



Research Genetic Cancer Centre

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# Personalised Cancer Testing

- Early detection
- Personalised treatment of cancer
- Chemosensitivity testing

R.G.C.C. International GmbH offers a range of individualised tests from a world-class molecular oncology laboratory in Greece.

These tests can:

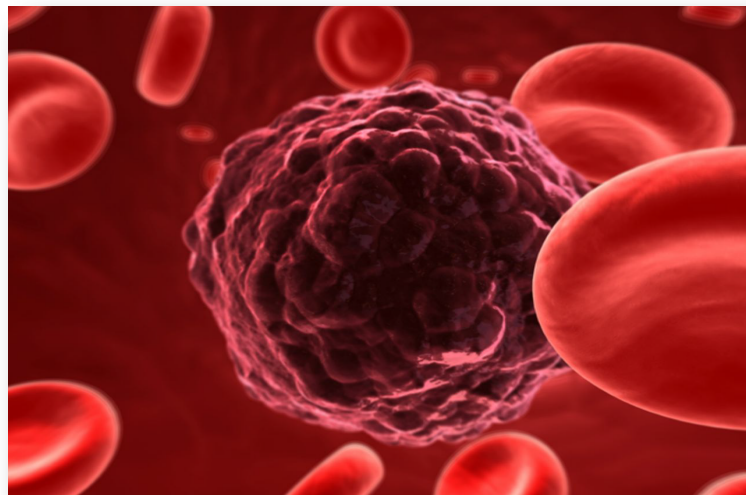
- 1) detect early signs of a developing cancer,
- 2) help to monitor existing cancers and
- 3) produce an individual profile of which cancer drugs and which natural substances can be used to achieve the best treatment outcome.

## Circulating Tumour Cells

CTCs are cancer cells, which have broken away from the primary tumour and have entered the blood stream where they circulate and have the potential to generate metastatic disease. These cells can be isolated and identified, and there is growing interest in their detection for the following purposes:

- The early detection and diagnosis of new cancers
- Monitoring of existing cancers
- Prognosis – providing information about the risk of recurrence of a current or old cancer

R.G.C.C. International GmbH offers general assays for CTCs and for specific cancers, including breast, colorectal, prostate, malignant melanoma and sarcomas.



# Chemosensitivity testing

Cancer doctors principally rely on the statistical analysis of large treatment trials, to decide which drugs to use for specific cancers. There is a growing interest in personalized cancer therapy, which involves identifying those treatments, which may work best for an individual's cancer. Chemosensitivity testing is one method of doing this.

Chemosensitivity testing involves testing an individual's cancer cells in the laboratory to see which drugs demonstrate the best response. It therefore provides guidance about which treatments may be best for the individual in clinical practice.

The R.G.C.C. International GmbH test is a blood test (or sometimes tissue). Tumor cells are identified and isolated from the sample for the following analysis:

- Viability testing of chemotherapy drugs
- Genetic profiling for guidance about targeted therapies eg monoclonal antibodies
- Viability testing (and identification of mechanisms of action), of natural substances which may be used as part of a complementary treatment strategy .

The results are presented in a written report which your doctor can use to help guide your treatment options and choices.

In addition, R.G.C.C. International GmbH can provide information about how an individual will 'handle' specific chemotherapy agents. Our genetic makeup determines whether we are 'accumulators' or 'rapid metabolizers' of certain drugs. This can play a critical role in determining how effective a specific treatment is likely to be for us, and how significant the side effects will be.

## Who are these tests for?

- People who want to actively engage in reducing their risk of developing cancer in the future
- People with an increased risk of cancer e.g. due to family history or lifestyle / environmental issues who want the opportunity to engage in a screening programme for early detection and diagnosis.
- People with a current diagnosis of cancer who want more information about treatment options for them as an individual – including natural treatments.

