

# ONCONOMICS PLUS RGCC®

**SAMPEL**

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**[www.rgcc-group.com](http://www.rgcc-group.com)**

Patient NAME	DATE OF BIRTH	DISEASE Breast	STAGE IV	Physician NAME Dr. Setiady Hardjo (Indonesia)
SPECIMEN 8ml Blood, 10ml Blood	VIAL IDs 130581, 130583			

## REPORT SUMMARY

CTCs COUNT: Isolated 3.4 cells/7.5 ml , SD +/- 0.3 cells

### SENSITIVITY - GENE EXPRESSION

#### Sensitivity

High sensitivity: alkylating factors, Gemcitabine

Partial sensitivity: epothilones, inhibitors of topoisomerase II, taxanes, eribulin, alkaloids of vinca, MTX, Pemetrexed

#### Expression

Over expression: C-erb-B1, EGF, ESR1, PGR, IGF-r 1, IGF-r 2, TGF-b, HDAC, HAT, VEGF, ANG 1, ANG 2

Down regulation: P180, HSP90, HSP27

### NATURAL SUBSTANCES SENSITIVITY

#### Class I

##### Cytotoxic Agents

Artecin, Agaricus Blazei Murill,  
Artesunate, Ascorbic acid, Bio D Mulsion  
NuMedica D3, Butyric Acid, C-statin,  
Cordyceps Sinensis, DCA  
(dichloroacetate), Frankincense, Onkobel  
Pro, Oxaloacetate (Cronaxal), Salicinium,  
Super Artemisinin

#### Class II

##### Immunostimulants / Immunomodulators

#### Class III

##### PK Inhibitors

Angiostop, Apigenin, CoQ10, Curcumin  
(turmeric), Genistein, Indol 3 Carbinol,  
Naltrexone, Pure Quercetin, Quercetin,  
Resveratrol, Vasculatin

\* Disclaimer! The natural substances that are tested in our lab facilities are not bonded from restriction for medical use.

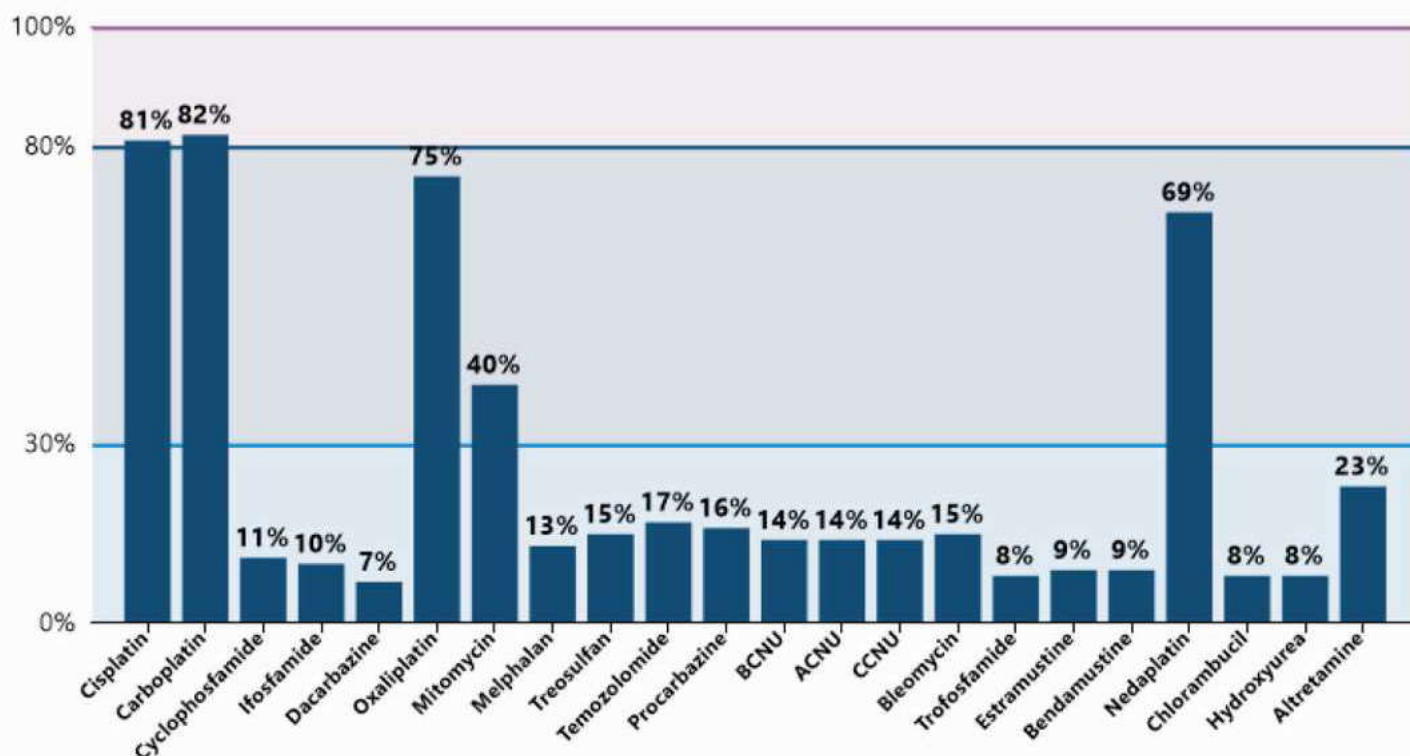
## Conclusion Results

- The neoplastic cells have the greatest sensitivity in Cisplatin, Carboplatin, Abraxane, Gemcitabine
- Also can be used Everolimus/Temsirolimus, Palbociclib
- The specific tumor appears to have resisting populations because of the MDRI overexpression that can be reversed by the use of inhibitors of ABCG2 pumps

— No sensitivity — Partial sensitivity — High sensitivity

## Alkylating Agents

High sensitivity: Cisplatin, Carboplatin

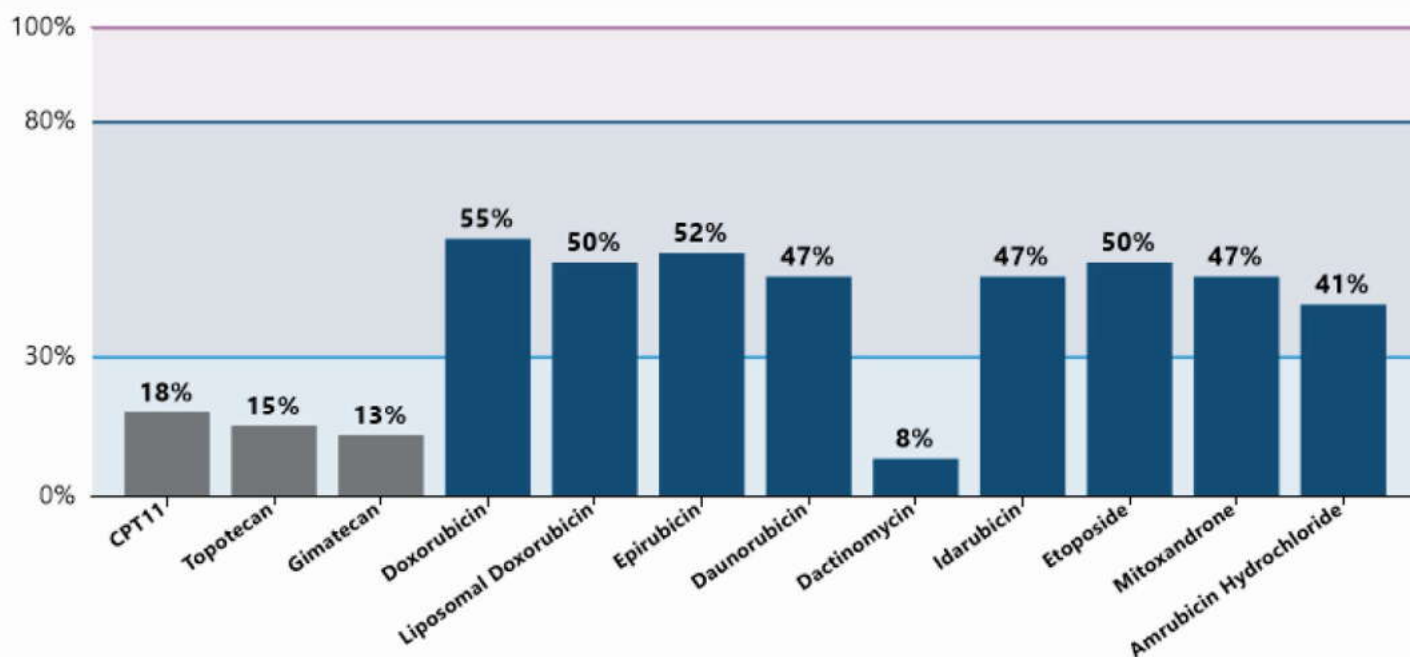


## Inhibitors of Topoisomerase I & II

High sensitivity:

