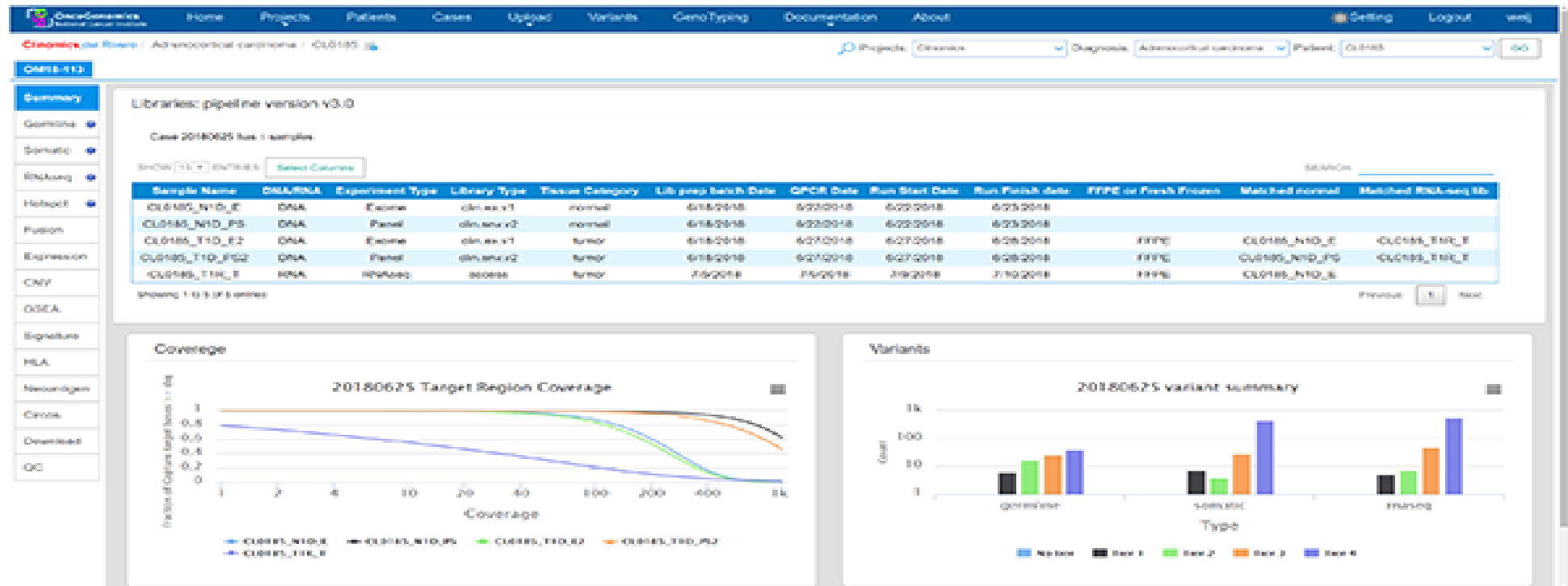
ClinOmics Data Portal

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



Patient Summary

Patient Summary Page



QC report

QC Report: Sequencing Statistics & Genotyping

Run Statistics

Summary	Close	Coverage	Transcript Coverage	Hotspot	Contours	Compare	DNA GC	RNA GC	RNA GC v2	FASTQC	Genotyping	Versions
Summary												
Genome												
Genetic												
RNAseq												
Hotspot												
Fusion												
Expression												
CNV												
GSEA												
Signature												

Showing 1 to 4 of 4 entries

100% threshold

Genotyping

Summary	Close	Coverage	Transcript Coverage	Hotspot	Contours	Compare	DNA GC	RNA GC	RNA GC v2	FASTQC	Genotyping	Versions
Summary												
Genome												
Genetic												
RNAseq												
Hotspot												
Fusion												
Expression												
CNV												
GSEA												

