Therapy Select

Individualized Cancer Therapy:
Drug Treatment
Testing before Therapy

Presentation

by Dr. Frank Kischkel

Therapy Select

Individualized Cancer Therapy:
Drug Treatment
Testing before Therapy

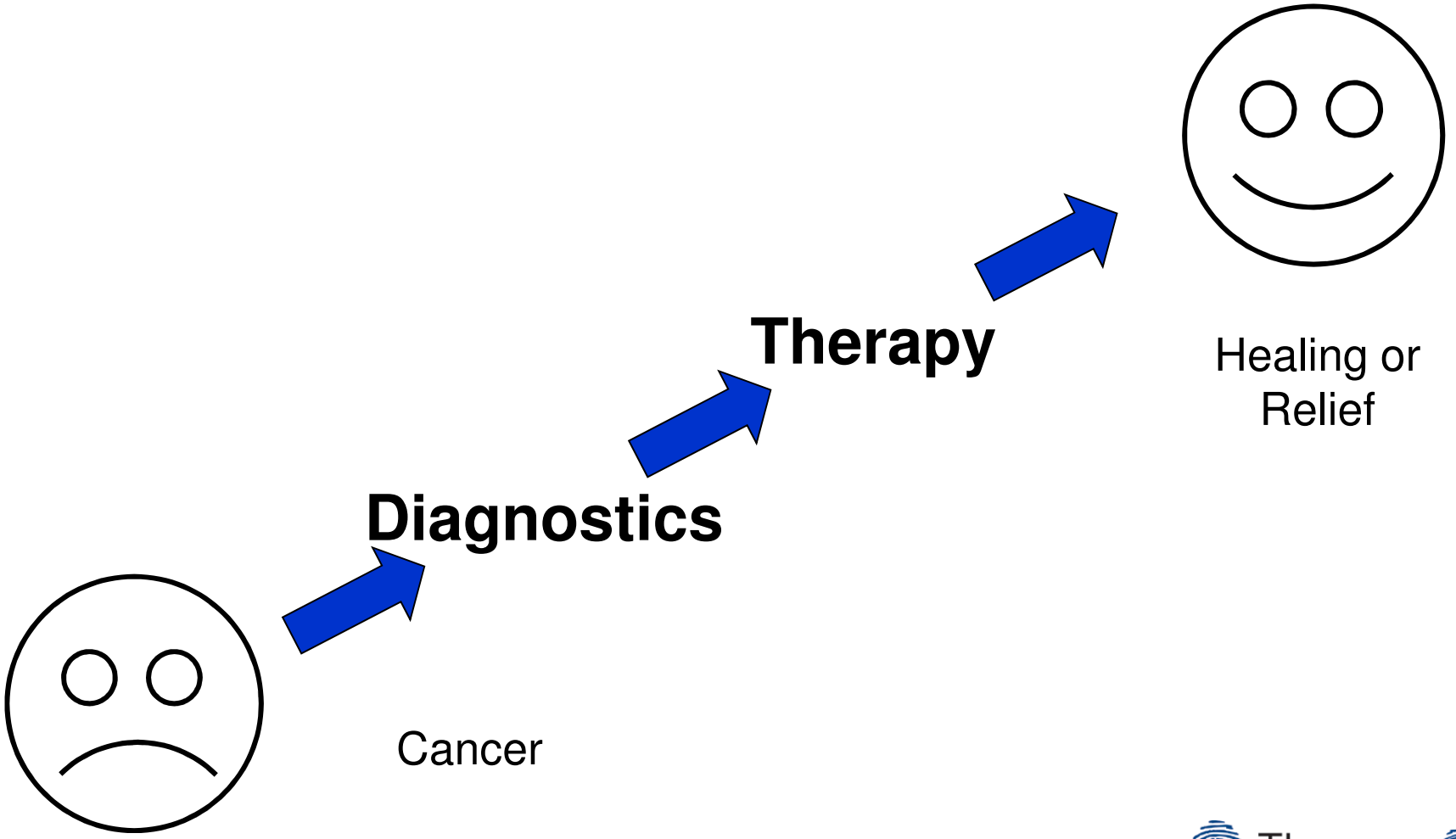
CTR-Test®

Chemotherapy-Resistance-Test

ONCOMPASS Cancer Diagnostics

KPS

Individualized Cancer Therapy



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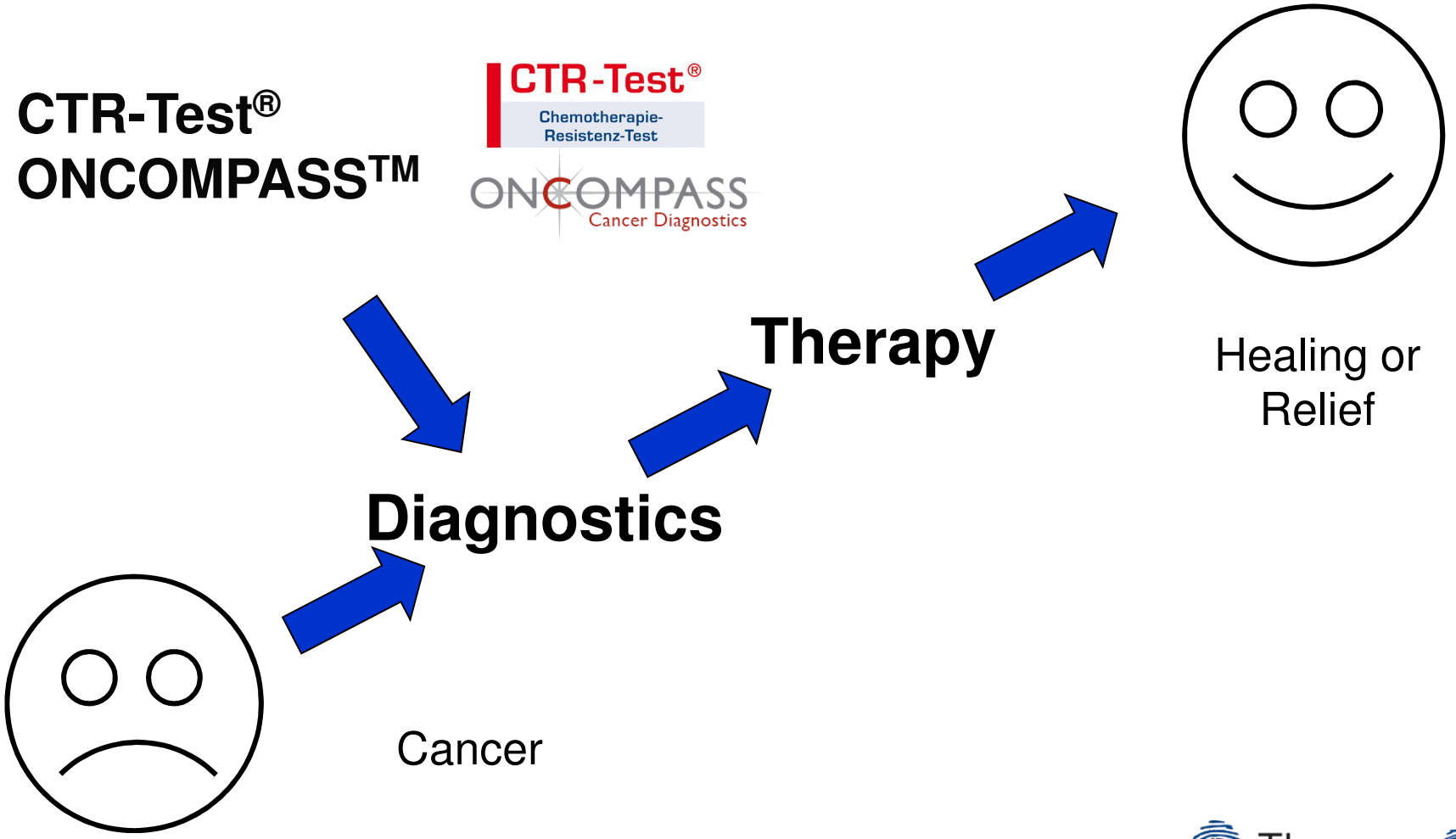
Individualized Cancer Therapy

CTR-Test®
ONCOMPASS™

CTR-Test®
Chemotherapie-Resistenz-Test
ONCOMPASS Cancer Diagnostics



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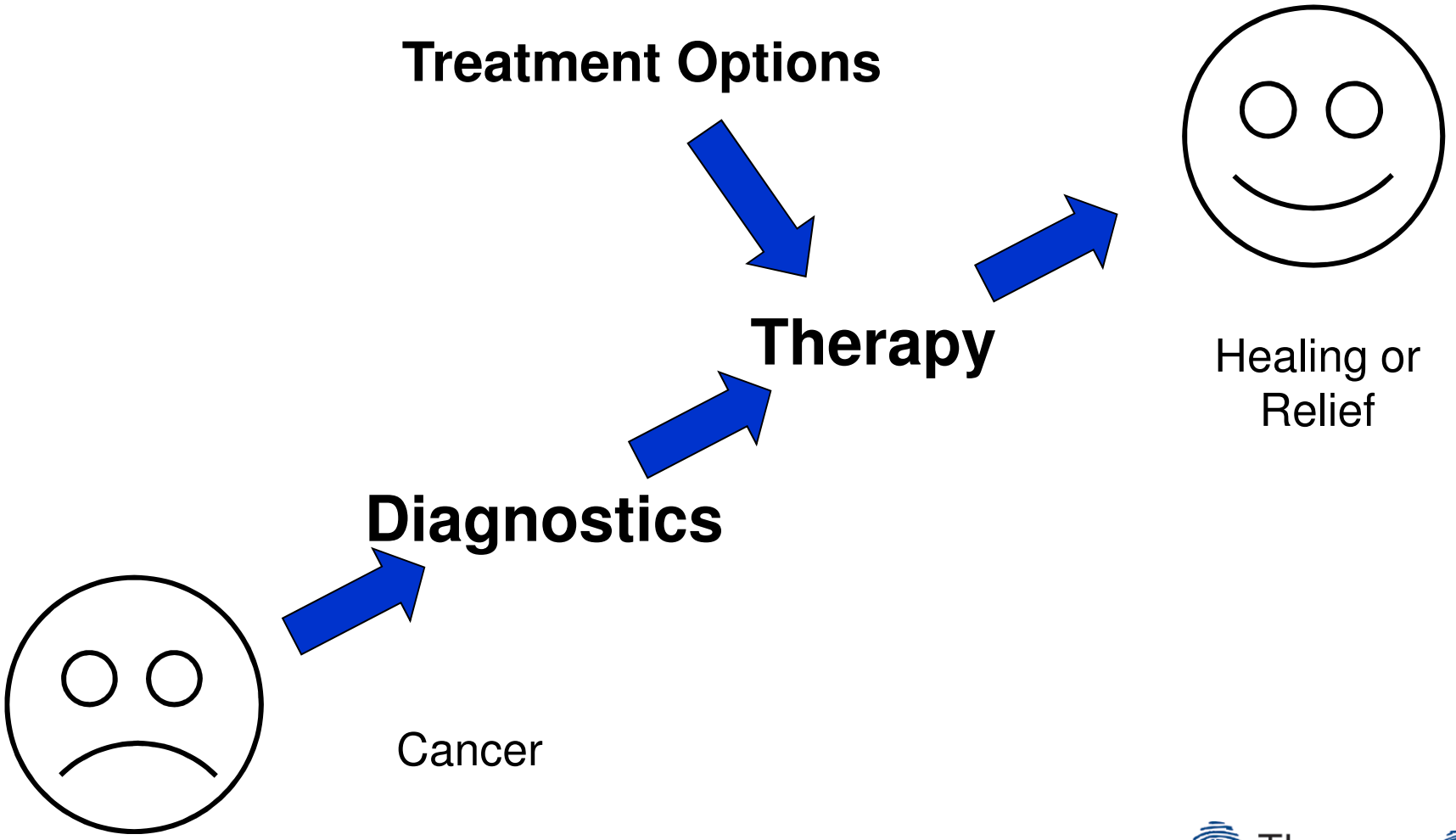
Individualized Cancer Therapy