## Who is R.G.C.C. International GmbH?

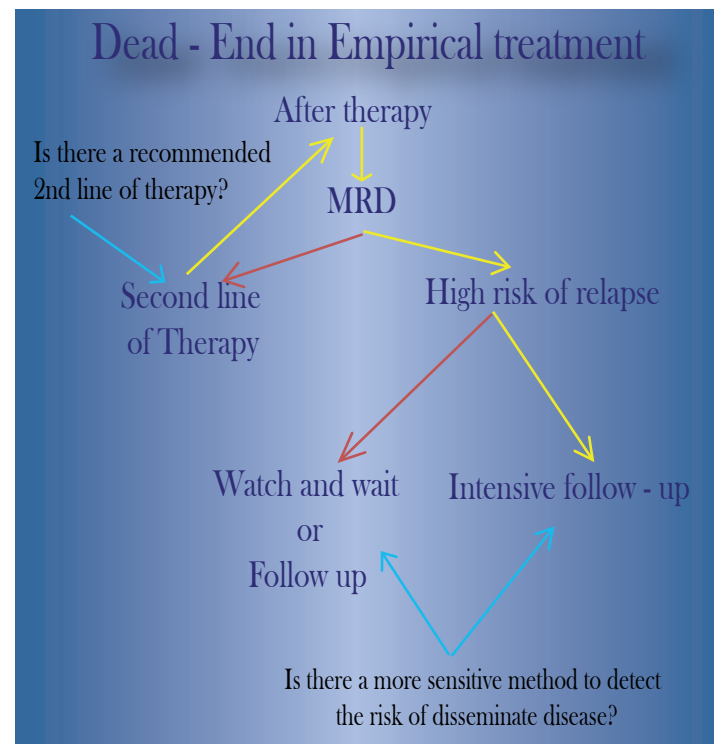
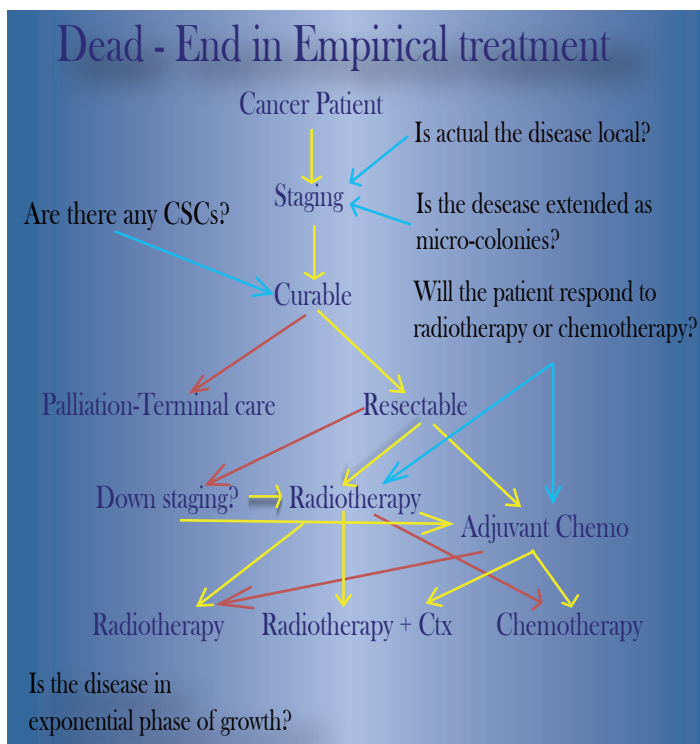
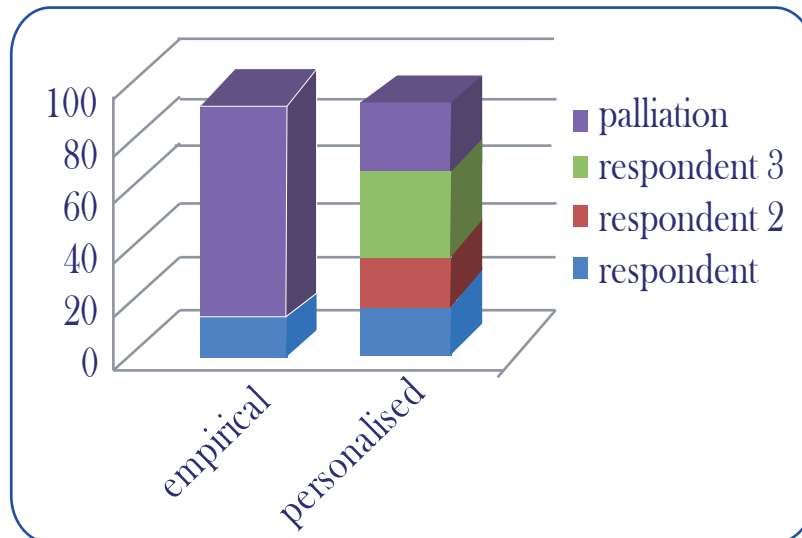
R.G.C.C. International GmbH is a world-class laboratory which specialises in medical genetics and in particular cancer genetics, providing a global service. The Director and founder is Dr Ioannis Papisotiriou MD.