Showing 1 to 4 of 4 entries

100% threshold

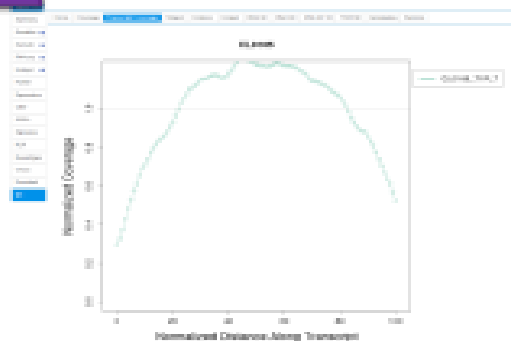
QC Report: Coverage

QC Report: Coverage

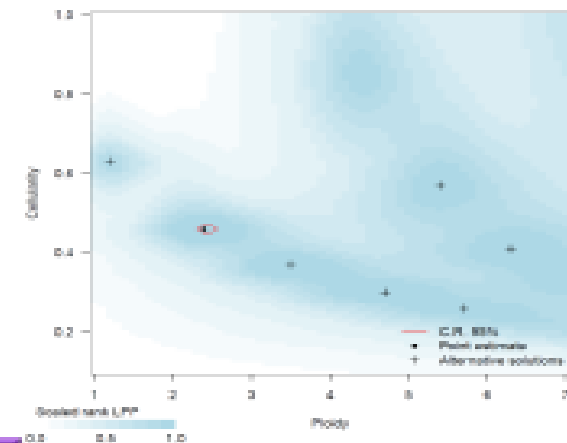
Circos



RNA Coverage



Tumor Content



Hotspot Coverage



Germline and Somatic Mutations

[illegible]

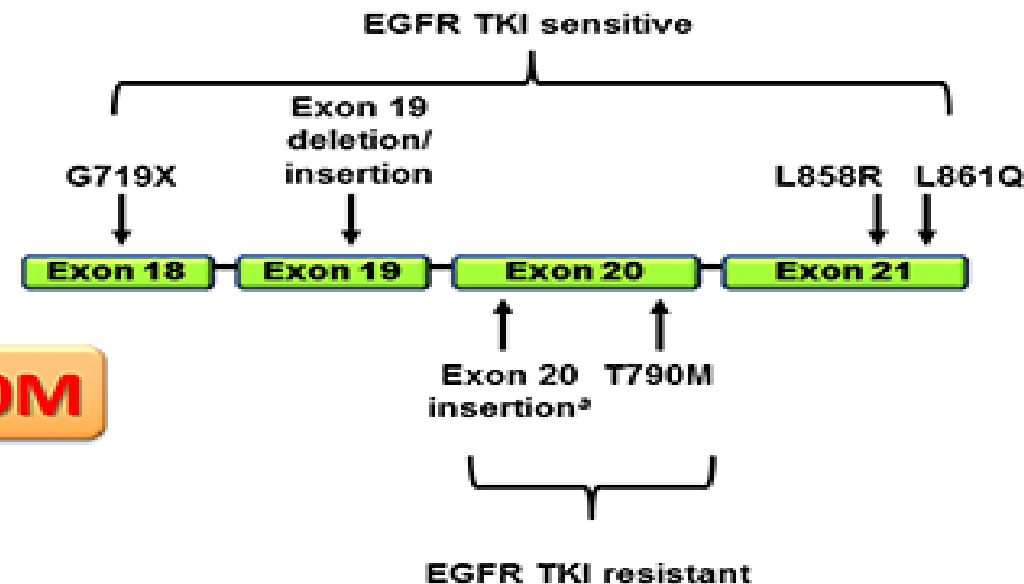
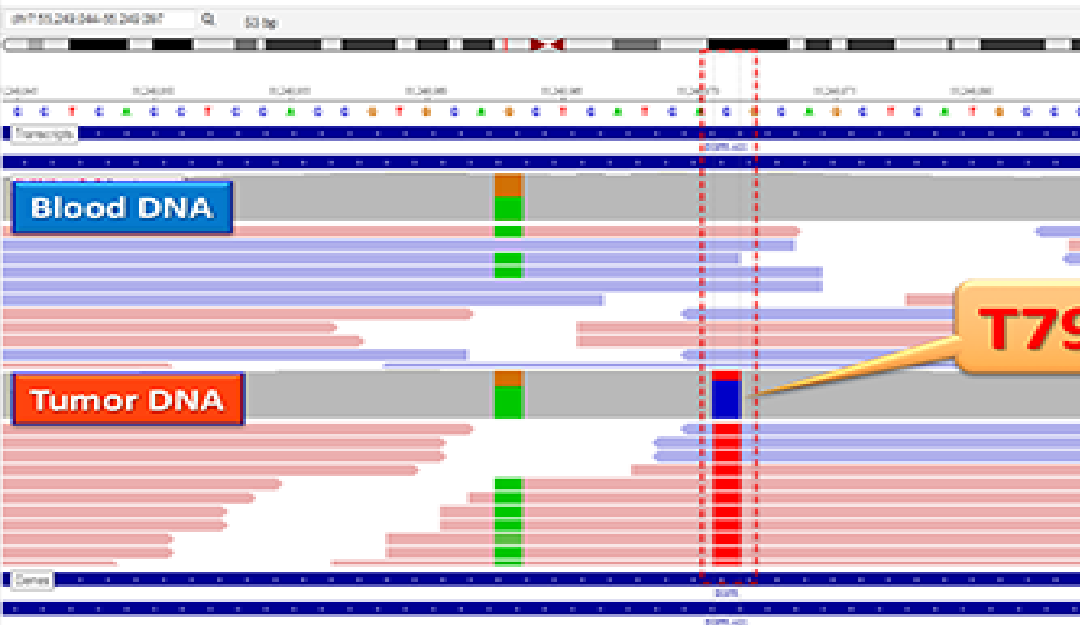
EGFR mutations

