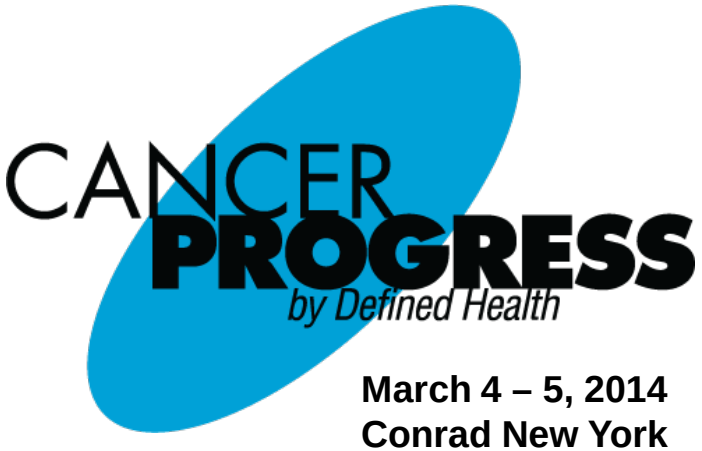
Big Data and Cancer: Transforming Patient Care by Turning Data into Decisions



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Big Data and Cancer: Transforming Patient Care by Turning Data into Decisions

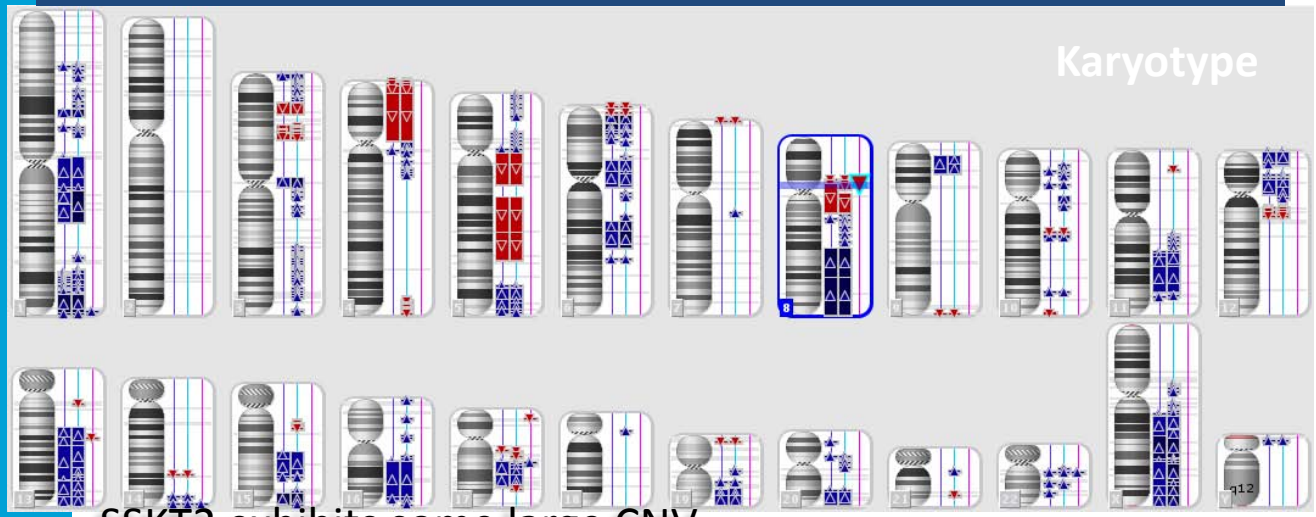
Moderator:

- Colin Hill, Chief Executive Officer, President & Chairman, GNS Healthcare

Panelists:

- Alexis Borisy, Entrepreneur in Residence, Third Rock Ventures
- Joel Dudley, PhD, Director of Biomedical Informatics and Assistant Professor of Genetics and Genomics Sciences, Icahn School of Medicine at Mount Sinai
- Brian Leyland-Jones, MD, VP, Molecular and Experimental Medicine, Avera Health
- Michael Kolodziej, MD, National Medical Director, Oncology Strategies, Aetna Ventures, LLC
- Timothy J. Thompson, CEO, Intervention Insights

SSKT2 Basic CNV Report



SSKT2 exhibits some large CNV changes, particularly on chromosomes 1, 4, 5, 6, 8, 13, and X. You'll note the two sets of bars (in a few cases 3). The first two bars are the replicate samples. 85% of the CNVs were concordant between the two tumor samples. Highlighted is chr 8 where there was a homozygous loss of ADAM 3A and 5P in all three samples, it has recently been linked to glioma development.