# Scientific Evidence

- It is well established by literature and validation that the overall response rate from empirical chemotherapy varies from 5 to 7.5% (Royal North Shore Hospital Clin Oncol (R Coll Radiol) 2005 Jun;17(4):294).
- Pharmaceutical industry assesses and validates candidate drugs by utilizing extensive chemosensitivity assays under the term of High Throughput Screening (HTS).
- Cancer is caused by severe damaged genetic material which leads to random genetic instability. So, each malignancy behaves differently to each individual.
- Each person has different genetic fingerprinting from the others. This classifies people to:
  - Rapid metabolizers (individuals that metabolize fast the drug without receive any benefit from it).
  - Accumulators (individuals that cannot excrete the byproducts of a drug and that causes severe side effects and toxicities).
  - Normal metabolizers (these individuals can normally metabolize a drug to its active form and excrete the byproducts normally).

Hence based on the above, each patient and each malignancy has its own identity and behaves individually and differently from person to person.

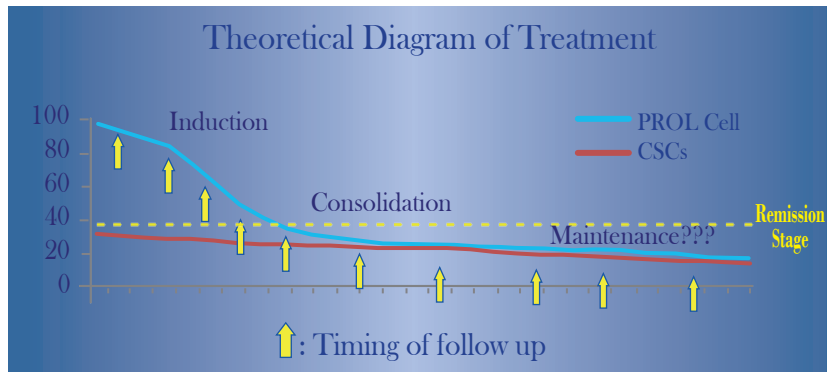
Therefore personalized treatment becomes essential in order to generate better rates of successful treatments in cancer. (DIAGRAMM: NSCLC of case treated with empirical lines vs personalised options)



# Therapeutic Concept

The tumor is consisted from several subgroups of cells (subpopulations) with different features. One of the subset actually drives the progress of the disease, the resistance to therapy and the relapse. This subset is called cancer stem cell like cells or tumor initiating cells. When a patient is treated and the cancer cells may be destroyed, then when the compatible diagnostic does not discover any signal, the cancer cells may consist a population of  $10^9$  to  $10^{12}$  cells. This limit defines the remission stage of a patient. At that stage only the cancer stem cells may survive and colonize into distant organs and generate metastases in time.

Hence the usage of our test is to detect in which therapeutic approach the cancer cell may respond and also during remission, it is essential to detect, discover and explore the features of the disseminated cancer stem cell like, in order to delay further the risk of relapse and also to generate options to treat even these kinds of cells. The main goal is to discover, analyze and screen the cancer cells in every step of the disease.