EGFR mutations in NSCLC

GV view of patient: CL0040 case: OM18-007 Total 4 sample(s)

Click (check sample to load)

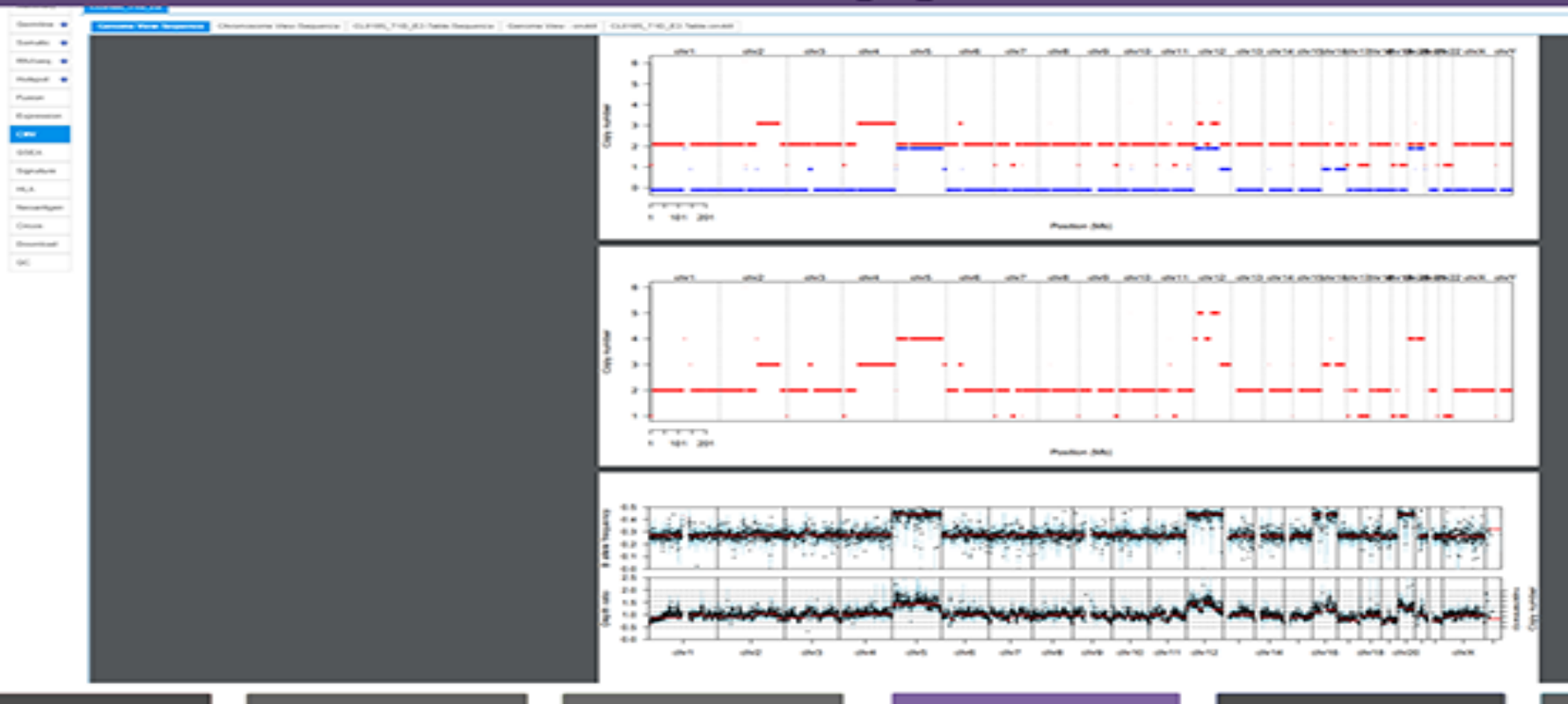
CL0040_T10_E Exome, normal (Exome, normal) CL0040_T10_E Exome, tumor (Exome, tumor) CL0040_T10_P Panel, normal (Panel, normal) CL0040_T10_P Panel, tumor (Panel, tumor)