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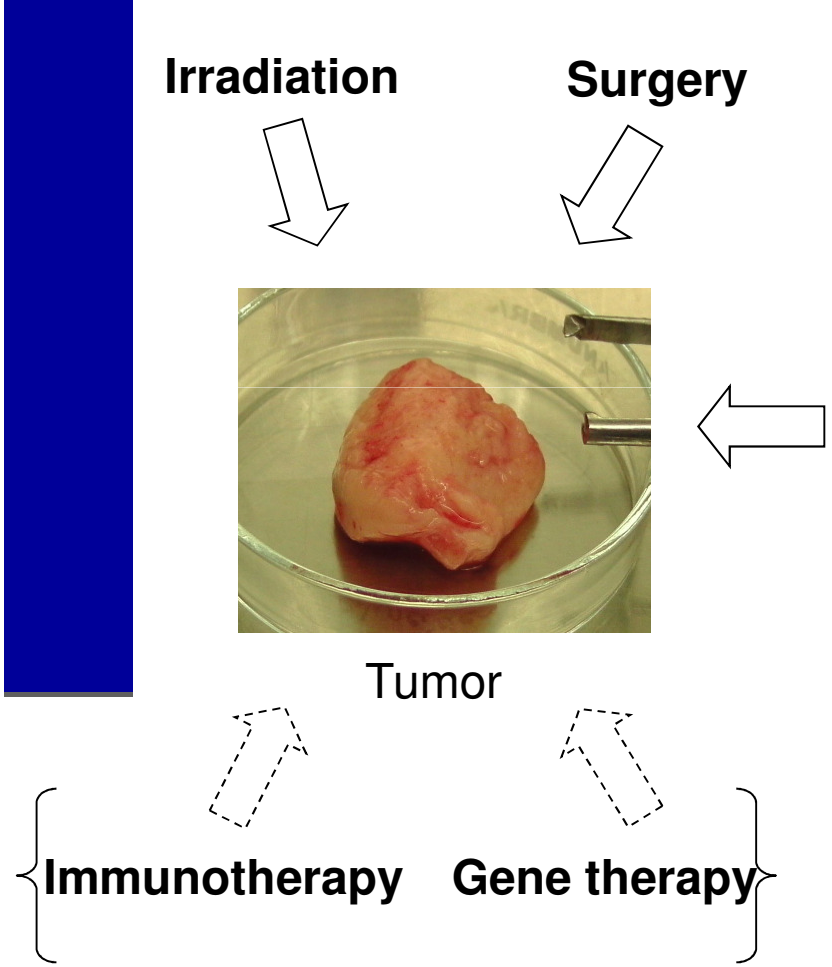
Treatment Options for Cancer



Medication

Type	Action	Target
Chemotherapeutic drugs	Cell division	TC
Hormones	Cell division	TC
Inhibitors of signal transduction	Inside (Tumor) cells	TC, VC
Antibodies (monoclonal)	Outside (Tumor) cells	TC, VC, IC
Cytokines	Immuno-modulation	IC

TC … Tumor cells; VC … Vascular cells; IC … Cells of the immune system

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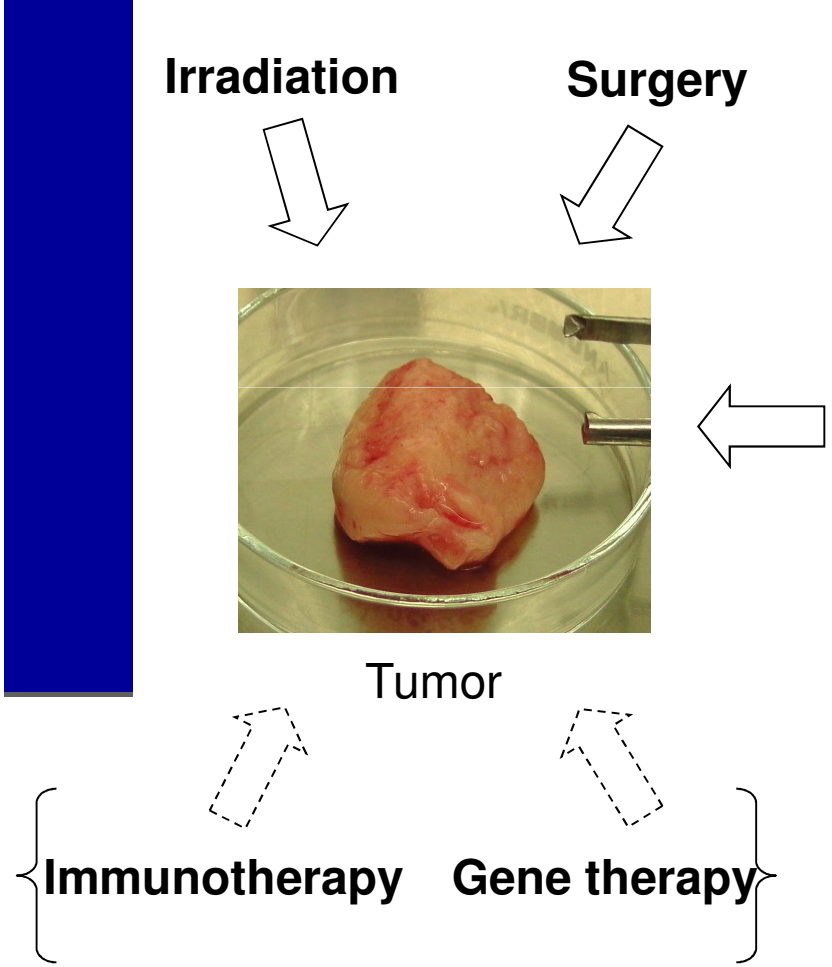
Treatment Options for Cancer



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TC … Tumor cells; VC … Vascular cells; IC … Cells of the immune system

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CTR-Test® Can Evaluate Drugs That Act Against Cancer Cells Directly

CTR-Test®
Chemotherapie-Resistenz-Test

Medication

Type	Action	Target
Chemotherapeutic drugs	**Cell division**	**TC**
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ONCOMPASS Can Evaluate Targeted Drugs

ONCOMPASS Cancer Diagnostics

Medication

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Chemotherapeutic drugs	**Cell division**	**TC**
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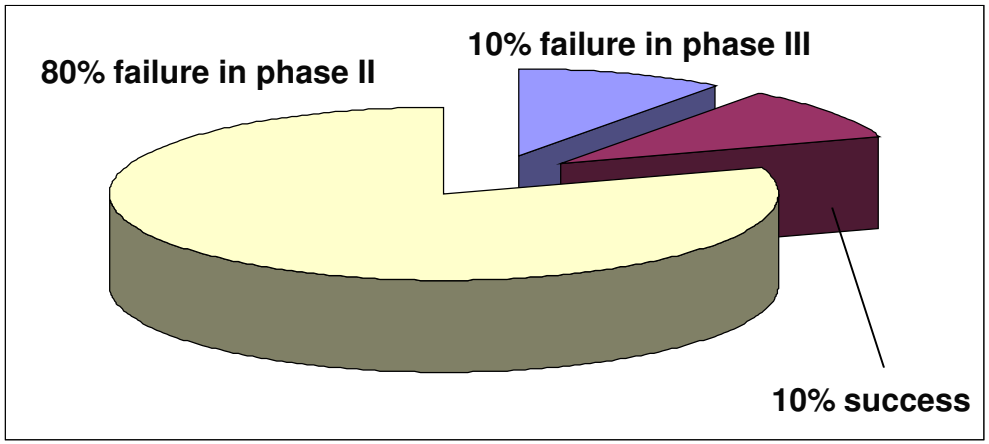
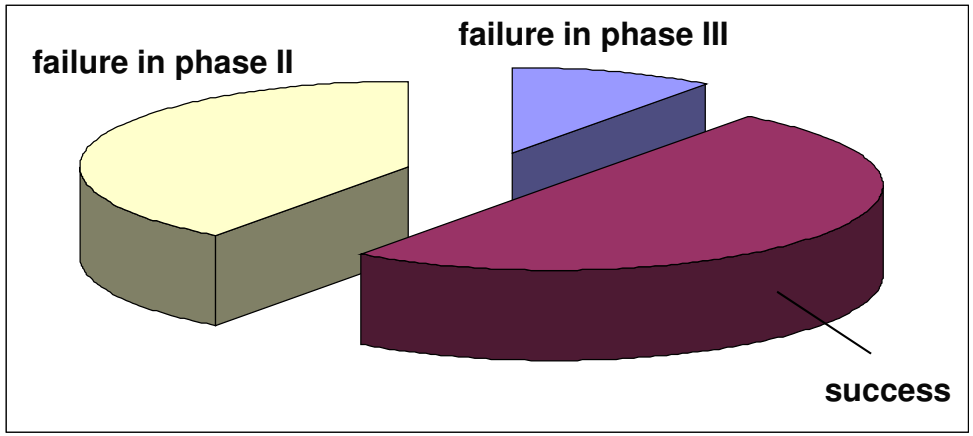
Increased Success Rate of Clinical Trials by Using Companion Diagnostics

Current success rate of clinical trials in cancer



Source: MedCity News - http://www.medcitynews.com

Putative increased success rate of clinical trials in cancer by using companion diagnostics



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Chemotherapy-Resistance-Test

CTR-Test®

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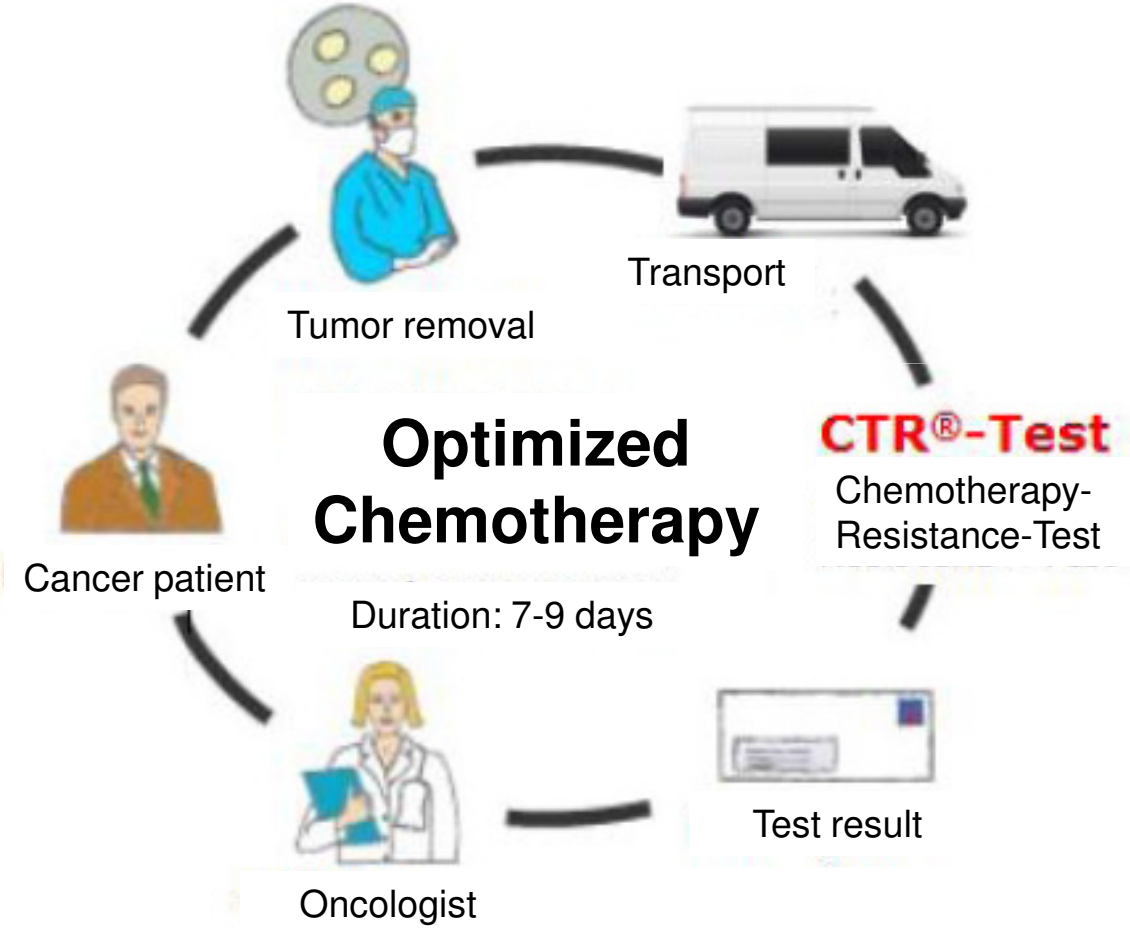
The Logistic Chain