CytoRegion	Chromosome	CN State
APC	5	1
BAP1	3	1
FGFR3	4	1
IRF4	6	1
MAP3K1	5	1
MLL2	12	1
MYST3	8	1
PBRM1	3	1
PIK3R1	5	1
PRKDC	8	1
RAD50	5	1
SETD2	3	1
TGFBR2	3	1

CNV Losses

CNV Gains

CytoRegion	Chromosome	CN State
AKT3	1	4
BTK	X	4
IGF1R	15	4
PAK3	X	4
ARFRP1	20	3
ATM	11	3
AURKA	20	3
BCORL1	X	3
BRIP1	17	3
CBFB	16	3
CCND2	12	3
CD79B	17	3
CDH1	16	3
CDKN2A	9	3
CDKN2B	9	3
CTCF	16	3
DDR2	1	3
EPHA3	3	3
FGF14	13	3
FGF23	12	3
FGF6	12	3
FGFR4	5	3
FLT4	5	3
GNA13	17	3
GNAS	20	3
IRS2	13	3
KDM5A	12	3
KRAS	12	3
MAP2K1	15	3
MCL1	1	3
MRE11A	11	3
NOTCH2	1	3
NPM1	5	3
NTRK1	1	3
NUP93	16	3
PPP2R1A	19	3
PRDM1	6	3
RB1	13	3
RNF43	17	3
SPOP	17	3
STAG2	X	3

Nov 2013, Tristan M. Carland, PhD

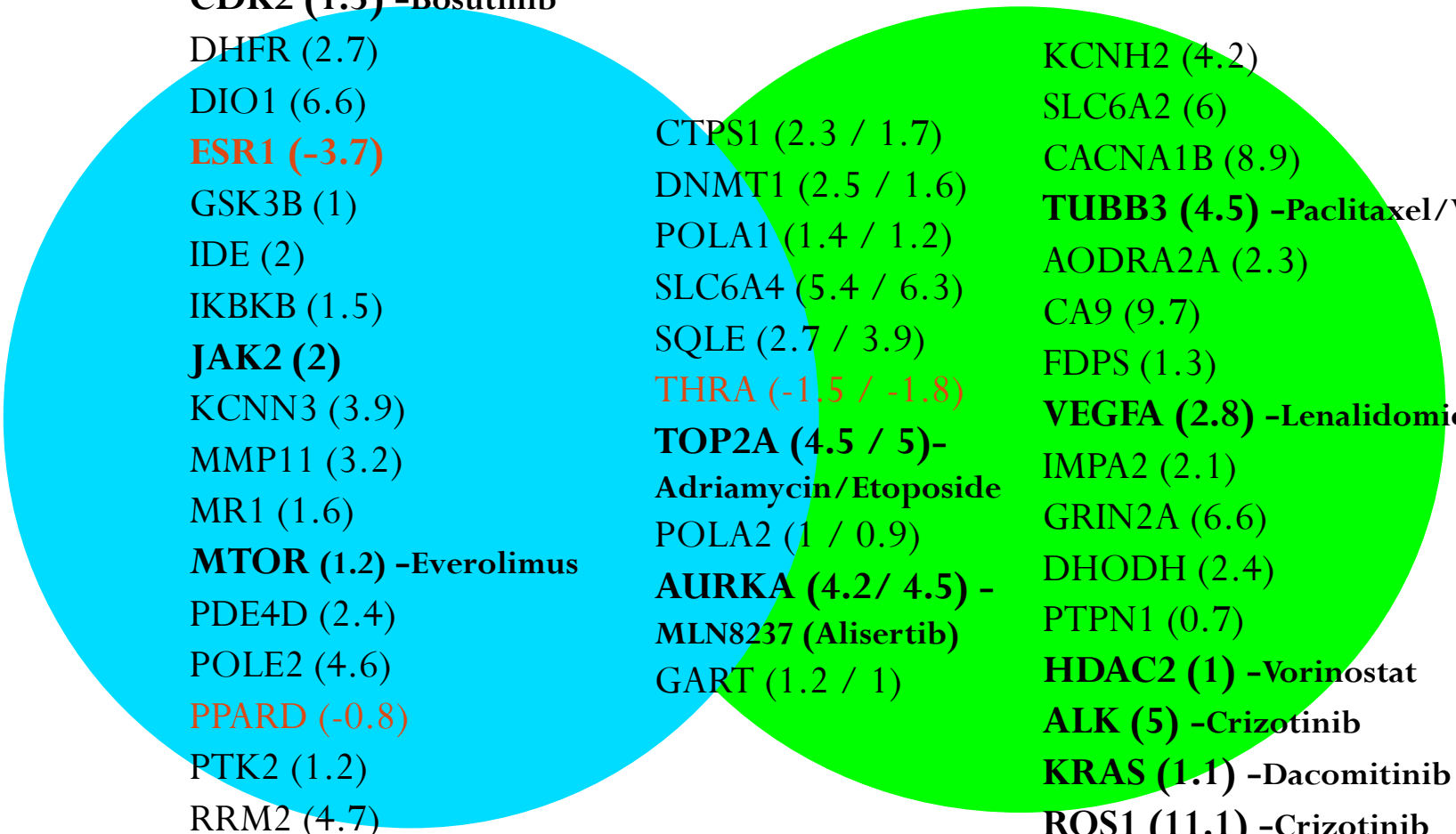
RNA Seq (sample #1)