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

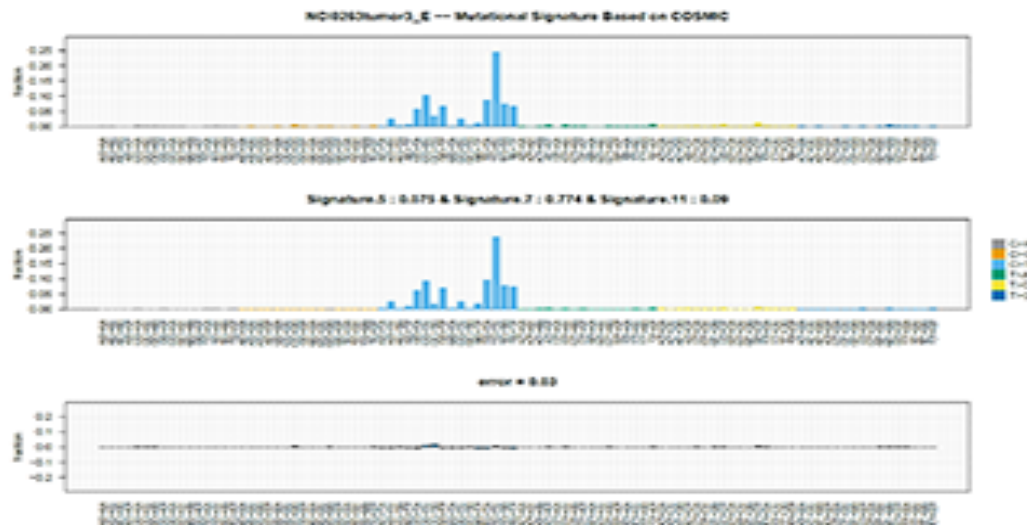
Tumor Copy Number

Tumor Copy Number

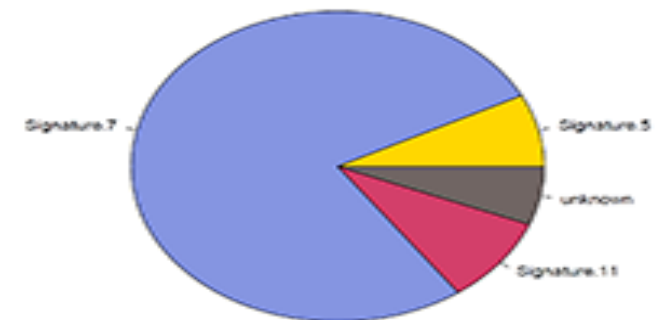


Mutation Signatures

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, by formation of pyrimidine-pyrimidine photodimers) and these mutations are being repaired by transcription-coupled nucleotide excision repair.

Cosmicdb: 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 Río' / 'Adrenocortical carcinoma' / 'CL0185'. Search filters are set to 'Projects: Clinomics', 'Diagnosis: Adrenocortical carcinoma', and 'Patient: CL0185'. The left sidebar lists various genomic analysis categories, with 'Somatic' selected. The main content area shows the 'Mutation_Burden' tab for sample 'OM18-113'. It includes a 'Callers' dropdown set to 'MuTect' and a 'Records: 2/6' indicator. A table displays the mutation burden data for two samples, with the 'Burden Per MB' column highlighted by a red box. The table shows two entries: one for 'Adrenocortical carcinoma' (CL0185_T1D_E2, Exome) with a burden of 612 and 13.54 MB, and another for 'Adrenocortical carcinoma' (CL0185_T1D_PS2, Panel) with a burden of 36 and 14.6 MB. The interface also features a 'Select Columns' button, a 'Show 15 entries' option, and a search bar.