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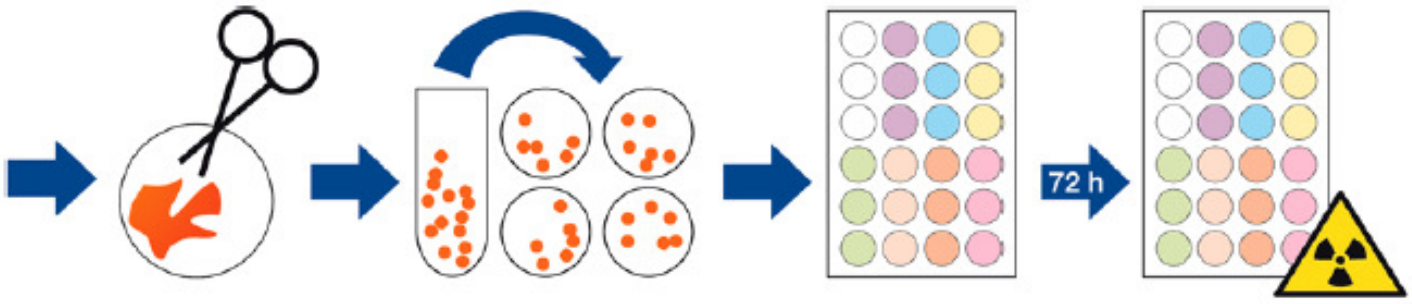
The Procedure

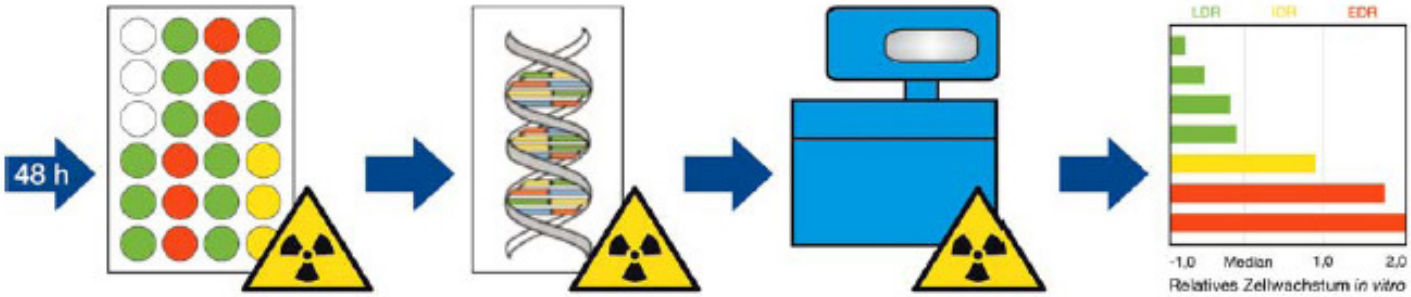


1 Tumor preparation

2 Plating of tumor cell suspension

3 Addition of chemotherapeutic drugs

4 Addition of 3H-labeled thymidine



5 Different cell growth

6 Isolation of genomic DNA

7 Reading of incorporated 3H-activtiy

8 Computing test result

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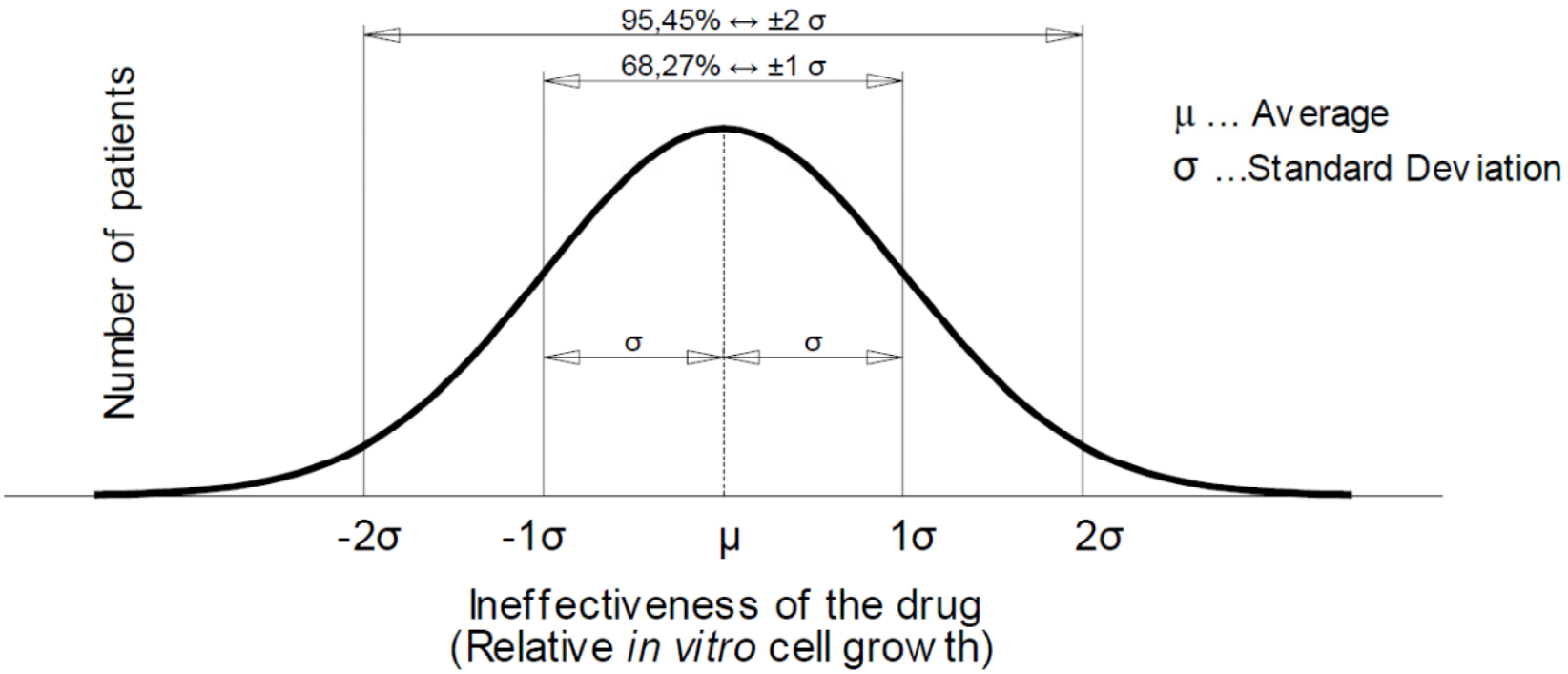
The Test Report

Standard distribution of a drug effect



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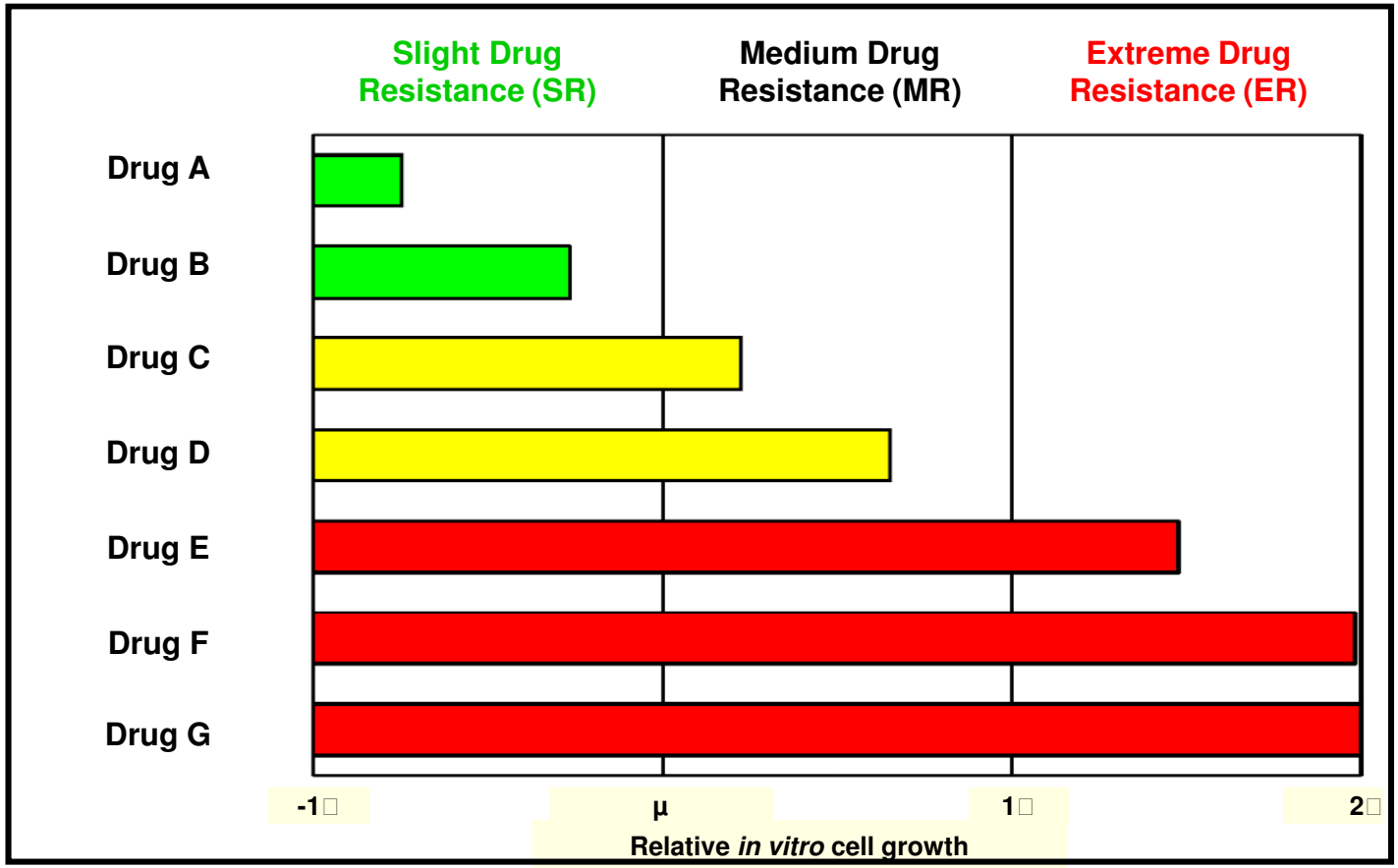
The Test Report