Drug	Target_Expressed	Target_Expressed_FC
Adriamycin	TOP2A	4.52
Alitretinoin	RXRB	-1.01
AMG337	MET	-2.65
BGJ398	FGFR1	-1.86
Crizotinib	MET	-2.65
Dacarbazine	POLA2	0.94
Etoposide	TOP2A	4.52
GSK2141795 (GSK795)		
Interferon		
MLN8237	AURKA	4.2
Paclitaxel		
Pemetrexed	DHFR GART	2.68 1.18
Sorefenib	BRAF	1.58
Tamoxifen	ESR1	-3.72
Temsirolimus	MTOR	1.16
Vinblastine		
Vorinostat		
XL184	MET	-2.65

RNA seq (sample #2)

Drug	Target_Expressed	Target_Expressed_FC
Adriamycin	TOP2A	4.95
BGJ398	FGFR1	-3.43
Crizotinib	ALK ROS1	4.95 11.13
Dacarbazine	POLA2	0.85
Etoposide	TOP2A	4.95
GSK2141795 (GSK795)		
MLN8237	AURKA	4.49
Paclitaxel	TUBB3	4.53
Pemetrexed	GART	0.99
PF-00299804	KRAS	1.1
Sorefenib	PDGFRB	-2.33
Vinblastine	TUBB3	4.53
Vorinostat	HDAC2	1