OncoGenomics National Cancer Institute

Home Projects Patients Cases Upload Variants GenoTyping Documentation About

Setting Logout weij

Clinomics del Río / 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

Records: 2/6

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**

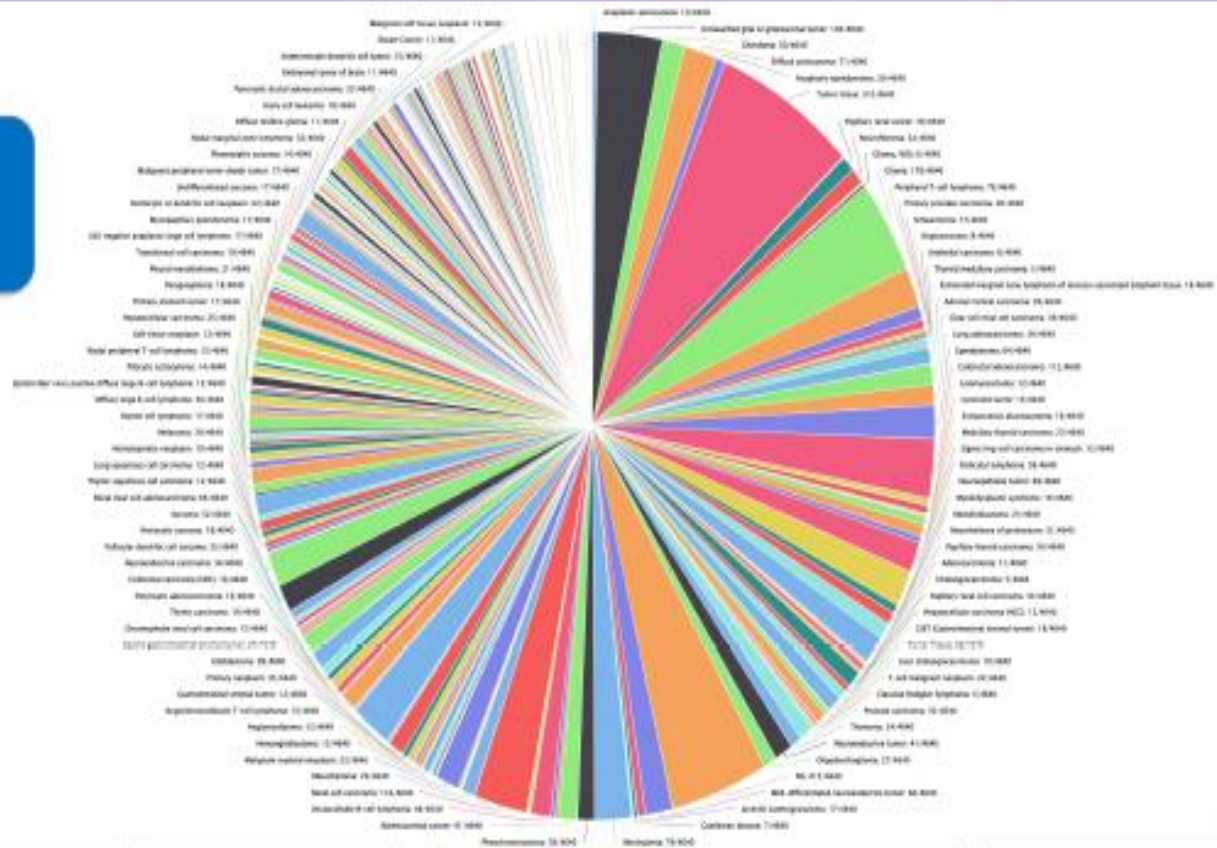
COMPASS

COMPASS Program (LP, 2019-)

11/1/2023:

Patients = 4640

Diagnosis = 496



Conclusions

Conclusions

- Next-generation sequencing is an important genomic tool to study the genomics and epigenetics of tumors
- Genomic research has significantly advanced our understanding of human cancers
- Routine integrated omics analyses of patient tumors can pinpoint rational molecular targets to improve the outcomes of childhood cancers

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