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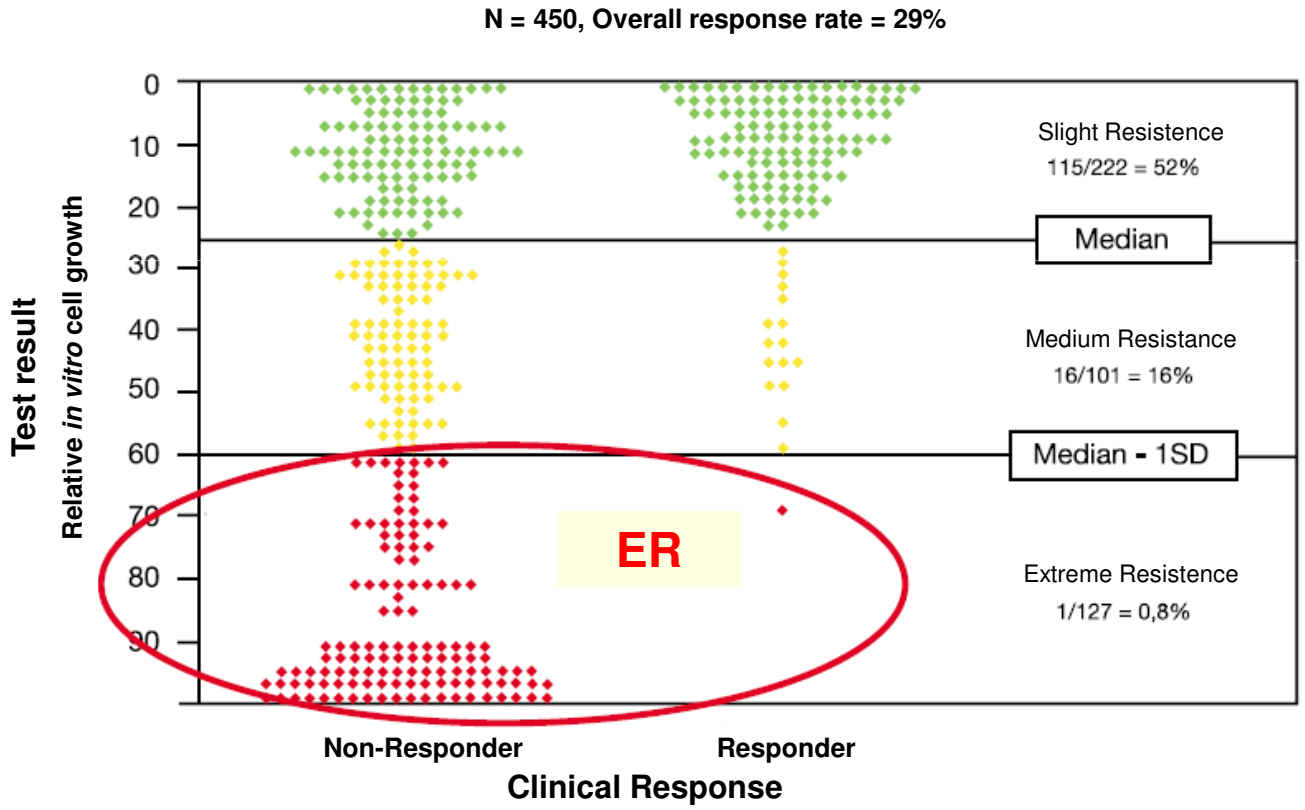
Correlation of CTR-Test® Result and Clinical Response



Kern DH, Weisenthal LM (1990) J Natl Cancer Inst. 82(7):582-8

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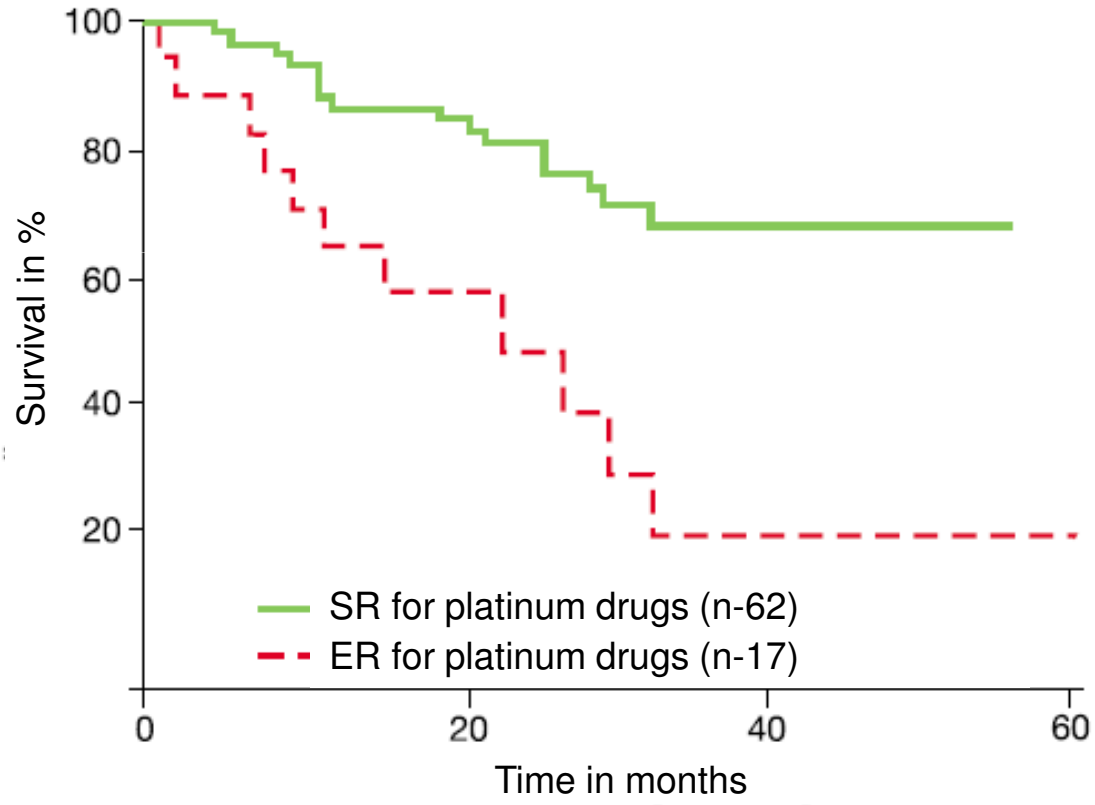
Correlation of CTR-Test® Result and Overall Survival



Holloway et al. (2002) Gynecologic Oncology 87(1):8-16

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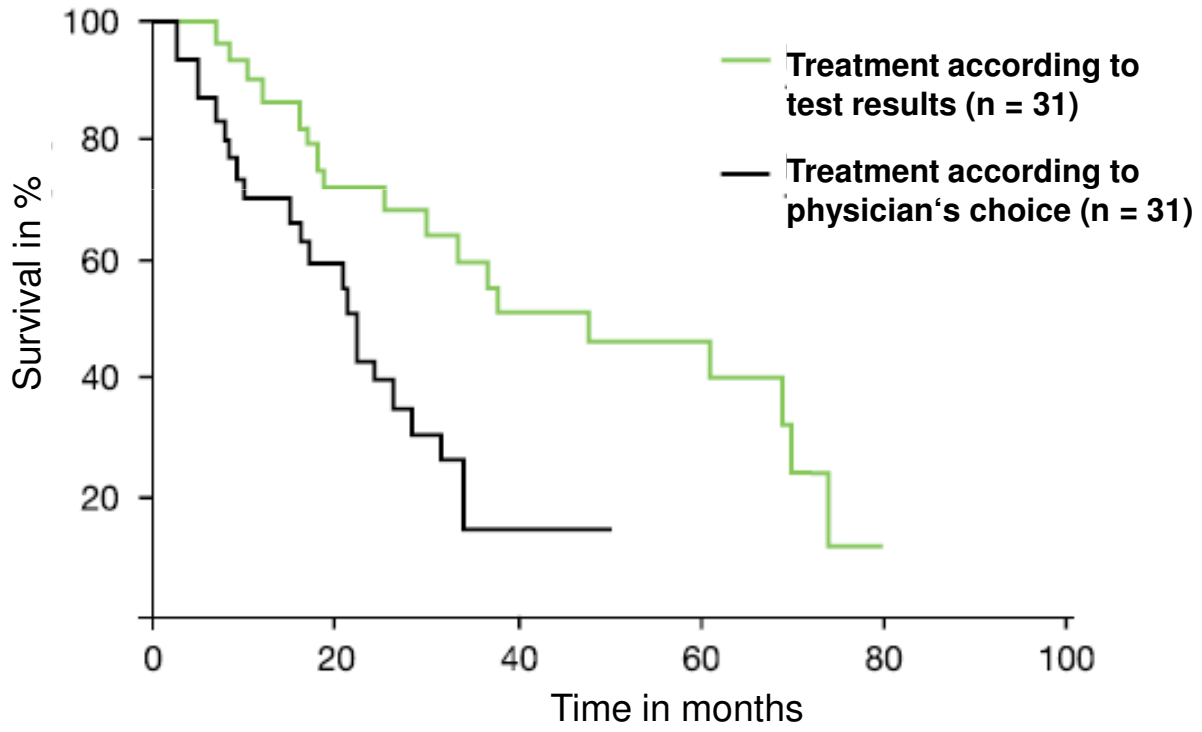
Extended Survival by Treatment According to Test Result

- Ovarian cancer, platinum-sensitive group



Loizzi et al. (2003) Am J Obstet Gynecol 189(5): 1301-1307

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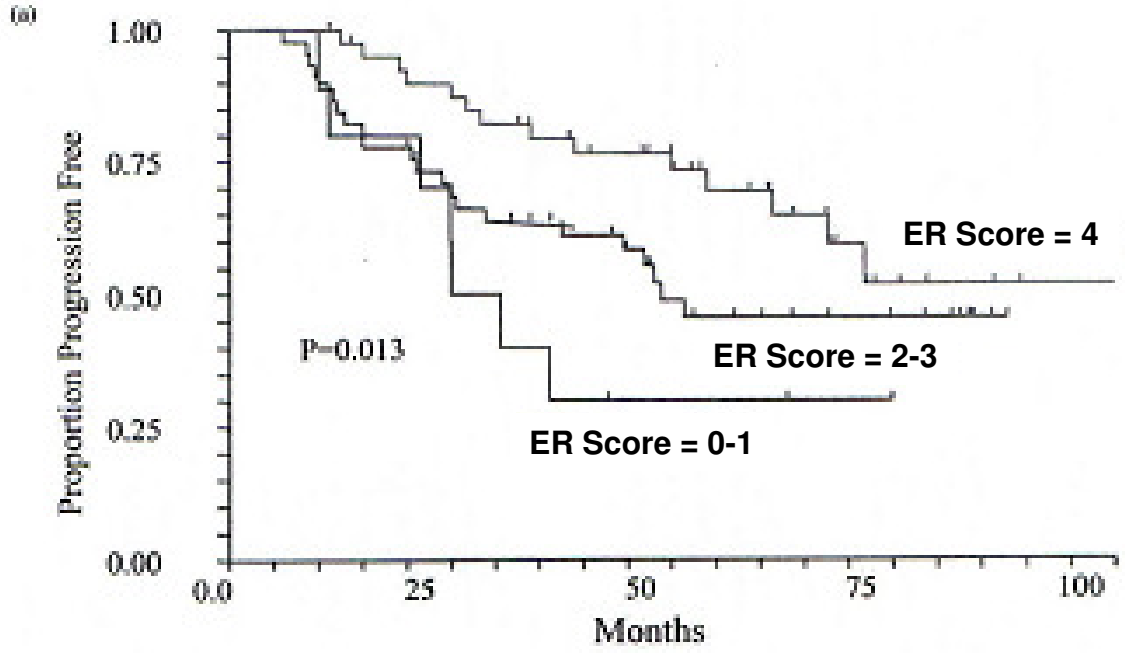
Best Drug Combination Correlates with Single Active Drugs

- Kaplan-Meier progression free survival curves for patients with ER scores of 4 vs. 2-3 vs. 0-1.



Mehta RS et al. (2001) Breast Cancer Research and Treatmant 66(3): 225-237.