Inhibitors of Topoisomerase I

Inhibitors of Topoisomerase II



No sensitivity

Partial sensitivity

High sensitivity

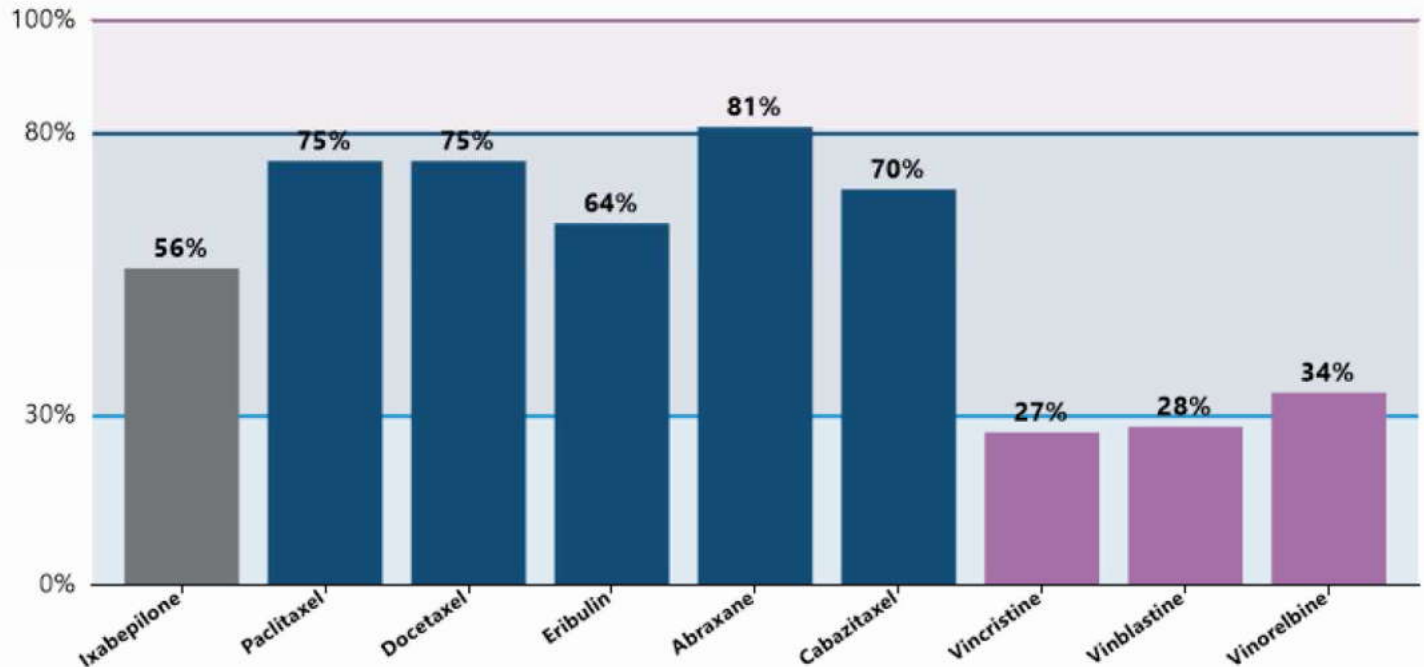
## Epothilones & Nucleus Spindle Stabilizer I & II