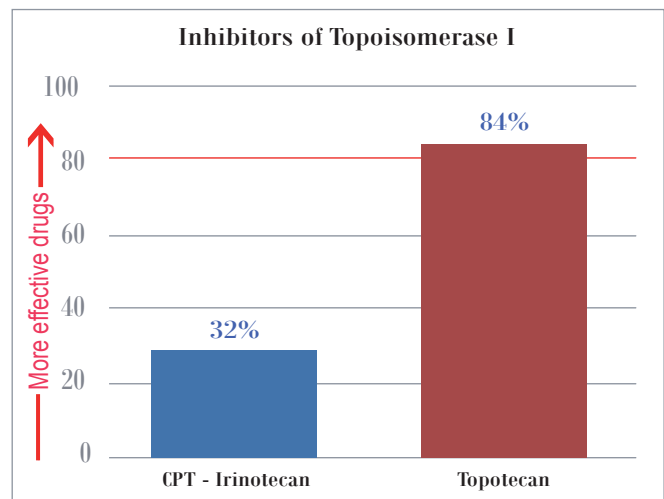
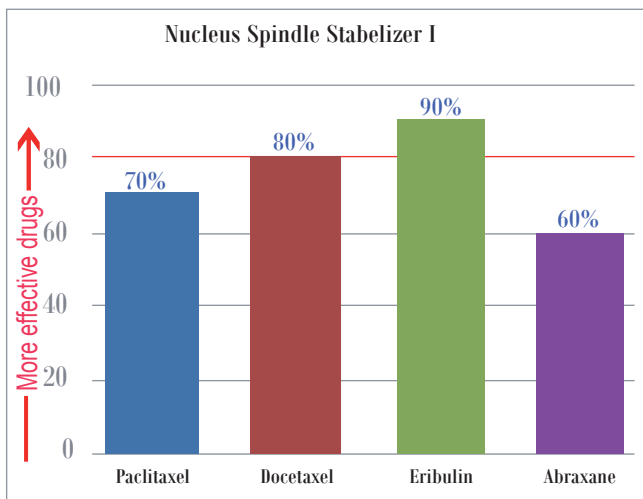


## Chemosensitivity / Chemoresistance

**Oncostat Plus**  
former TUP Plus

### Chemosensitivity for Cytotoxic drugs, targeted therapies (MOAB & TKIs) & Natural substances.

This test includes the chemosensitivity / chemoresistance assessment for cytotoxic drugs, monoclonal antibodies, small molecules that inhibit specific targets (TKI etc), the assessment of natural substances and extracts for an anticancer potency.



Samples at: <http://www.rgcc-genlab.com/?tests>

\* CTCs : Circulating Tumor Cells

## **Oncostat** *former TUP*

### **Chemosensitivity for Cytotoxic drugs**

This test includes the chemosensitivity / chemoresistance assessment for cytotoxic drugs, monoclonal antibodies, small molecules that inhibit specific targets (TKI etc).

## **Oncostat Extracts** *former TUP Extracts*

### **Chemosensitivity only for Natural Substances**

This test includes only the assessment of natural substances and plant extracts for potency against cancer patients derived CTCs.

## **Screening & Follow Up Tools**

### **Oncocount**

#### **CTC Number Only**

This test has as an outcome only the enumeration of CTCs, it does not include any other information concerning CTCs.

### **Oncotrail**

#### **CTC Number & Immunophenotype for specific types of malignancies**

This test is a tailor made test for specific type of malignancies such as breast cancer (Oncotrail for breast), prostate cancer (Oncotrail for prostate), Sarcoma etc. This test includes only relevant markers for a specific type of malignancy which makes the test a good tool for follow up control.

### **Oncotrace**

#### **CTC Number & Immunophenotype for all types of malignancies**

This test has as an outcome the concentration of CTCs and also the immunophenotype control of this kind of cells.

## Profile of humoral and cellular immunity and cachexia

This test uses specific cellular markers and cytokine production to detect the type or types of cells that are responsible for the activation or repression of the immune system of a patient.

Two different assays are used for the result export.

ELISA assay is used for the detection of cytokines produced by specific cells in serum sample.

On the other hand flow cytometry is used for the enumeration of specific markers on peripheral blood cells.

Both assays are then compared to a control sample and the results are represented as the following table:

## Immunity activation/suppression

Hematopoietic cells	Cell Type		Markers / cytokines		Control	Results		
CD45 positive cells	B cells	Plasma cells	CD19				↑	
		Naïve B cells	CD20				↓	
		Memory cells	CD28				-	
	T cells	CD8 (Cytotoxic T Lymphocytes, CTLs)	CD62L					
			CD4 (T helper cells, T <sub>H</sub> )	<i>Th1 (cell mediated immunity)</i>	IFN-γ (interferon gamma)			
		<i>Th2 (humoral immunity)</i>		IL-4 (Interleukin 4)				
				IL-6 (Interleukin 6)				
			IL-2 (Interleukin 2)					
		<i>Th3 (suppressed immunity)</i>	TNF-α (Tumor Necrosis Factor alpha)					
			T regulatory cells (Tregs)	CD25	CTLA4			
		Memory cells	CD28					
	Antigen Presenting Cells (APCs)	Dendritic cells (DCs)	CD80					
CD86								