SSKT 2



downregulated
upregulated

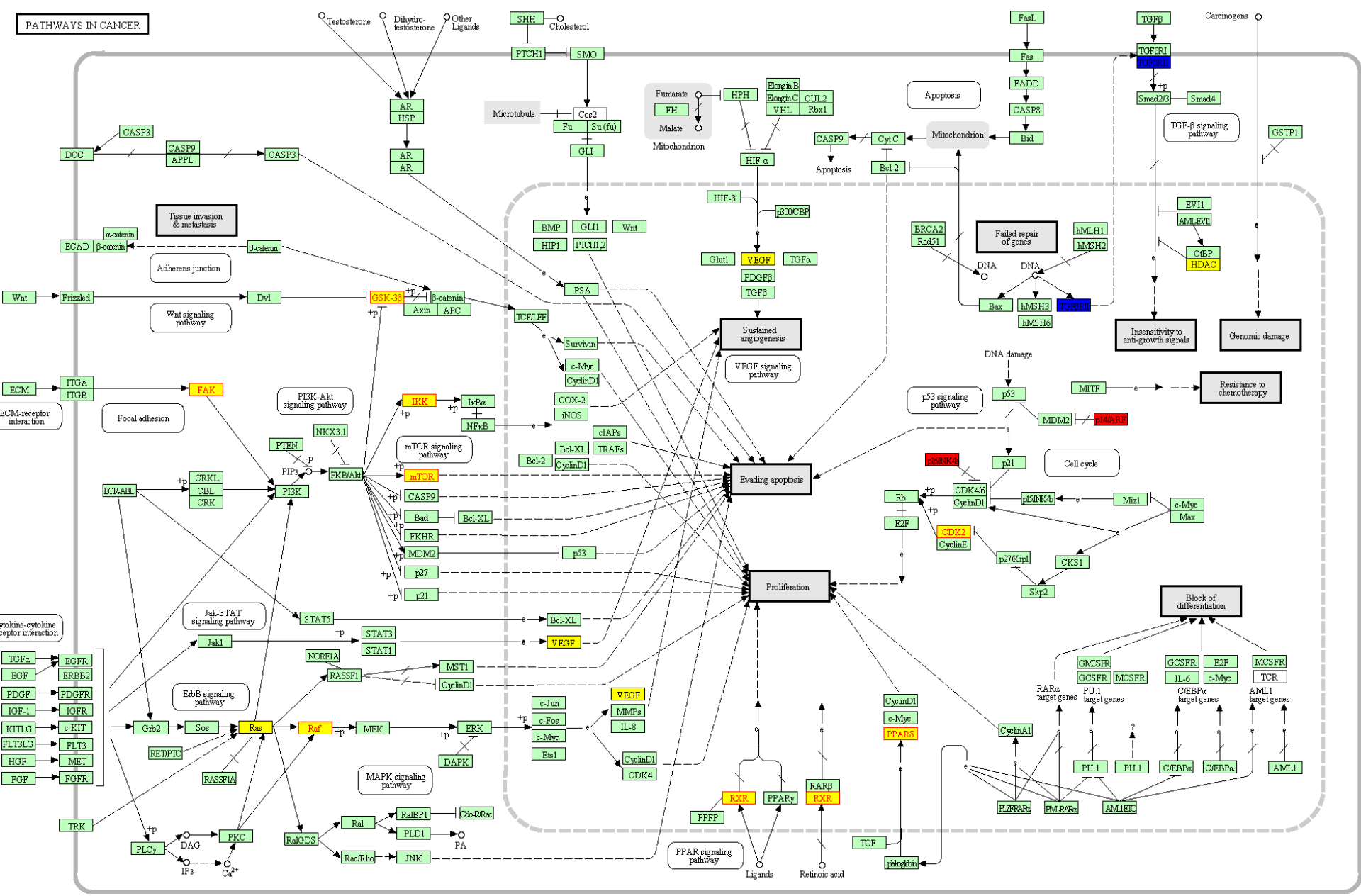
values: log2 fold change

THERAPEUTIC INSIGHT by Defined Health
DefinedHealth unconventional insight
CANCER PROGRESS by Defined Health

RNA-seq & CNV Concordance

Gene	Chromosome	CN State	Gain/Loss	SSKT2_T1	SSKT2_T2
AURKA	20	3	Gain	Up (4.2)	up (4.5)
BRIP1	17	3	Gain	up (5)	up (5.8)
CDKN2A	9	3	Gain	up (4.4)	up (4.7)
FGFR3	4	1	Loss	up (3.5)	NA (1.4)
PIK3R1	5	1	Loss	NA (-0.1)	down (-2.3)
PRKDC	8	1	Loss	up (3.2)	NA (0.8)
TGFBR2	3	1	Loss	down (-2.5)	down (-2.9)

Red: Upregulated and Gain
Blue: Downregulated and loss
NA: not diff. expressed or no reliable expression value



Blue: Downregulated & CNV: Loss

Red: Upregulated & CNV: Gain

BRIP1 BRCA1 interacting protein C-terminal helicase 1 [*Homo sapiens* (human)]