High sensitivity: **Abraxane**

Epothilones

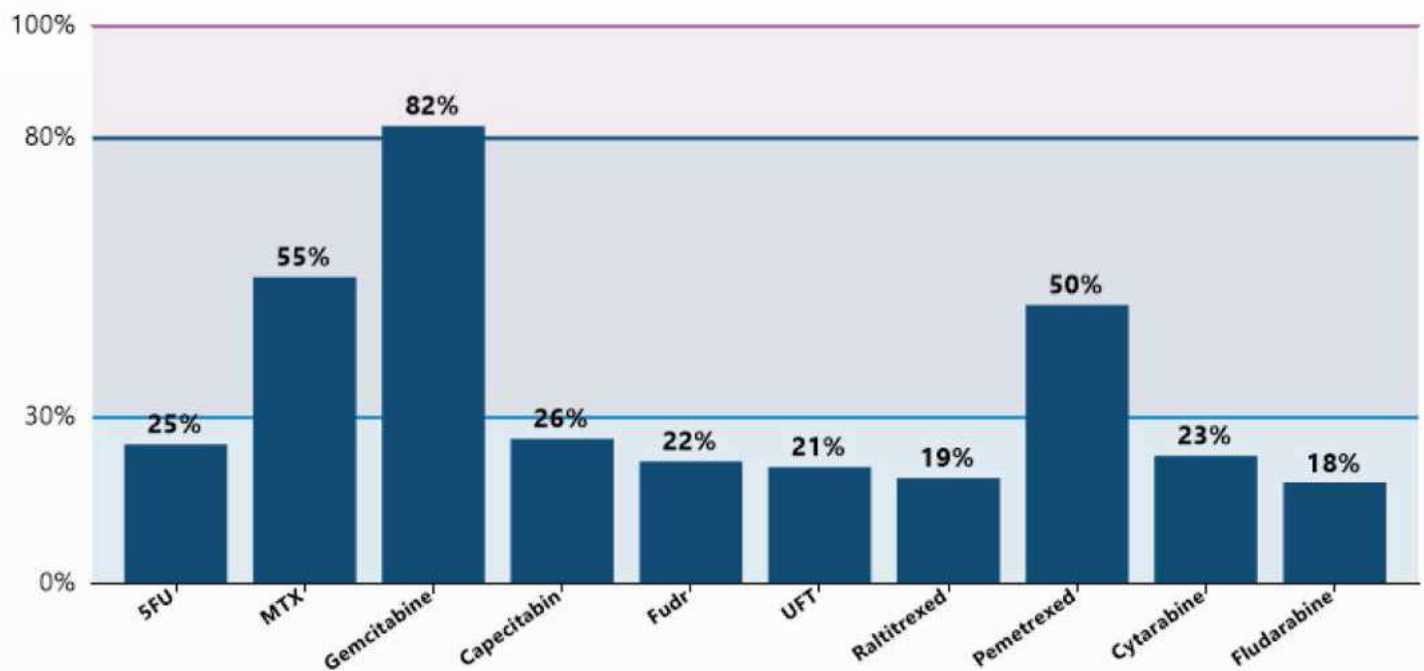
Nucleus Spindle Stabilizer I

Nucleus Spindle Stabilizer II

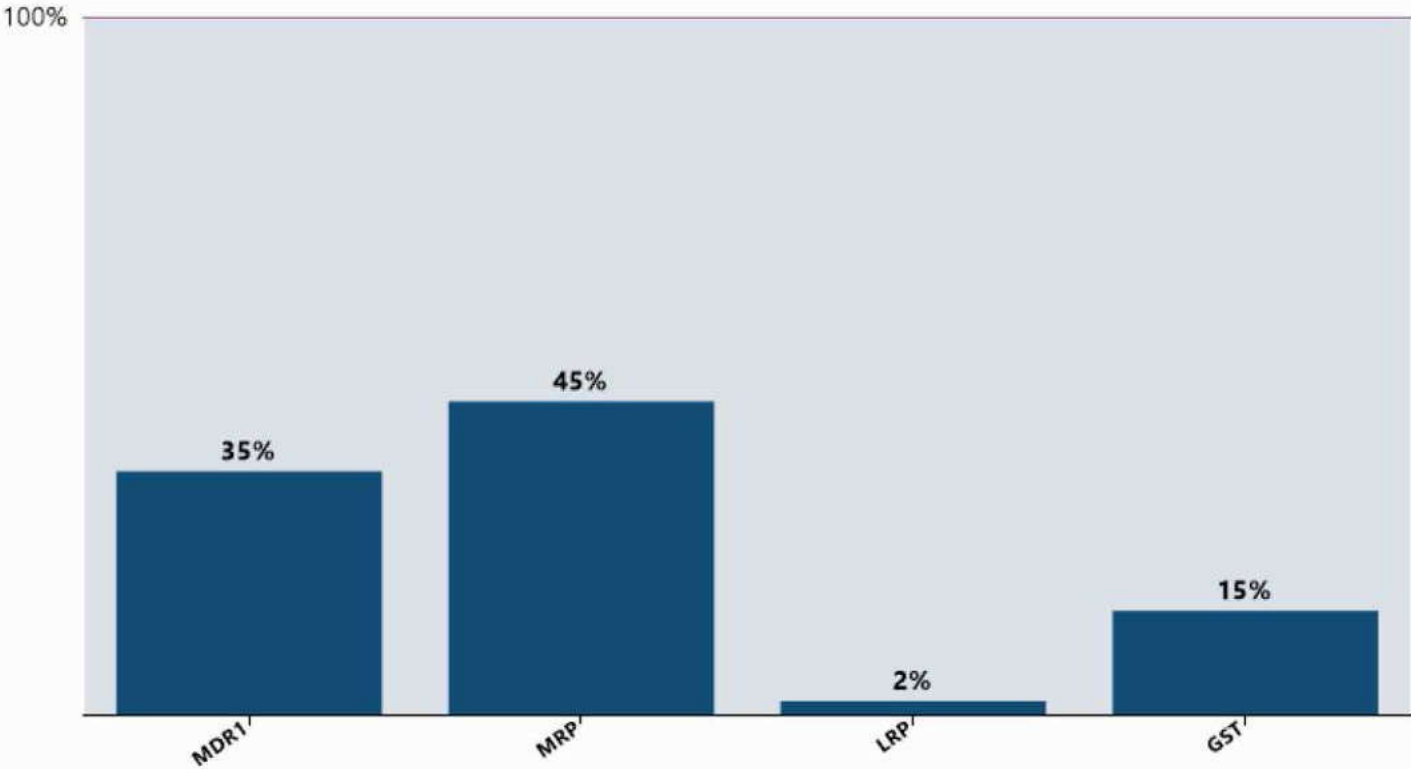


## Nucleoside Analogues

High sensitivity: **Gemcitabine**

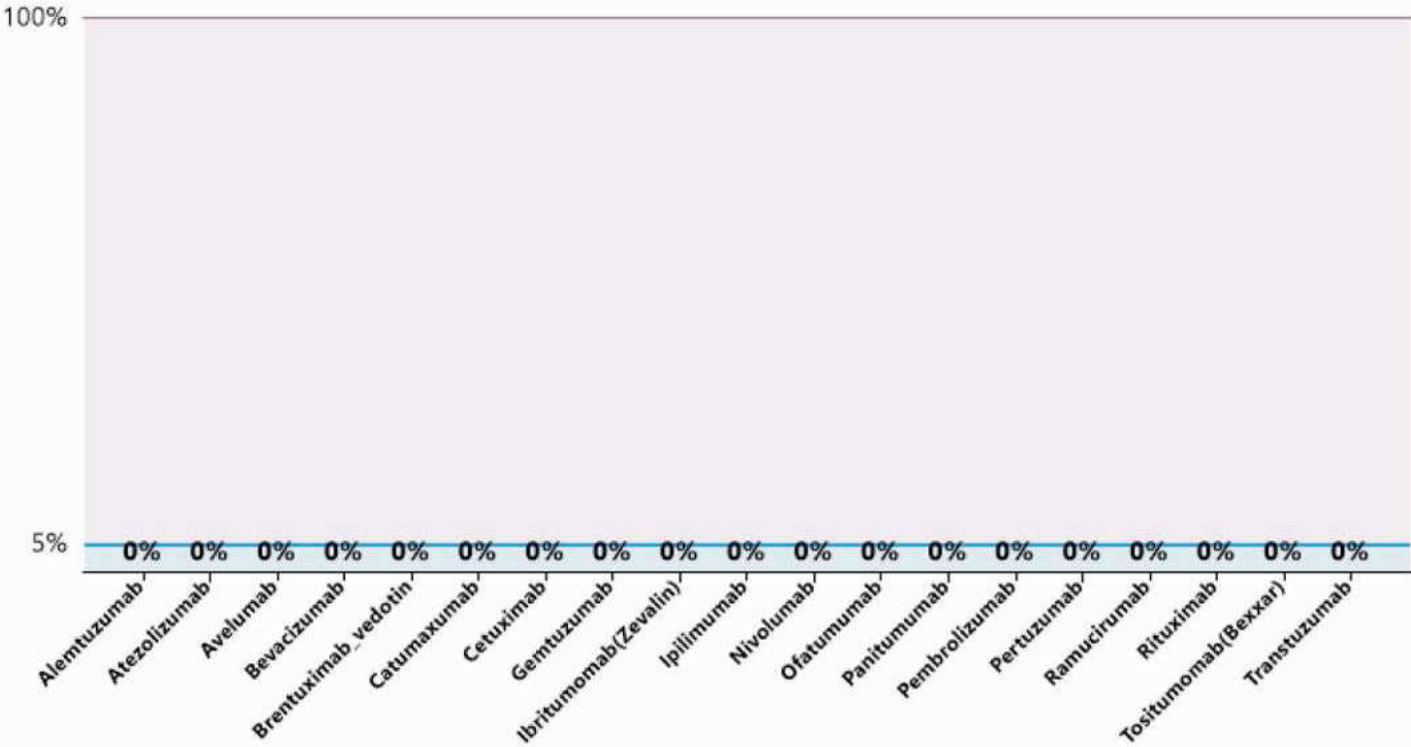


## Resistance Factors



## Moab - Monoclonal Antibodies

No sensitivity    Sensitivity

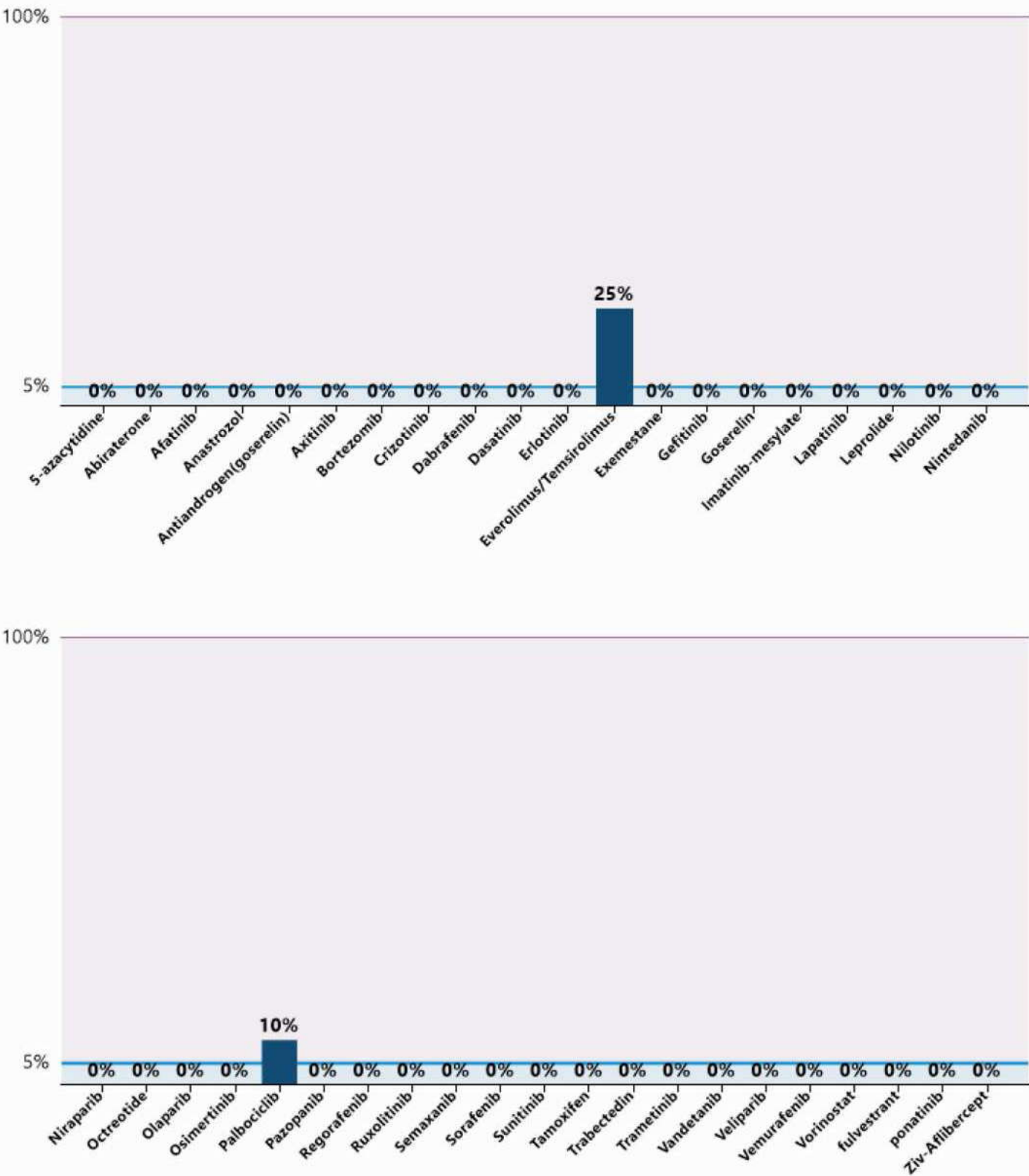




No sensitivity

Sensitivity

SMW - Small Molecular weight molecule



## Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
p180	Preprotein for Cellular stress	HIGH RISK	Tyrosin kinase growth f.	-40	HIGH RISK
Bcr-abl	Fusion Protein	LOW RISK	Resist phenotype	0	LOW RISK
PTEN	Repair Related Gene	HIGH RISK	Tumor Suppressor Gene	30	HIGH RISK
COX2	Eicosanoid related protein	LOW RISK	Tumour Growth	0	LOW RISK
5-LOX			Tumour Growth	0	LOW RISK
NFkB	Proteasome inhibitors	LOW RISK	Transcription fact	0	LOW RISK
IkB(a,b,c)			Inhibitor of NFkB	0	LOW RISK
ALK	Proto-Oncogene	LOW RISK	Acute Leukemia kinase	0	LOW RISK
EML-4-ALK			Fusion EML with ALK	0	LOW RISK
NPM-ALK			Fusion NPM with ALK	0	LOW RISK
RET			Proto-Oncogene	0	LOW RISK

### Preprotein for Cellular stress

-40%

p180

### Fusion Protein

Bcr-abl | 0%

### Repair Related Gene

PTEN | 30%

### Eicosanoid related protein

COX2 | 0%

5-LOX | 0%

### Proteasome inhibitors

NFkB | 0%

IkB(a,b,c) | 0%

### Proto-Oncogene

ALK | 0%

EML-4-ALK | 0%

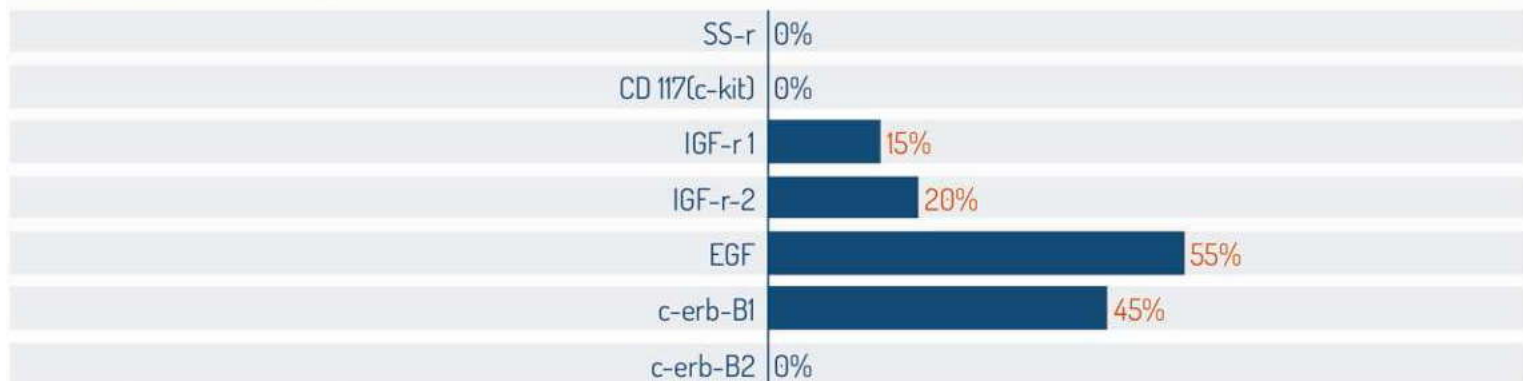
NPM-ALK | 0%

RET | 0%

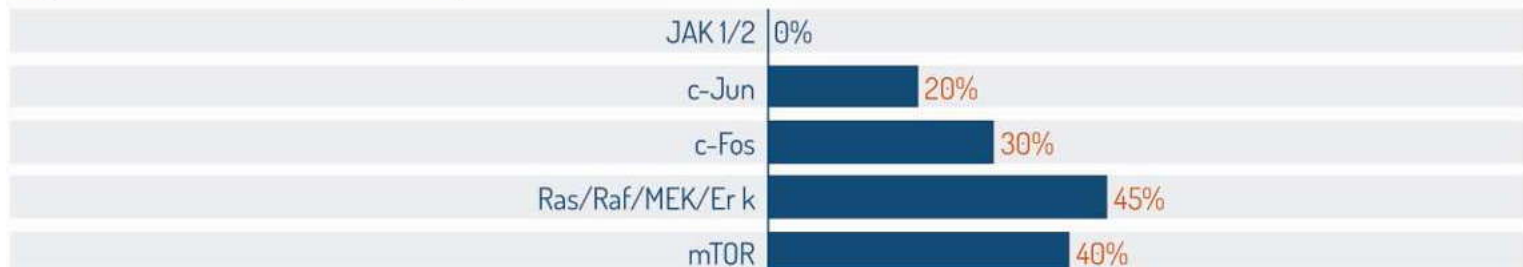
# Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
SS-r	Growth Factor Receptor	HIGH RISK	Somatostatin receptor	0	LOW RISK