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ONCOMPASS

Cancer Diagnostics

KPS DIAGNOSTICS GmbH

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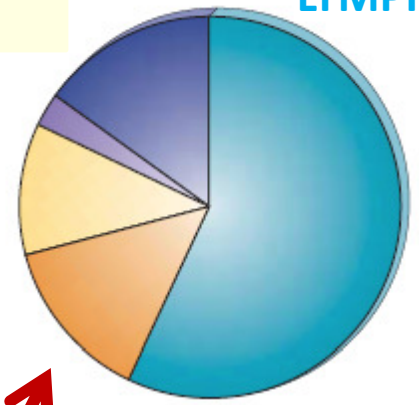
A CENSUS OF HUMAN CANCER GENES IN 2004

Symbol	Name	GeneID	Chr	Chr Band	Cancer Somatic Mut	Cancer Germline Mut	Tumour Types (Somatic Mutations)	Tumour Types (Germline Mutations)	Cancer Syndrome	Tissue Type	Cancer Molecular Genetics	Mutation Type	Translocation Partner
AKT1	v-akt murine thymoma viral oncogene homolog 1	207	14	14q32.32	yes		breast, colorectal, ovarian, NSCLC			E	Dom	Mis	
AKT2	v-akt murine thymoma viral oncogene homolog 2	208	19	19q13.1-q	yes		ovarian, pancreatic			E	Dom	A	
ALDH2	aldehyde dehydrogenase 2 family (mitochondrial)	217	12	12q24.2	yes		leiomyoma			M	Dom	T	HMGA2
ALK	anaplastic lymphoma kinase (Ki-1)	238	2	2p23	yes	yes	ALCL, NSCLC, Neuroblastoma, Brea	neuroblastoma	Familial neuroblastor	L, E, M	Dom	T, Mis, A	NPM1, TPM3, TFG, TI
APC	adenomatous polyposis of the colon gene	324	5	5q21	yes	yes	colorectal, pancreatic, desmoid, hep	colorectal, pancreatic, desmoid, hepa	Adenomatous polypo	E, M, O	Rec	D, Mis, N, F, S	
ATRX	alpha thalassemia/mental retardation syndrome X-linked	546	X	Xq21.1			Pancreatic neuroendocrine tumors			E	Rec	Mis, F, N	
BRAF	v-raf murine sarcoma viral oncogene homolog B1	673	7	7q34	yes		melanoma, colorectal, papillary thyroid,	borderline ov, Non small-cell lung	cancer (NSCLC), chol	E	Dom	Mis, T, O	AKAP9, KIAA1549
BRCA1	familial breast/ovarian cancer gene 1	672	17	17q21	yes	yes	ovarian	breast, ovarian	Hereditary breast/ova	E	Rec	D, Mis, N, F, S	
BRCA2	familial breast/ovarian cancer gene 2	675	13	13q12	yes	yes	breast, ovarian, pancreatic	breast, ovarian, pancreatic, leukemia	Hereditary breast/ova	L, E	Rec	D, Mis, N, F, S	
CDKN2A- p16(INK4a)	cyclin-dependent kinase inhibitor 2A (p16(INK4a)) gene	1029	9	9p21	yes	yes	melanoma, multiple other tumour typ	melanoma, pancreatic	Familial malignant m	L, E, M, O	Rec	D, Mis, N, F, S	
CDKN2A- p14ARF	cyclin-dependent kinase inhibitor 2A-- p14ARF protein	1029	9	9p21	yes	yes	melanoma, multiple other tumour typ	melanoma, pancreatic	Familial malignant m	L, E, M, O	Rec	D, S	
CTNNB1	catenin (cadherin-associated protein), beta 1	1499	3	3p22-p21.3	yes		colorectal, ovarian, hepatoblastoma,	others, pleomorphic salivary adenoma		E, M, O	Dom	H, Mis, T	PLAG1
DAXX	death-domain associated protein	1616	6	6p21.3	yes		Pancreatic neuroendocrine tumors			E	Rec	Mis, F, N	
EP300	300 kd E1A-Binding protein gene	2033	22	22q13	yes		colorectal, breast, pancreatic, AML,	ALL, DLBCL		L, E	Rec	T, N, F, Mis, O	MLL, RUNXBP2
ERBB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2,	2064	17	17q21.1	yes		breast, ovarian, other tumour types,	NSCLC, gastric		E	Dom	A, Mis, O	
ERCC2	excision repair cross-complementing rodent repair deficien	2068	19	19q13.2-q13.3	yes			skin basal cell, skin squamous cell, ri	Xeroderma pigmento	E	Rec	Mis, N, F, S	
ERCC3	excision repair cross-complementing rodent repair deficien	2071	2	2q21	yes			skin basal cell, skin squamous cell, ri	Xeroderma pigmento	E	Rec	Mis, S	
ERCC4	excision repair cross-complementing rodent repair deficien	2072	16	16p13.3-p13.13	yes			skin basal cell, skin squamous cell, ri	Xeroderma pigmento	E	Rec	Mis, N, F	
ERCC5	excision repair cross-complementing rodent repair deficien	2073	13	13q33	yes			skin basal cell, skin squamous cell, ri	Xeroderma pigmento	E	Rec	Mis, N, F	
FBXW7	F-box and WD-40 domain protein 7 (archipelago homolog,	55294	4	4q31.3	yes		colorectal, endometrial, T-ALL			E, L	Rec	Mis, N, D, F	
FGFR2	fibroblast growth factor receptor 2	2263	10	10q26	yes		gastric. NSCLC, endometrial			E	Dom	Mis	
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M recep	3572	5	5q11	yes		hepatocellular ca			E	Dom	O	
KRAS	v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog	3845	12	12p12.1	yes		pancreatic, colorectal, lung, thyroid,	AML, others		L, E, M, O	Dom	Mis	
MADH4	Homolog of Drosophila Mothers Against Decapentaplegic	4089	18	18q21.1	yes	yes	colorectal, pancreatic, small intestin	gastrointestinal polyps	Juvenile polyposis	E	Rec	D, Mis, N, F	
MAP2K4	mitogen-activated protein kinase kinase 4	6416	17	17p11.2	yes		pancreatic, breast, colorectal			E	Rec	D, Mis, N	
MDM2	Mdm2 p53 binding protein homolog	4193	12	12q15	yes		sarcoma, glioma, colorectal, other			M, O, E, L	Dom	A	
MLH1	E. coli MutL homolog gene	4292	3	3p21.3	yes	yes	colorectal, endometrial, ovarian, CNS	colorectal, endometrial, ovarian, CNS	Hereditary non-polyp	E, O	Rec	D, Mis, N, F, S	
MSH2	mutS homolog 2 (E. coli)	4436	2	2p22-p21	yes	yes	colorectal, endometrial, ovarian	colorectal, endometrial, ovarian	Hereditary non-polyp	E	Rec	D, Mis, N, F, S	
MSH6	mutS homolog 6 (E. coli)	2956	2	2p16	yes	yes	colorectal	colorectal, endometrial, ovarian	Hereditary non-polyp	E	Rec	Mis, N, F, S	
MSI2	musashi homolog 2 (Drosophila)	124540	17	17q23.2	yes		CML			L	Dom	T	HOXA9

SANGER DATABASE

LEUKEMIAS
LYMPHOMAS

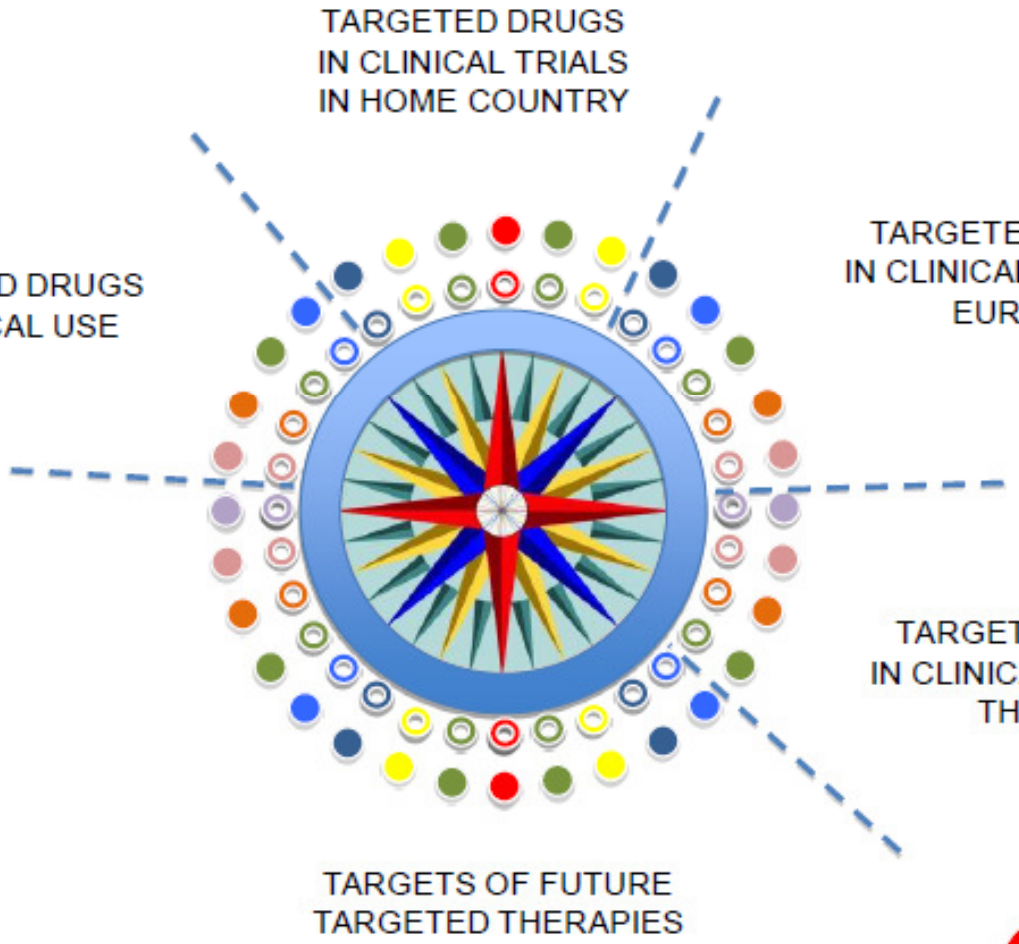


460 CANCER GENES

100 CANCER GENES IN EPITHELIAL CANCERS

1% of all genes
90% somatic mutations
20% germline mutations
10% show both somatic and germline mutations