Gene ID: 83990, updated on 17-Nov-2013

Organism

Homo sapiens

Lineage

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo

Also known as

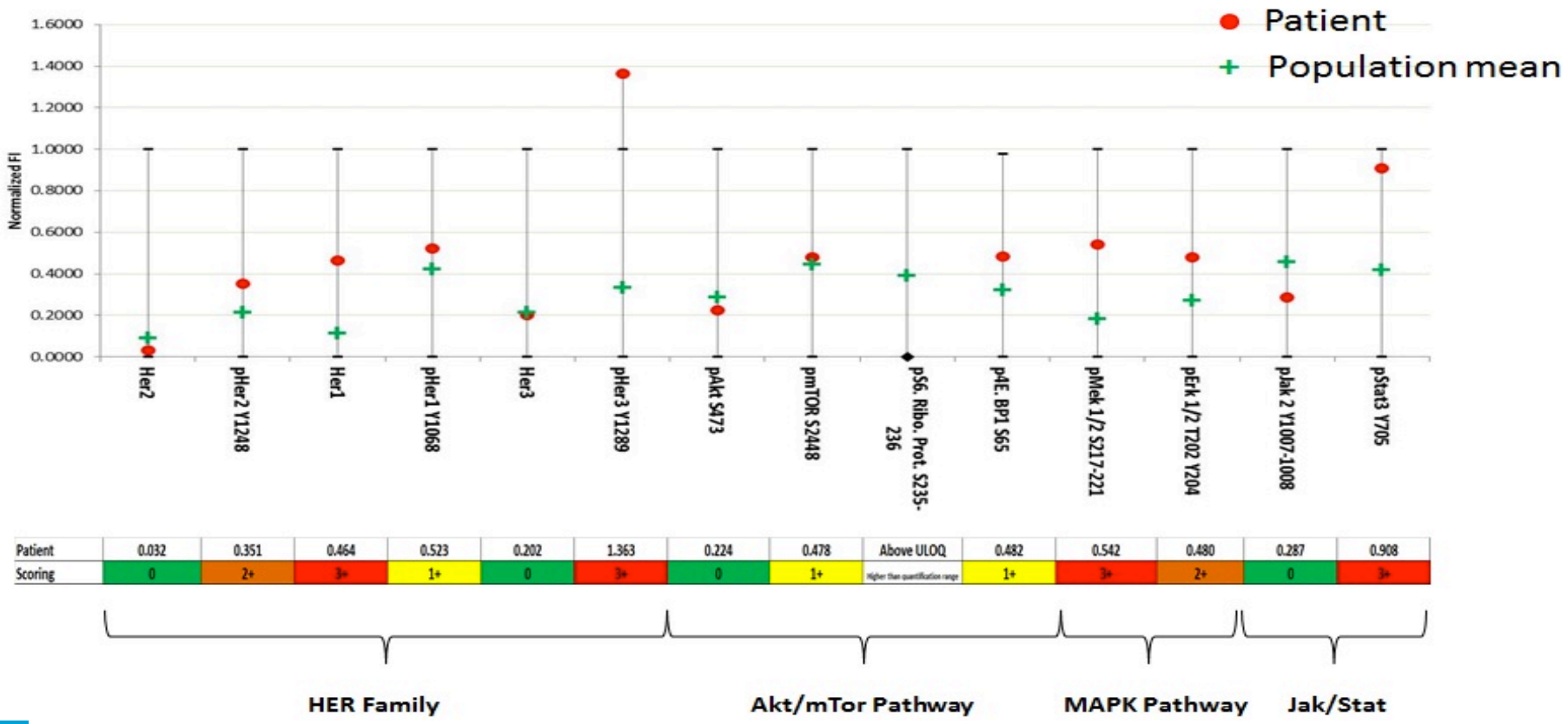
OF; BACH1; FANCJ

Summary

The protein encoded by this gene is a member of the RecQ DEAH helicase family and interacts with the BRCT repeats of breast cancer, type 1 (BRCA1). The bound complex is important in the normal double-strand break repair function of breast cancer, type 1 (BRCA1). This gene may be a target of germline cancer-inducing mutations. [provided by RefSeq, Jul 2008]

Location: 17q22.2

TheraLink Results



Summary

- Woman with triple negative breast cancer
  - Already has received multiple chemotherapy regimens: Including taxanes x 2, fluoropyrimidine, and anthracycline

Recommended Treatment Schema

- Everolimus 10 mg/day po x 21 days of 28 day cycle plus one of the following:
- carboplatin (AUC 2) weekly (Day 1,8,15) or
- cisplatin 20mg/m2 weekly (Day 1,8,15)

References:

- Anticancer Res. 2012 Aug;32(8):3435-41. **The mTOR inhibitor everolimus in combination with carboplatin in metastatic breast cancer**
- Cancer Chemother Pharmacol. 2012 Mar;69(3):591-8. doi: 10.1007/s00280-011-1734-5. Epub 2011 Sep 13.**A phase I study of daily everolimus plus low-dose weekly cisplatin for patients with advanced solid tumors**

Our values guide our approach to creating a better health care system

Our cause

To make quality health care more affordable and more accessible

Our strategy

To be the global leader in empowering people to live healthier lives

Clinical Policy Unit Function

- Aetna's Clinical Policy Unit is responsible for evaluating medical technologies to determine whether they are "experimental and investigational" and "medically necessary" as defined in applicable coverage documents

- Aetna has developed more than 600 Clinical Policy Bulletins (CPBs).

- The goal is to develop objective, clinically supported and defensible determinations.

Clinical Coverage Criteria

The following criteria are considered in evaluating a medical technology:

- The technology must have final approval from the appropriate governmental regulatory bodies, when required
- The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes
- The technology must improve net health outcome
- The technology must be as beneficial as any established alternatives
- The improvement must be attainable outside investigational settings

EVIDENCE

cost

ASSESSING GENOMIC ASSAYS: ACCURACY AND CLINICAL RELEVANCE

Analytical performance: Is the quantification of the analyte(s) of interest reliable and reproducible?
Clinical validity: How well does the test relate to the clinical outcome of interest?
Clinical utility: Does the information provided make a contribution to and improve current optimal management of the patient's disease?
Economic value: Assessment of cost savings and/or cost-effectiveness

Measures are interrelated

Analytic performance must be evaluated in context of the clinical use
Clinical validity must be assessed in context of analytic performance