CD 117(c-kit)			Proliferate growth factor receptor	0	LOW RISK
IGF-r1			Insulin like growth factor receptor	15	HIGH RISK
IGF-r-2			Insulin like growth factor receptor	20	HIGH RISK
EGF			Tumour Growth	55	HIGH RISK
c-erb-B1			Her1	45	HIGH RISK
c-erb-B2			Her/neu2	0	LOW RISK
JAK 1/2	Signal Transduction Pathway	HIGH RISK	Single transduction pathway	0	LOW RISK
c-Jun			Proto-Oncogene	20	HIGH RISK
c-Fos			Proto-Oncogene	30	HIGH RISK
Ras/Raf/MEK/Er k			Transduction pathway	45	HIGH RISK
mTOR			Transduction pathway	40	HIGH RISK
Progesterone Receptor	Hormone Receptors	HIGH RISK	Growth Factor Receptor	10	HIGH RISK
Estrogene Receptor			Growth Factor Receptor	25	HIGH RISK
NR3C4-A			Nucleous receptor group III Class 4(andro...	0	LOW RISK
NR3C4-B			Nucleous receptor group III Class 4(andro...	0	LOW RISK

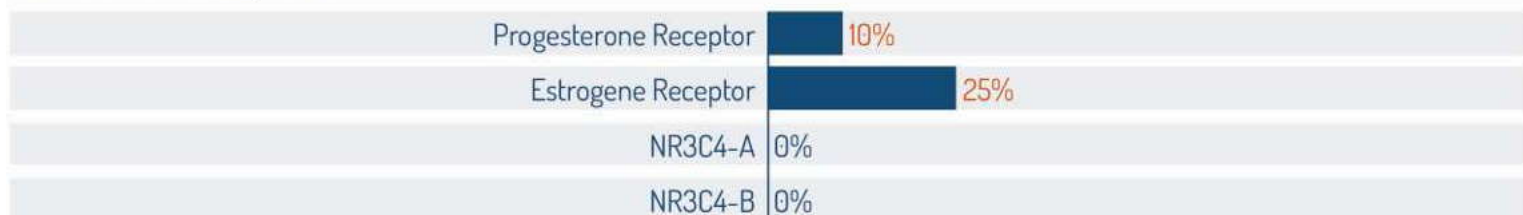
## Growth Factor Receptor



## Signal Transduction Pathway



## Hormone Receptors





## SELF REPAIR - RESISTANCE

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
TGF-b	Signal transduction	HIGH RISK	Tumour Growth	20	HIGH RISK
HSP27	Radiotherapy / Hyperthermia sensitivity	SENSITIVE	Heat Shock Protein	-40	SENSITIVE
HSP72			Heat Shock Protein	-5	SENSITIVE
HSP90			Heat Shock Protein	-15	SENSITIVE
DNA methyltransferase	Resistant Phenotype Markers	HIGH RISK	DNA methylation	-35	HIGH RISK
DNA demethylase			DNA methylation	0	LOW RISK
06-methyl-DNA- tran			DNA methylation	-50	HIGH RISK
Histone deacetylase			DNA coiling (nucleosome)	5	LOW RISK
HAT			Histone acetyl transferase	55	HIGH RISK
CXCR4			Resistant Phenotype	-35	HIGH RISK
CXCL12			Resistant Phenotype	0	LOW RISK
Gamma GC			Resist to alkylating drugs	0	LOW RISK
HDAC			Histone deacetylase	40	HIGH RISK