ONCOMPASS



TARGET

TARGETED DRUG

PROPRIATORY TECHNOLOGIES IN MOLECULAR DIAGNOSTICS AND BIOINFORMATICS FOR PERSONALIZED CANCER THERAPY

START

GOAL

CANCER GENOME PROJECT

TARGETED RESEQUENCING OF PATIENT SAMPLES

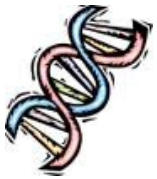
DATA ANALYSIS

MOLECULAR INTERPRETATION

CLINICAL NAVIGATION

PATIENT ASSISTANCE

PHYSICIANS



SEQUENCE

MUTATIONS

DRUGS

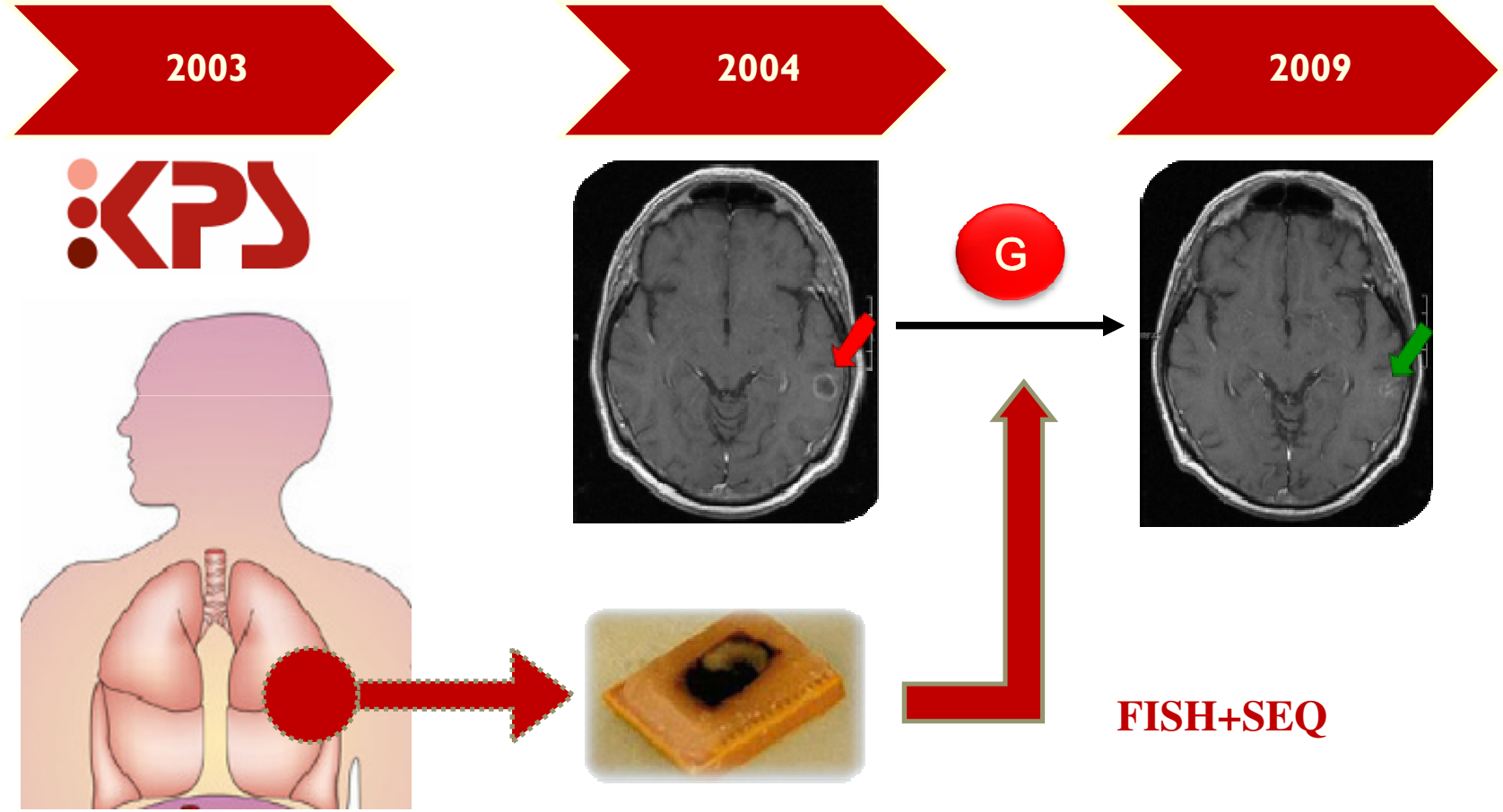
WHERE?

HOW?

CANCER GENES

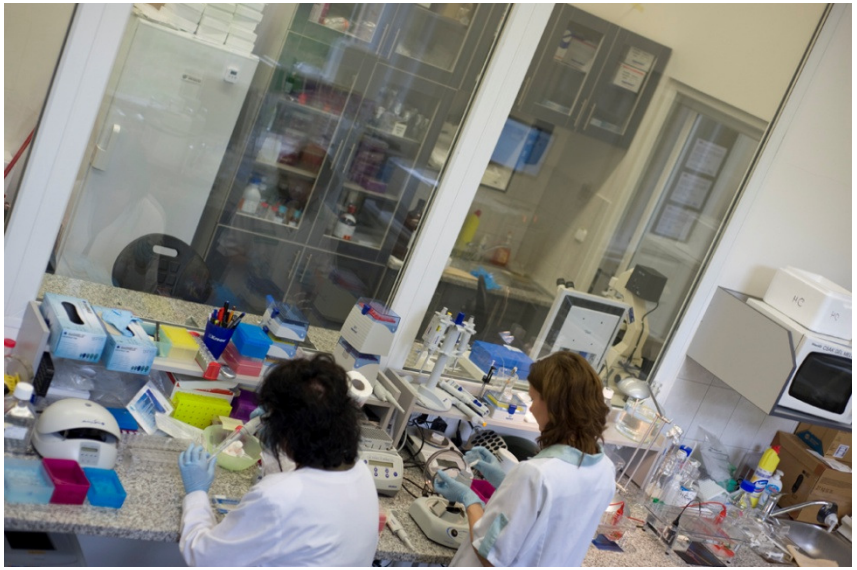
THERAPY

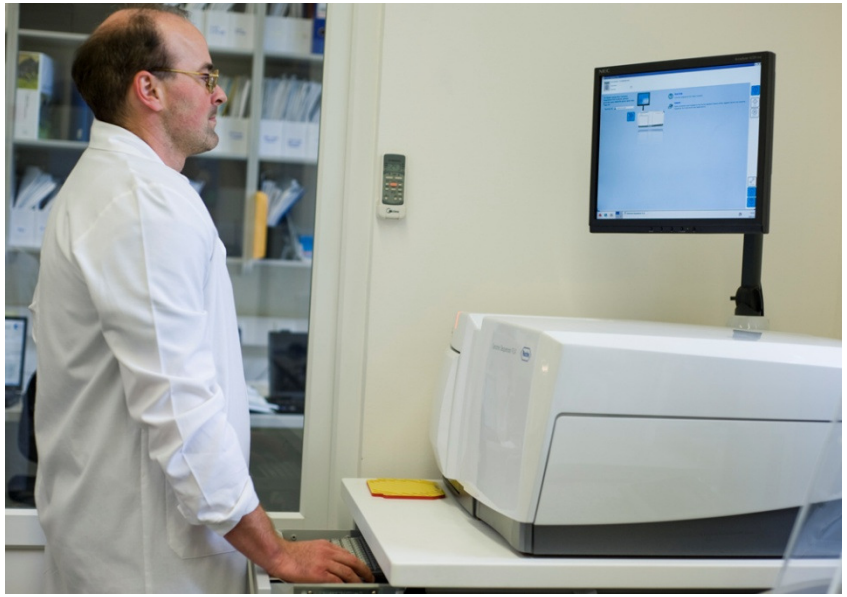
FIRST PROSPECTIVE TREATMENT OF A EGFR MUTANT NSCLC PATIENT



Modern treatment of lung cancer: case 1. Amplification and mutation of the epidermal growth factor receptor in metastatic lung cancer with remission from gefitinib. Schwab R, Pinter F, Moldavy J, Papay J, Strausz J, Kopper L, Keri G, Pap A, Petak I, Oreskovich K, Mangel L. J Clin Oncol. 2005 Oct 20;23(30):7736-8.

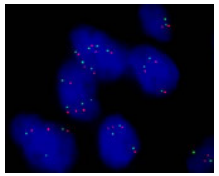
MOLECULAR DIAGNOSTIC LABORATORY

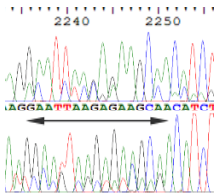




KPS DIAGNOSTICS:
CENTRAL LABORATORY SERVICES
FOR PERSONALIZED ANTI-CANCER THERAPIES

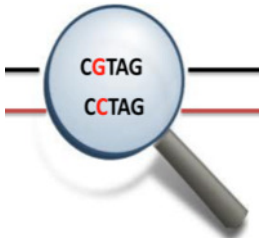
Molecular Diagnostics





- ✓ Optimized Cancer Panels for NGS sequencing
- ✓ Special technologies for small biopsies

Information Technology



- ✓ Special mathematical algorithms for data analysis
- ✓ Mutation database and pathway analysis for interpretation and decision support

Partners

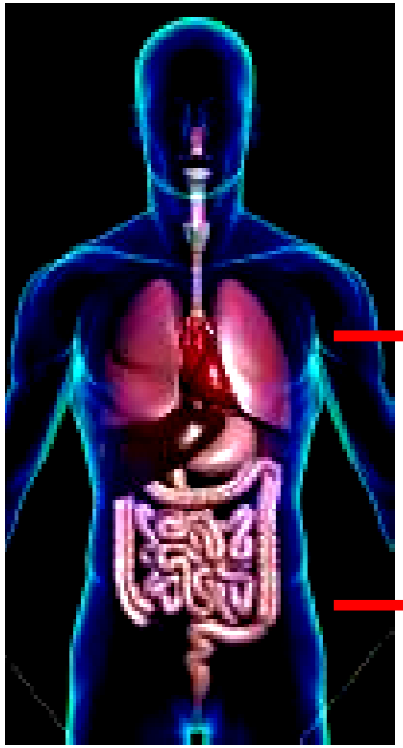
SAKK
Roche
SEEROG
AstraZeneca
AMGEN®
MERCK

Offices in Budapest, HU and in Heidelberg, GE

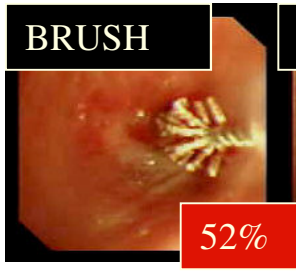
External Quality Assurance Programs of the European Association of Pathologists