## Signal transduction

TGF-b 20%

## Radiotherapy / Hyperthermia sensitivity

-40% HSP27

-5% HSP72

-15% HSP90

## Resistant Phenotype Markers

-35% DNA methyltransferase

DNA demethylase 0%

-50% 06-methyl-DNA- tran

Histone deacetylase 5%

HAT 55%

-35% CXCR4

CXCL12 0%

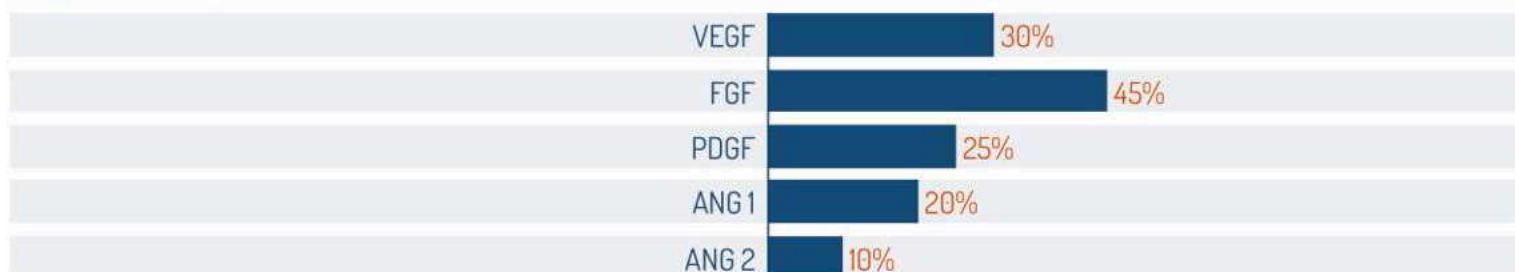
Gamma GC 0%

HDAC 40%

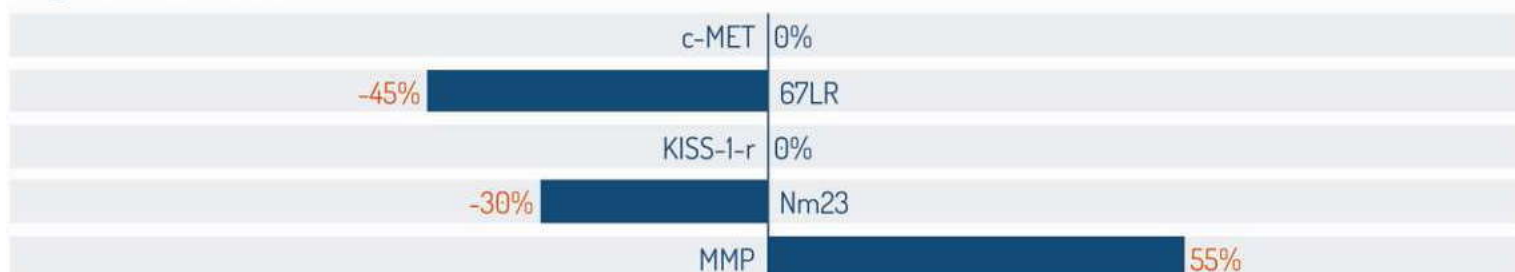
## ANGIOGENESIS - METASTASES

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
VEGF	Angiogenesis	HIGH RISK	Angiogenesis	30	HIGH RISK
FGF			Angiogenesis	45	HIGH RISK
PDGF			Angiogenesis	25	HIGH RISK
ANG 1			Angiogenin I	20	HIGH RISK
ANG 2			Angiogenin II	10	HIGH RISK
c-MET	Migration invasion	HIGH RISK	Mesenchymal to epithelial transition	0	LOW RISK
67LR			67 Laminin receptor	-45	HIGH RISK
KISS-1-r			Metastases regulator	0	LOW RISK
Nm23			Metastases regulator	-30	HIGH RISK
MMP			Metastases	55	HIGH RISK

### Angiogenesis



### Migration invasion



## CELL CYCLE REGULATION &amp; IMMORTALIZATION / APOPTOSIS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
E2F1	Increase Protein Synthesis	LOW RISK	Transcr. Fact of TS & topo I	0	LOW RISK
CDC6	Rapid Cell Cycle	LOW RISK	Initiation of DNA replication	0	LOW RISK
h-TERT	Immortalization	HIGH RISK	M2 crisis- aggressive phen	15	HIGH RISK
Bcl-2	Regulation of Apoptosis	HIGH RISK	Apoptosis	20	HIGH RISK
Bax			Apoptosis	-50	HIGH RISK
CD95 (fas-r)			Apoptosis related receptor	-10	HIGH RISK
p27	Cell Cycle Rate	HIGH RISK	Cell arrest (G0)	-45	HIGH RISK
p53			Cell cycle regulator	20	HIGH RISK
p16			Apoptosis	30	HIGH RISK

## Increase Protein Synthesis

E2F1 | 0%

## Rapid Cell Cycle

CDC6 | 0%

## Immortalization

h-TERT | 15%

## Regulation of Apoptosis

Bcl-2 | 20%

-50% | Bax

-10% | CD95 (fas-r)

## Cell Cycle Rate

-45% | p27

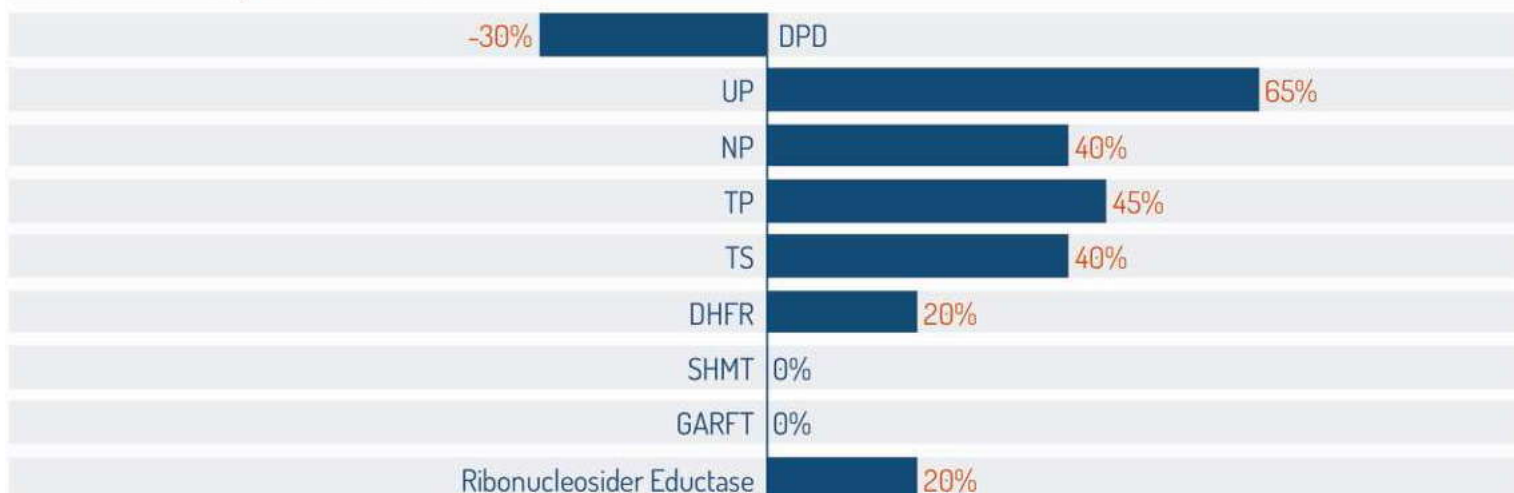
p53 | 20%

p16 | 30%

## DRUG METABOLISMS & TARGETS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
DPD	Nucleoside Import Transformation	HIGH RISK	Resist to 5FU	-30	HIGH RISK
UP			Resist to 5FU	65	HIGH RISK
NP			Resist to pyrim. Antagonist	40	HIGH RISK
TP			Resist to 5FU	45	HIGH RISK
TS			Rapid cell cycle (THFA)	40	HIGH RISK
DHFR			Rapid cell cycle (THFA)	20	HIGH RISK
SHMT			Rapid cell cycle (THFA)	0	LOW RISK
GARFT			Rapid cell cycle (THFA)	0	LOW RISK
Ribonucleosider Eductase			DNA synthesis	20	HIGH RISK
CES1&2 (carboxyesterase)	Activation of Camptothecin	HIGH RISK	Resist to camptothecin	55	HIGH RISK
CypB1	Xenobiotic	HIGH RISK	Xenobiotic metabolism	30	HIGH RISK
ERCC1	DNA Repair Related Gene	HIGH RISK	DNA repair mechanism	-35	HIGH RISK
RRM1			Nucleotide polymerizations	15	HIGH RISK

### Nucleoside Import Transformation



### Activation of Camptothecin



### Xenobiotic



### DNA Repair Related Gene





MARKERS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
CD33	Immune system regulation	LOW RISK	Myeloid Cell origin	0	LOW RISK
CD52	Immune system regulation	LOW RISK	Leukaemia Marker	0	LOW RISK
CD20	Development and differentiation of B cells into plasma cells	LOW RISK	Lymphoma Related Antigen	0	LOW RISK
EpCAM (EpCAm+ve)	Cell-cell adhesion	HIGH RISK	Epithelial Marker ( 2.9 cells/7.5 ml )	30	HIGH RISK
PD-L1	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK
PD 1	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK
PD-L2	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK

Immune system regulation



Immune system regulation



Development and differentiation of B cells into plasma cells



Cell-cell adhesion



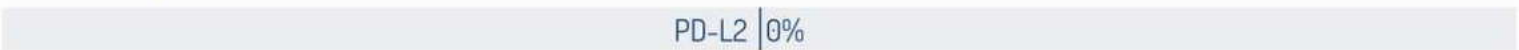
Immune system regulation



Immune system regulation



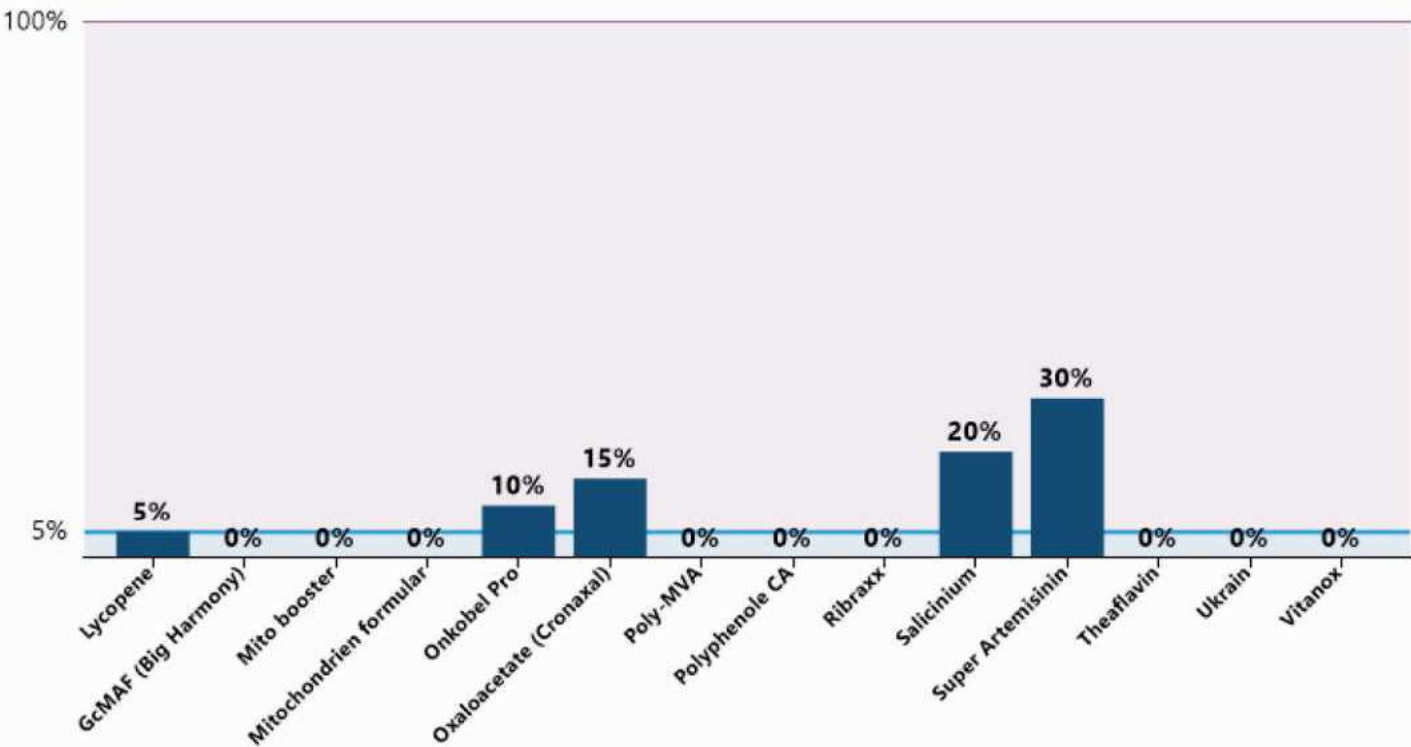
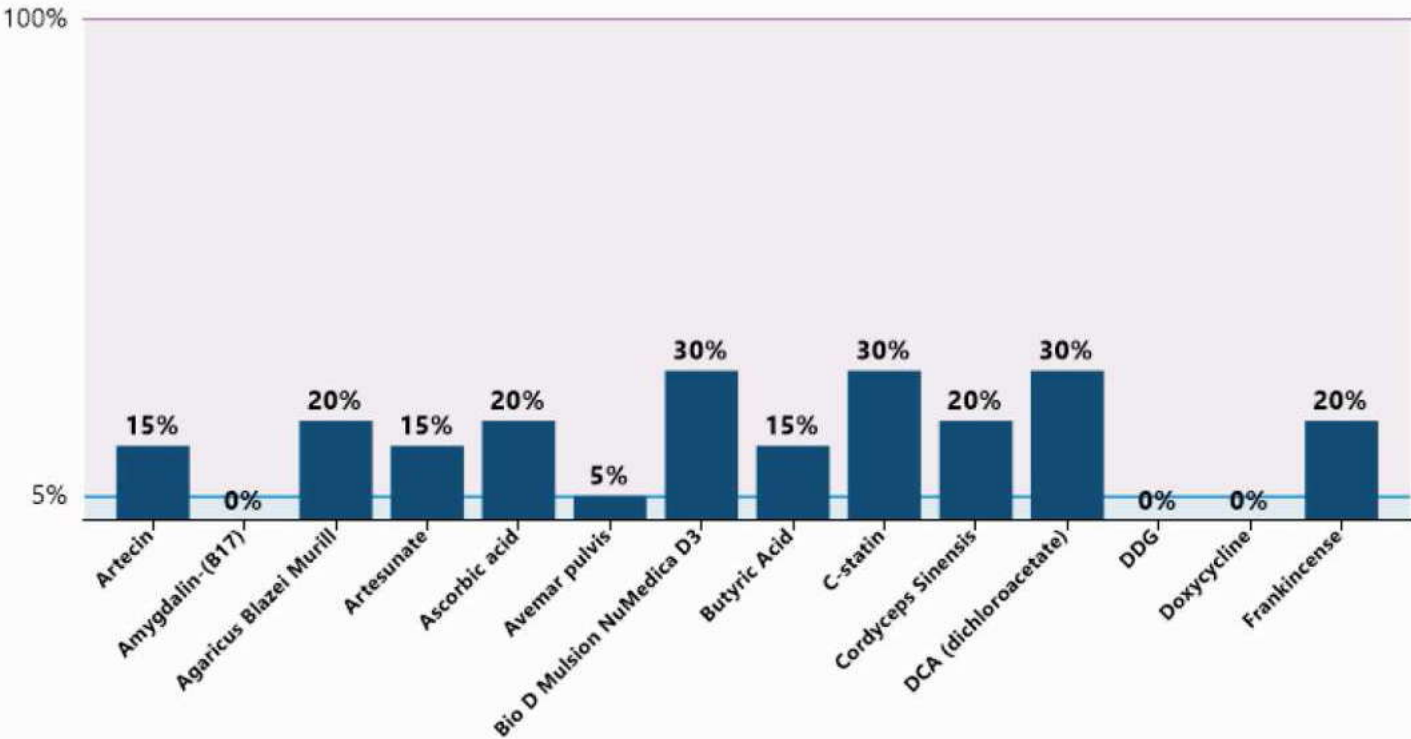
Immune system regulation