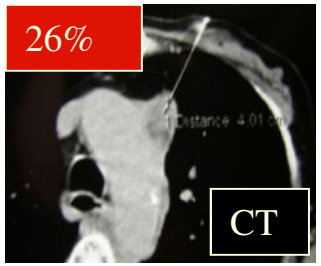
SYSTEM CERTIFICATION ISO 9001:2008 SGS

SAMPLE TYPES FOR MOLECULAR PATHOLOGY



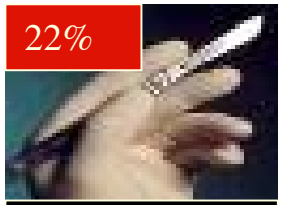
LUNG





CYTOLOGY SMEAR

EXCISOR

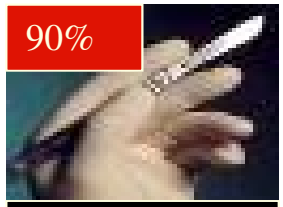


SURGICAL

FFPE BLOCK

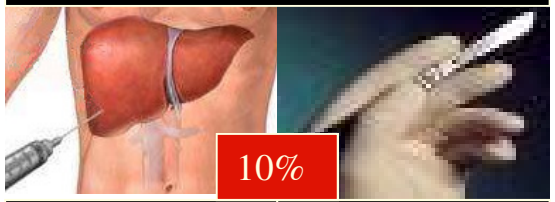
COLON

ENDSOCOPY



SURGICAL

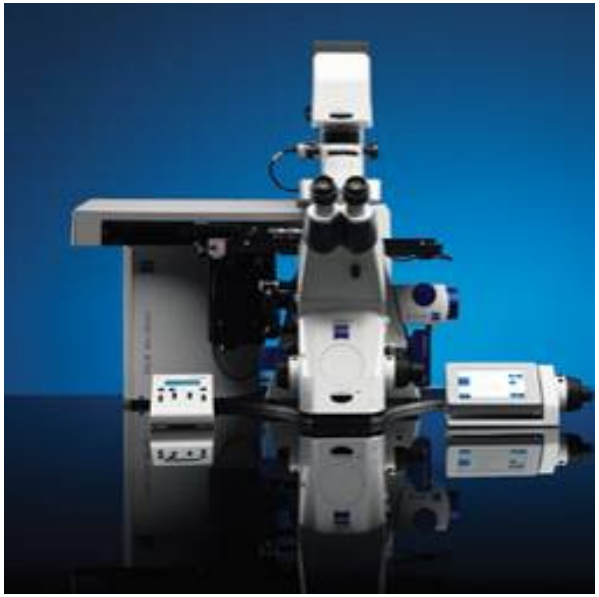
LIVER METASTASIS

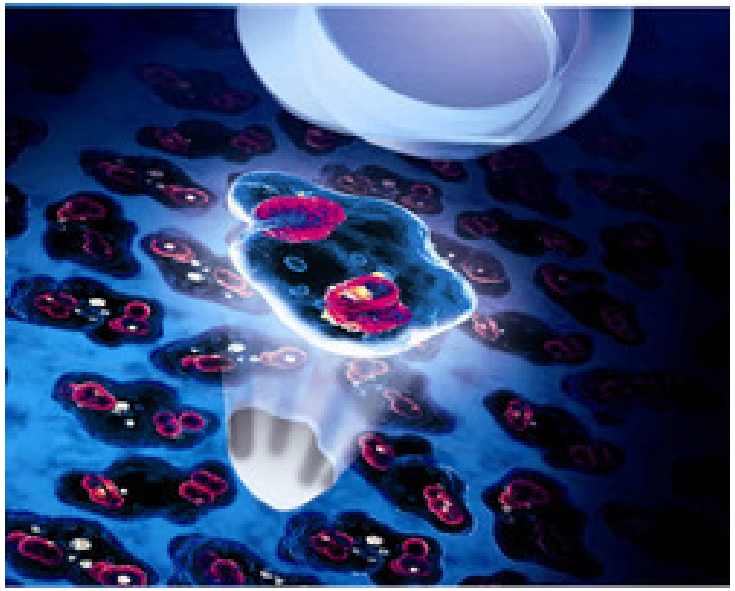


BIOPSY

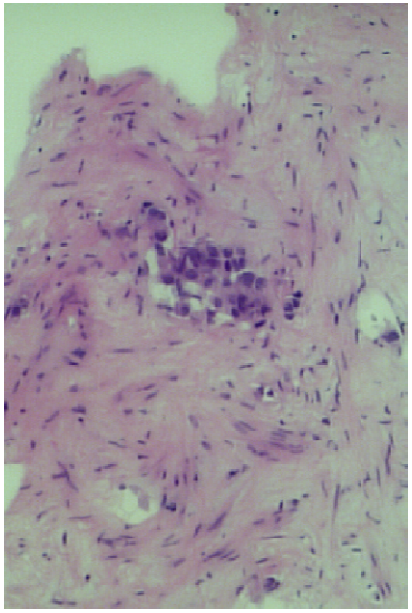
SURGICAL

SUCCESSFUL MULTIPLEX MOLECULAR PDX IN EXTREMELLY SMALL SAMPLES WITH ZEISS-PALM LASER CAPTURE MICROSCOPY BY TRANSFERING THE CELLS DIRECTLY FROM THE SLIDE TO THE PCR TUBE FOR AMPLIFICATION WITHOUT DNA EXTRACTION

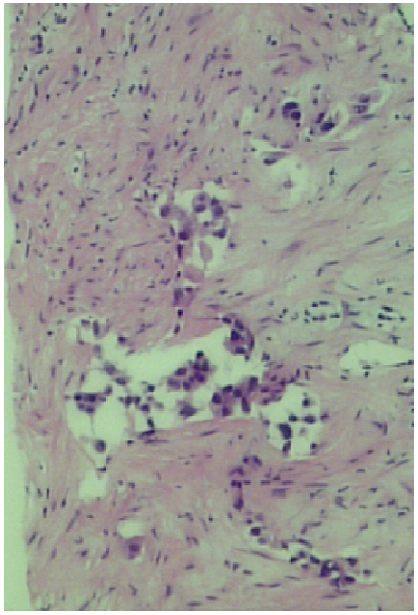




DETECTION OF EGFR MUTATION IN 84 CELLS



28 db



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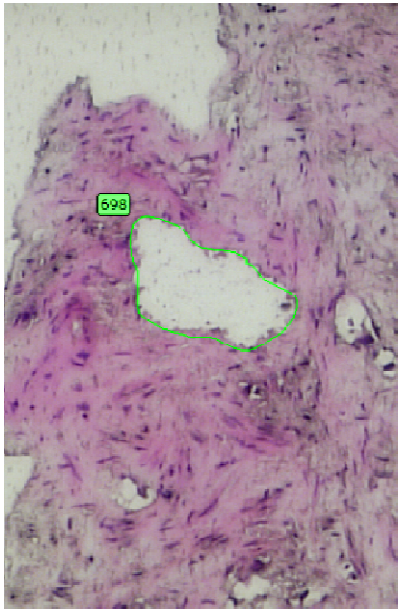
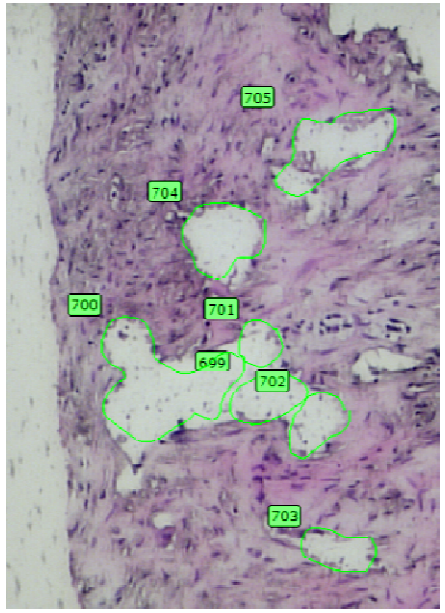
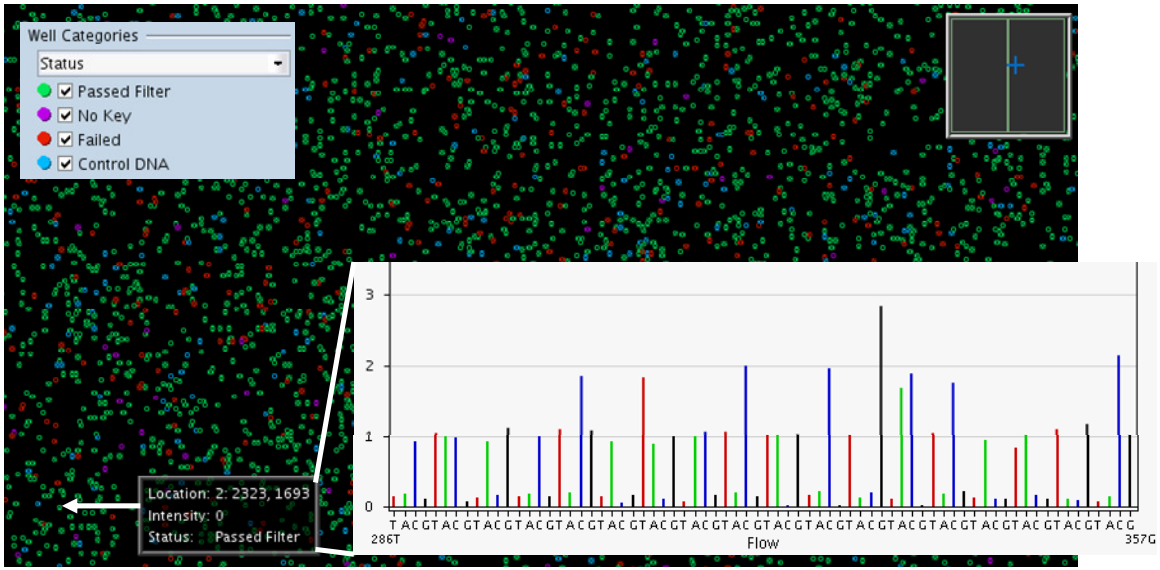