No sensitivity

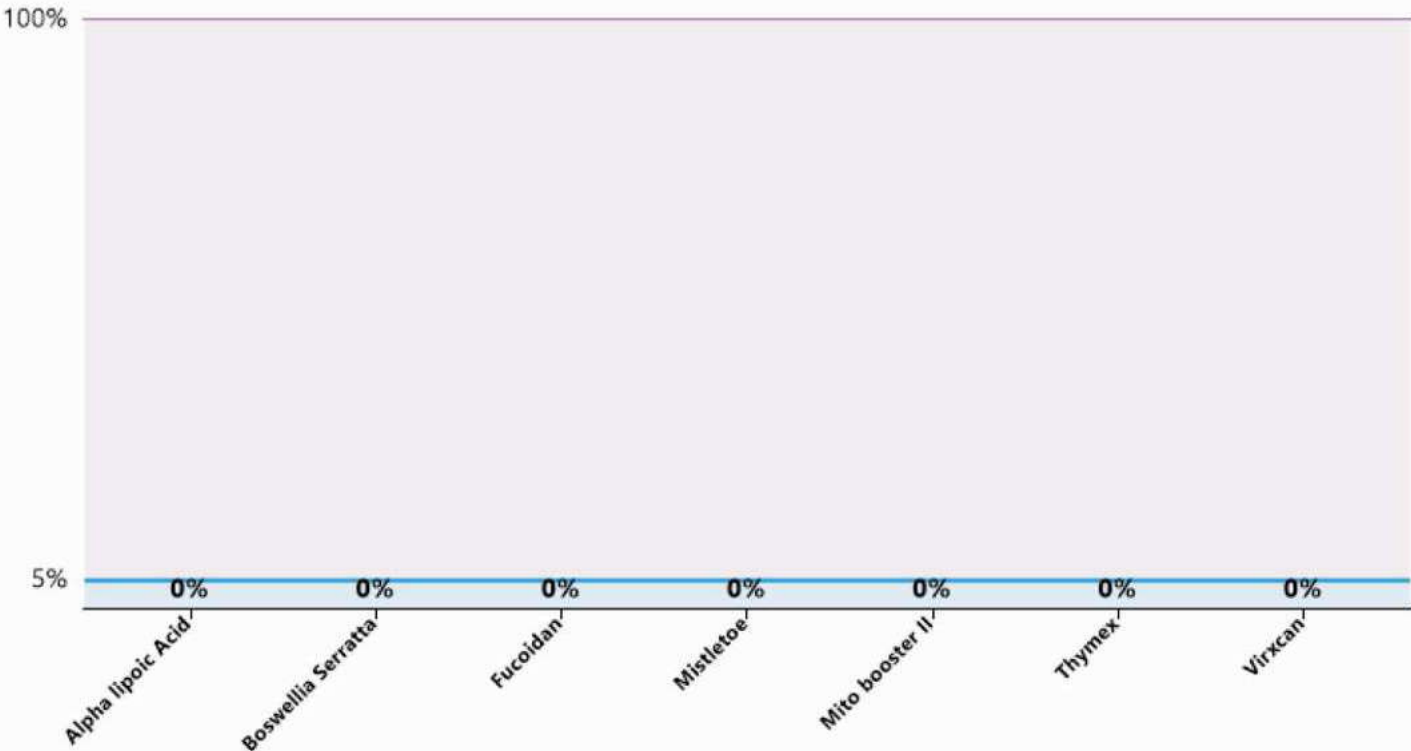
Sensitivity

Class I (Cytotoxic Agents)

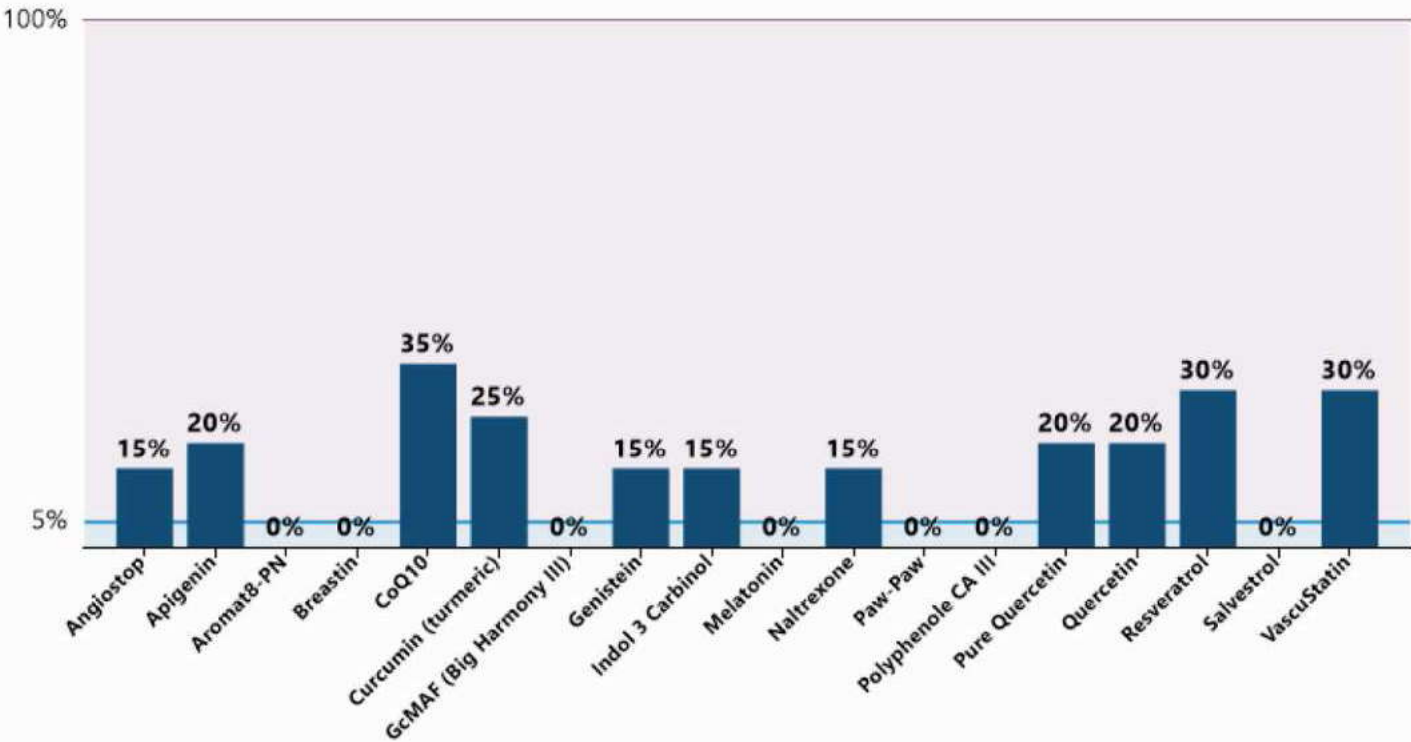


No sensitivity      Sensitivity

Class II (Immunostimulants / Immunomodulators)



Class III (PK Inhibitors)