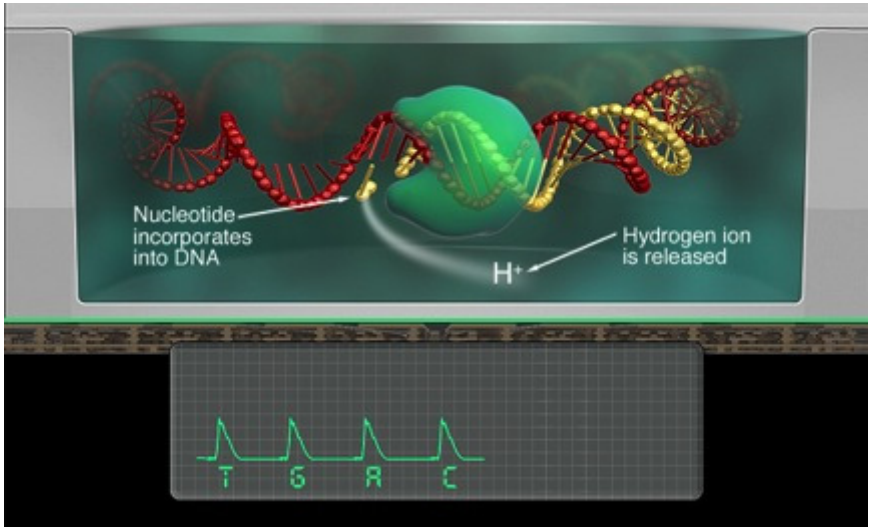


EGFR EXON 21
L858R

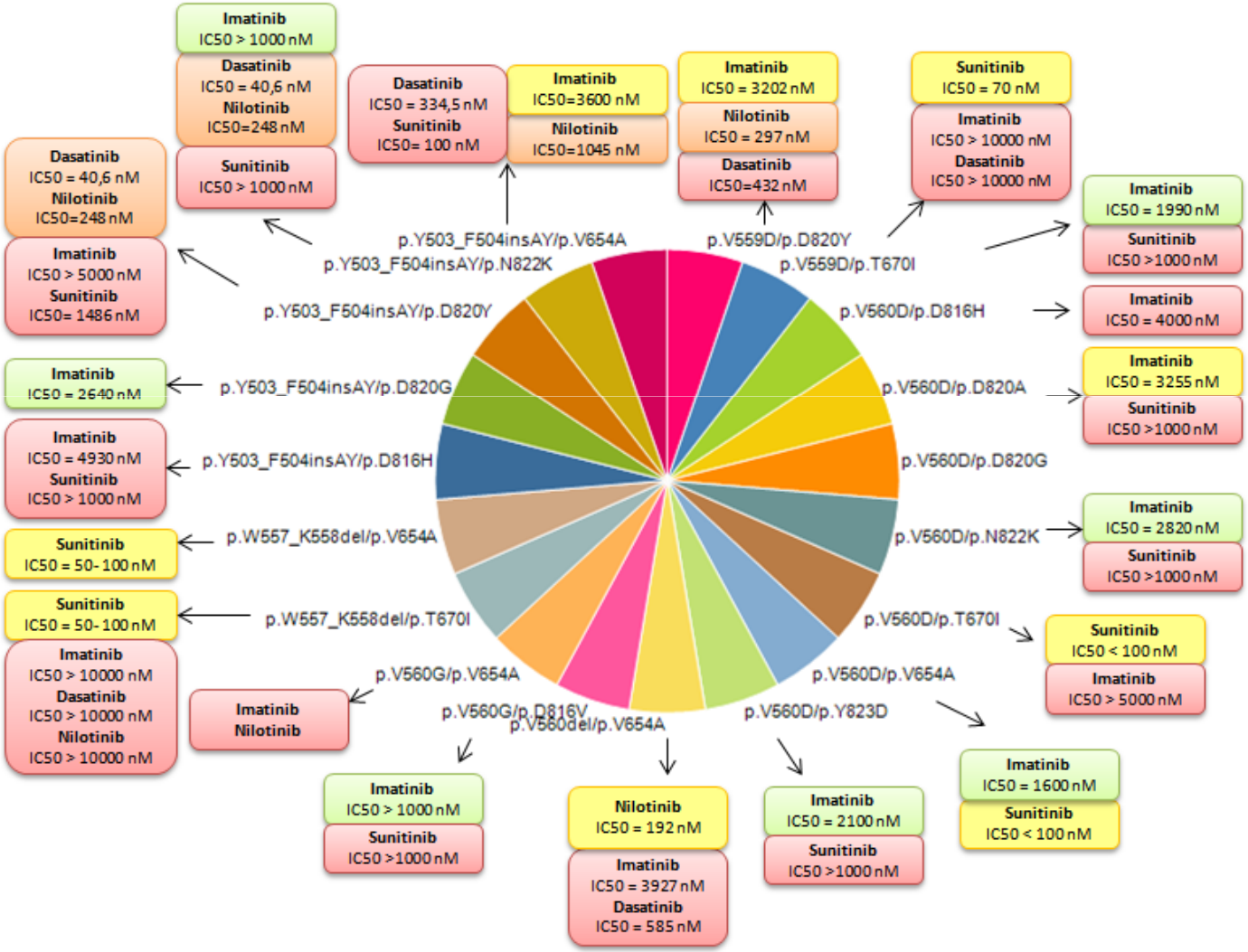
Response to gefitinib therapy

PIONEERING NEXT GENERATION SEQUENCING IN ONCOLOGY

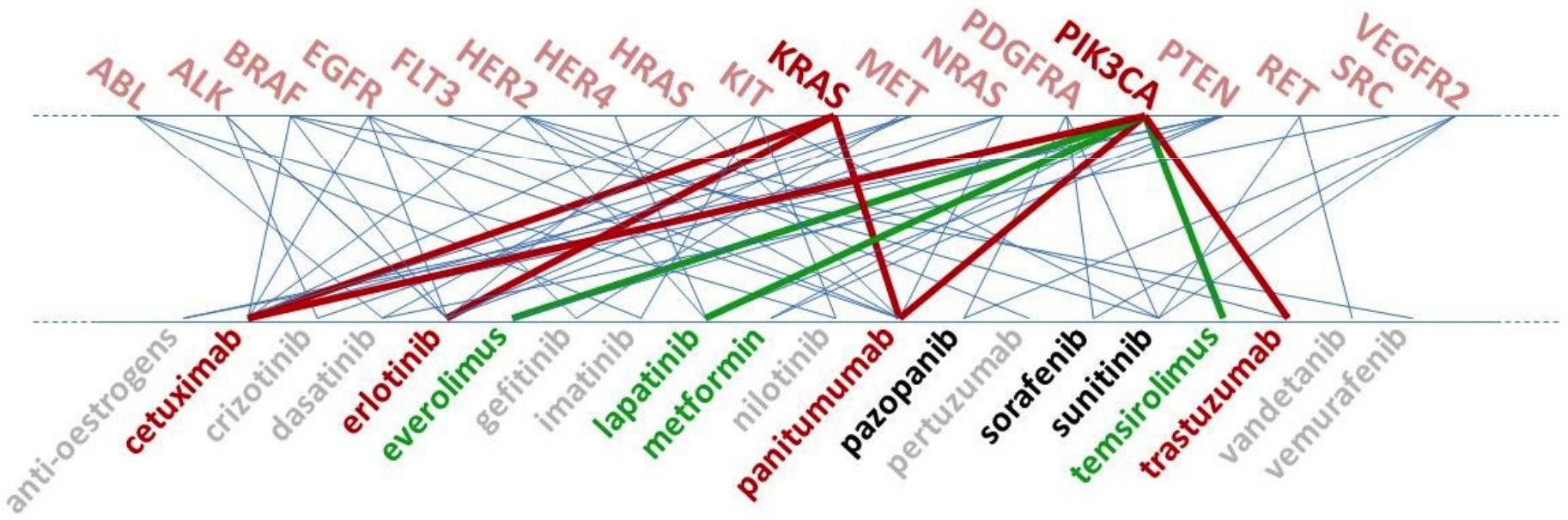




ONCOMPASS DRUG SENSITIVITY DATABASE

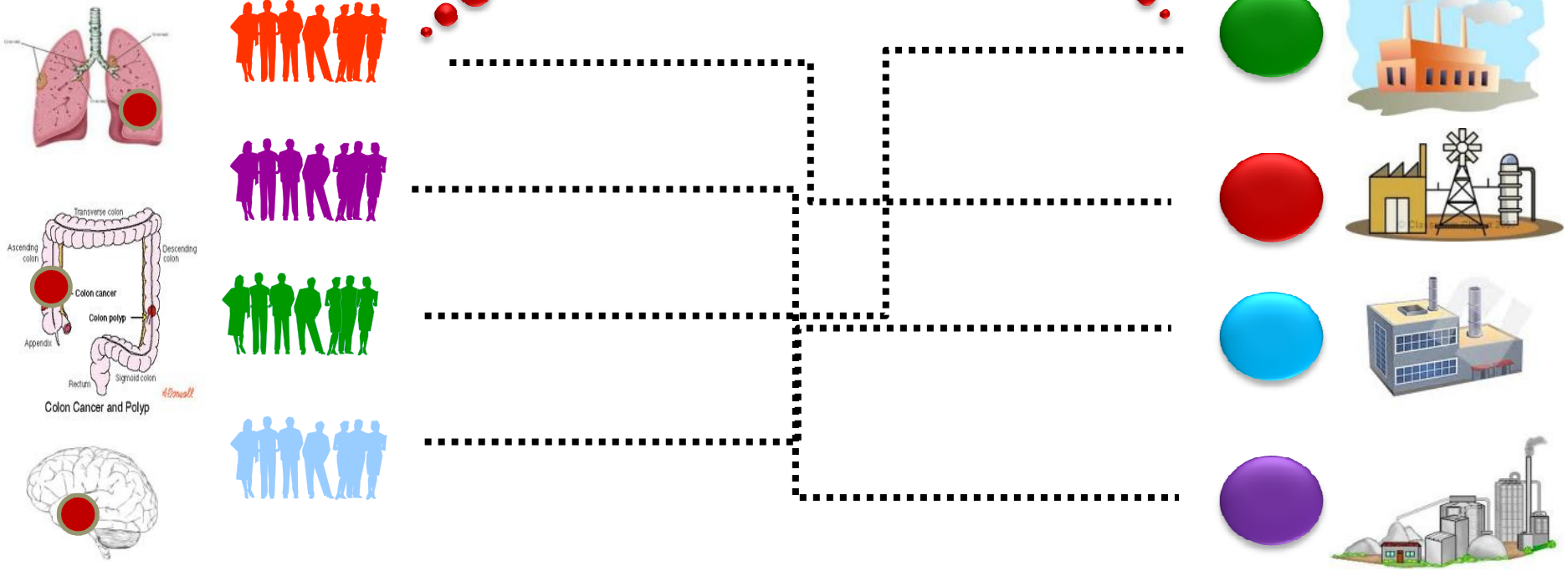


PROPRIATORY TECHNOLOGY TO FIND THE RIGHT DRUG FOR THE MUTATED GENES



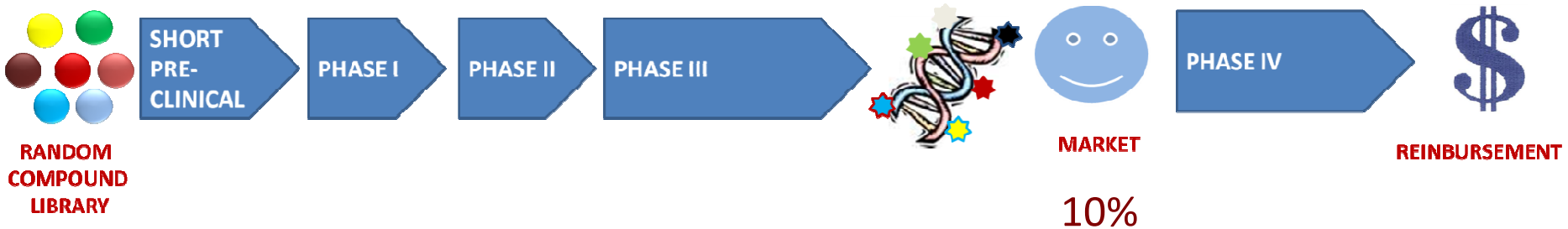
~100 TARGETS

~400 DRUGS



TARGET BASED PHASE 1b TRIALS

OLD MODEL

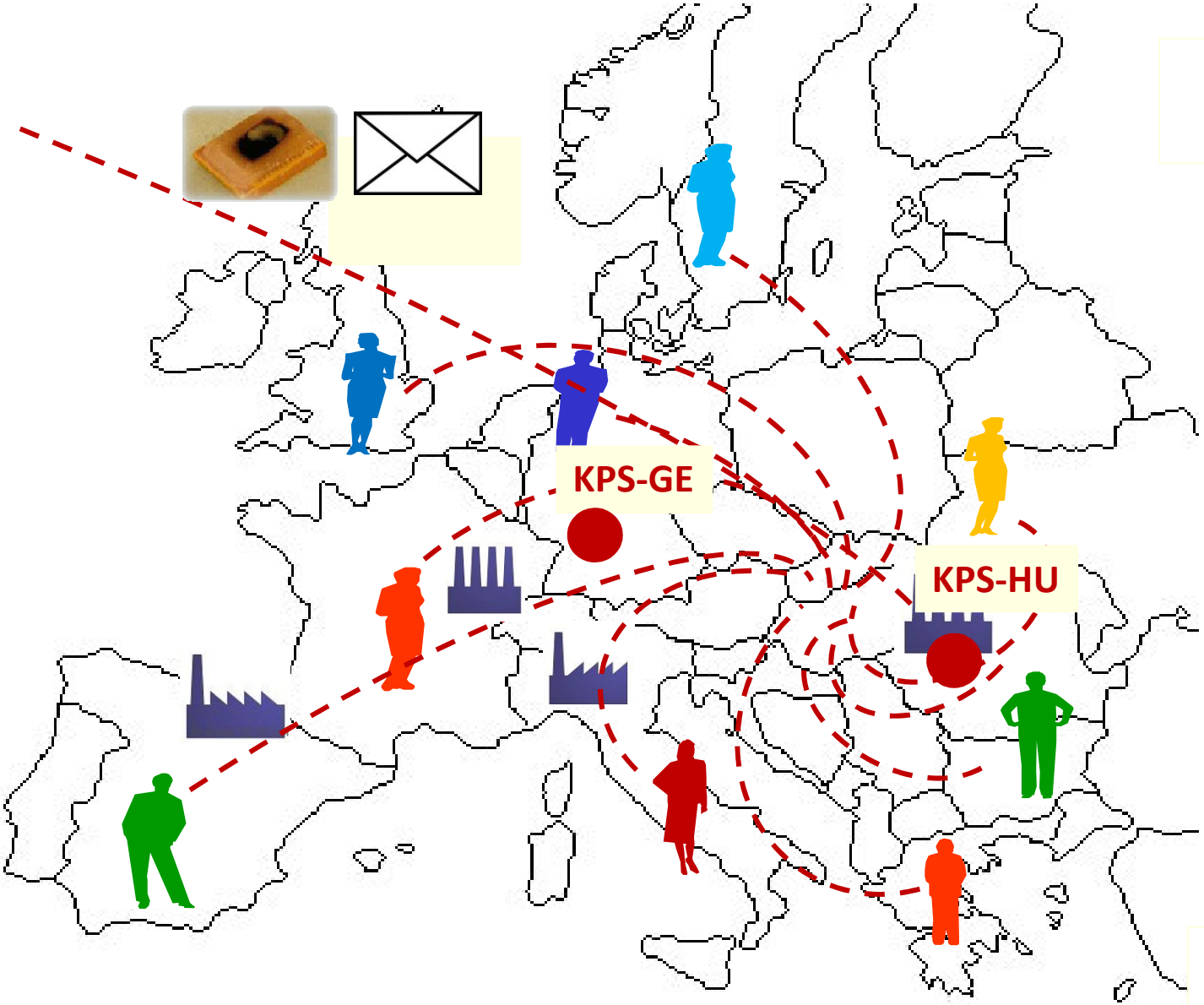


10%

NEW MODEL

25%

Oncompass Clinical Trial Navigator and Patient Assistance



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