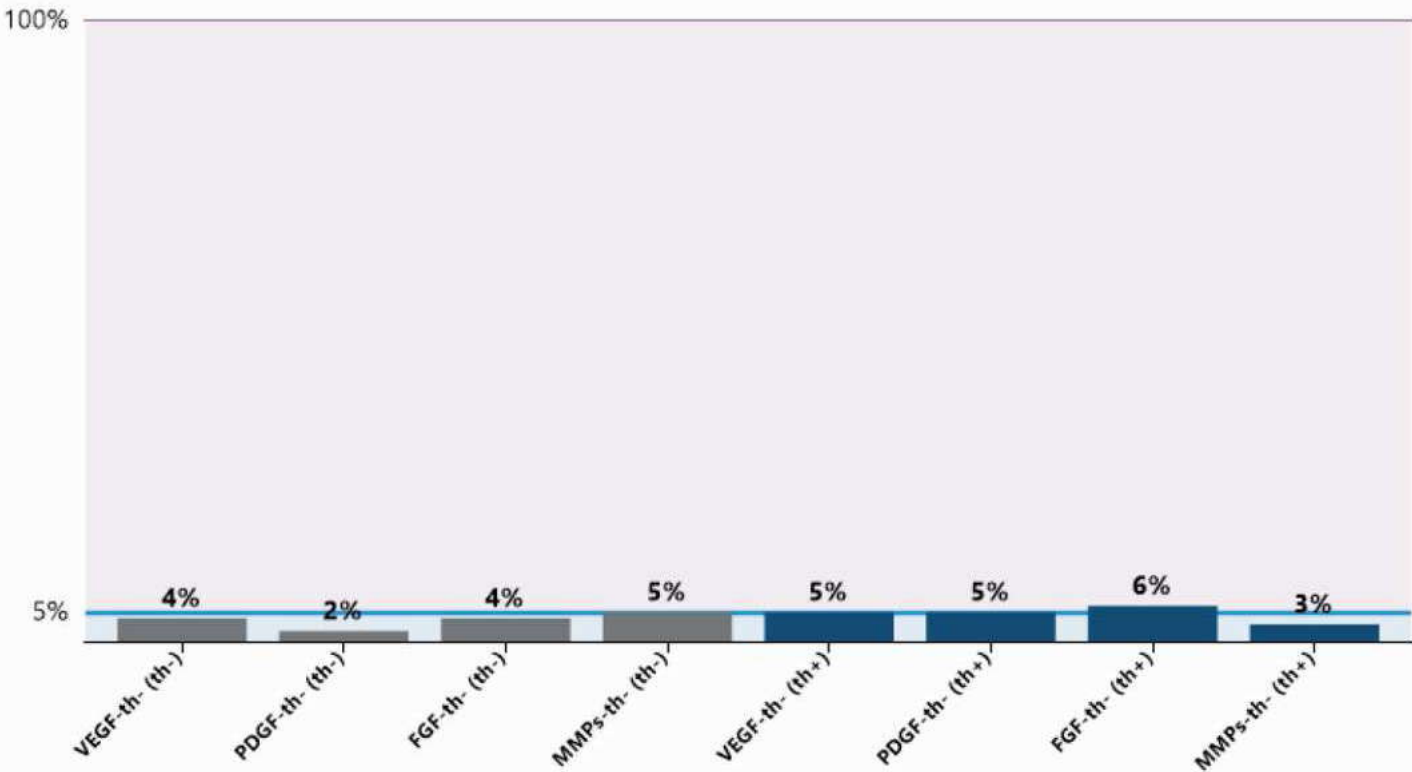
No sensitivity

Sensitivity

Malignant Cells - Thalidomide

th-

th+



NATURAL SUBSTANCES

SUBSTANCE NAME	VALUE W/O SUBSTANCE	VALUE WITH SUBSTANCE	EFFICACY
Ribociclib	12	19	Effective
Alpelisib	10	19	Effective
Letrozole	15	14	Not Effective
Metformin	11	10	Not Effective
Abemaciclib	12	14	Not Effective



## Information

## Laboratory Process

- Isolation of the malignant cells using flow cytometry and negative selection. The isolated cells were expanded and they splitter in two, from which, one part is going to viability assays and the other is going for transcriptomic micro-Arrays
- Isolation of mRNA
- Quality control of integrity of mRNA
- Reversed transcription of mRNA to cDNA
- Hybridisation of cDNA with micro-Arrays all genome transcriptomic micro-Arrays slide
- Analysis of the data and detection of repeatable patterns
- Normalization and assessment of clinical relevant probes

This Test report is issued based on testing the sample / specimen examined by the Laboratory. Modification of data, selective breeding and using portions of this test report is forbidden. The laboratory assumes no liability for improper use or improper interpretation of the results.

## Expression Rates

## Clinical relevant genes related with:

Isolation of mRNA	p53, p21, p16, DHFR, TS, SHMT
Drug targets	Topo I & II, TS, DHFR, ribonucleotide reductase etc.
Signal Transduction Pathway	EGFr, PDGFr, etc.
Epigenetic aberration	Dnmt1, DNA demethylase, etc.
Angiogenesis	VEGF-r, FGFr, PDGFr
Growth signal	c-erb-B1, c-erb-B2, bar-abl, etc
Repair after physical application (radiation, hyperthermia)	HSP27, HSP70, HSP90, HIF1a, etc.

Sincerely,



Dr. Ioannis Papasotiriou MD, PhD, SCym

## GROWTH FACTORS PROLIFERATION STIMULI

FUNCTION	NAME	NAME OFFICIAL	RELATED
Preprotein for Cellular stress	p180	RRBP1	Tyrosine kinase growth factor
Fusion Protein	Bcr-abl	BCR-ABL	Resist phenotype
Repair Related Gene	PTEN	PTEN	Tumor Suppressor Gene
Eicosanoid related protein	COX2 5-LOX	PTGS2 ALOX5	Tumour Growth Tumour Growth
Proteasome inhibitors	NFkB Ikb (a,b,c)	NFKB1 NFKBIA/B	Transcription Factor NFkB Inhibitors
Proto-Oncogene	ALK EML-4-ALK NPM-ALK RET	ALK EML4-ALK NPM-ALK RET	Acute Leukemia kinase Fused EML-ALK Fused NPM-ALK Proto-Oncogene
Growth Factor Receptor	SS-r CD 117 (c-kit) IGF-r 1 IGF-r 2 EGF C-erb-B2 C-erb-B1	SSTR3/5 KIT IGF1R IGF2R EGF ERBB2 EGFR	Somatostatin receptor Proliferate growth factor receptor Insulin like growth factor receptor Insulin like growth factor receptor Tumour Growth Receptor tyrosine-protein kinase Epithelial Growth Factor Recept...
Signal Transduction Pathway	JAK1/2 c-Jun c-Fos Ras-Raf-MEK-ERK mTOR	JAK1/2 FOS JUN ERK1/2 MTOR	Single transduction pathway Proto-Oncogene Proto-Oncogene Single transduction pathway Single transduction pathway
Hormone Receptors	Progesterone-Receptor Estrogen-Receptor NR3C4-A NR3C4-B	PGR ESR1 NR3C4A NR3C4B	Growth Factor Receptor Growth Factor Receptor Androgen Receptor Androgen Receptor

## SELF REPAIR - RESISTANCE

FUNCTION	NAME	NAME OFFICIAL	RELATED
Signal transduction	TGF-b	TGFB2	Tumour Growth
Radiotherapy / Hyperthermia se...	HSP27 HSP72 HSP90	HSPB1 HSPA1A HSP90AA1	Heat Shock Protein Heat Shock Protein Heat Shock Protein
Resistant Phenotype Markers	DNA methyltransferase I DNA-demethylase O6-methyl-DNA-tran Histone-deacetylase-dipeptide HAT CXCR4 HDAC CXCL12 Gamma GC	DNMT1 TET1 MGMT HDAC1 HAT1 CXCR4 HDAC2 CXCL12 GGCX	DNA methylation DNA methylation DNA methylation DNA Coiling Histone acetyl transferase Resist phenotype Histone deacetylase Resist phenotype Resist to alkylating drugs

## ANGIOGENESIS

FUNCTION	NAME	NAME OFFICIAL	RELATED
Angiogenesis	VEGF	VEGFA	Angiogenesis
	FGF	FGF1(3)	Angiogenesis
	PDGF	PDGFA(2)	Angiogenesis
	ANG 1	ANGPT1	Angiopoietin
	ANG 2	ANGPT2	Angiopoietin

## DRUG METABOLISMS & TARGETS

FUNCTION	NAME	NAME OFFICIAL	RELATED
Nucleoside Import Transformation	DPD	DPYD	Resist to 5FU
	UP	UPP1	Resist to 5FU
	NP	PNP	Purine Nucleoside Phosphorylase
	TP	TYMP	Resist to 5FU
	TS	TYMS	Rapid cell cycle (THFA)
	DHFR	DHFR	Rapid cell cycle (THFA)
	SHMT	SHMT1	Rapid cell cycle (THFA)
	GARFT	GART	Rapid cell cycle (THFA)
	Ribonucleoside reductase	RRM1	DNA synthesis
Activation of Camptothecin	CES1-2	CES1-2	Resist to camptothecin
Xenobiotic	CypB1	CYB1B1	Xenobiotic metabolism
DNA Repair Related Gene	ERCC1	ERCC1	DNA repair mechanism
	RRM1	RRM1	Nucleotide polymerizations

## MARKERS

FUNCTION	NAME	NAME OFFICIAL	RELATED
markers	CD33	CD33	Myeloid Cell origin
	CD52	CD52	Leukaemia Marker
	CD20	CD20	Lymphoma Related Antigen
	EpCAM	EPCAM	Epithelial Marker
	PD-L1	CD274	Immunoregulatory Factor
	PD 1	PDCD1	Immunoregulatory Factor
	PD-L2	PDCD1LG2	Immunoregulatory Factor



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- b. Bhagwat N, Carpenter EL. Flow Cytometric Methods for Circulating Tumor Cell Isolation and Molecular Analysis. *Adv Exp Med Biol*. 2017;994:105-118. doi: 10.1007/978-3-319-55947-6\_5. PMID: 28560670.
- c. Papasotiriou I, et al. Detection of Circulating Tumor Cells in Patients with Breast, Prostate, Pancreatic, Colon and Melanoma Cancer: A Blinded Comparative Study Using Healthy Donors. *Journal of Cancer Therapy*. 2015;6:543-553. <http://dx.doi.org/10.4236/jct.2015.67059>.
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