*This test will be a useful tool for practitioners dealing with patients with acute and chronic immune diseases.*

## Metastat

### *Markers on CTCs that point out the potent organ for relapse*

From literature numerous markers are associated with specific tumor organ metastases. The Metastat test is a collection of specific markers that are detected on specific organs.

Cells of the primary tumor that have the ability to metastasize, will express specific genes and proteins according to the organ that will metastasize, and that is given by the genetic information.

This test uses patient's blood samples that are analyzed with two different methods for the export of accurate results.

Real Time PCR detects the levels of these specific marker genes and flow cytometry the protein levels produced by these exact genes.

Results are compared to a control sample and the results are given with the following format

### Metastasis Markers

<u>Metastasis location</u>	<u>Marker</u>	<u>Sample levels</u>	<u>Normal levels</u>	<u>Results</u>
General	TGF- $\beta$ R2			
	ITGB-4 R			↓
	ITGB-5 R			
	ITGB-6 R			
Pleura	CCR6			
	Mesothelin			
Skin	CCR7			
Lung	IGF-R2			
	Phospho-ERK1/2			
Bone	Bone Morphogenetic Protein Receptors			
	CXCR4 and RANK			
	BST-2			
Liver	CXCR4			
	TRAIL-R2			
	FAS R			
	HGFR			
Brain	Phospho-STAT-3			
	CX3CR1			
	DSC-2			

*Metastat is a tool that will help practitioners in the prognosis of metastases trends in cancer patients and guide them in the choice of appropriate chemotherapy.*

*\*CTCs: Circulating Tumour Cells*



## *SNPs analysis of cytostatic drugs*

**Pharmacogenomics** is the science that examines the inherited variations in genes that dictate drug response and explores the ways these variations can be used to predict whether a patient will have a good response to a drug, a bad response to a drug, or no response at all.

**Single Nucleotide Polymorphisms (SNPs)** are DNA sequence variations that can affect how human develop diseases or respond to chemicals, drugs and other agents.

**ChemoSNiP** includes the study of SNPs of genes that are included in metabolism/detoxification of cytostatic or targeted drugs which are used as cancer therapy.

Categories	Genes/Drugs
<b>Phase I Drug Metabolism</b>	CYP2D6, CYP2C9, CYP1A2, CYP3A4 etc.
<b>Phase II Drug Metabolism</b>	NAT, GSTP, TPMT etc.
<b>Pharmacodynamics</b>	ABCB1, ABCG2 etc.
<b>Alkylating Agents</b>	Oxaliplatin, Cisplatin, Cyclophosphamide, Melphalan, Busulfan, Dacarbazine etc.
<b>Topo I Inhibitors</b>	Topotecan, Irinotecan etc.
<b>Topo II Inhibitors</b>	Doxorubicin, Epirubicin, Etoposide etc.
<b>Antimetabolites</b>	5-FU, Methotrexate, Gemcitabine,
<b>Spindle Poisons</b>	Docetaxel, Paclitaxel, Vincristine etc.

*The polymorphisms are related with response to drugs, risk of toxicity, clearance, stability and activity of enzymes, reaction velocity, progression of free survival and overall survival.*

***SNPs analysis of cancer therapy and support drugs***

**PharmacoSNiP** is based in the study of SNPs that related with the response or metabolism of broad spectrum of drug which are used in **cancer therapy** and **support**.

*The test includes SNPs related with:*

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Antibiotics
  - Inflammation
  - Thrombosis risk
  - Diabetes risk
  - Osteoporosis risk
- Heart Diseases risk, etc.

*Polymorphisms which are associated with resistance, response, risk for gastrointestinal bleeding, clearance etc.*

Indications of each test can be found at: <http://www.rgcc-genlab.com/?tests>

**Where can I get these tests?**



# R.G.C.C. International GmbH



Research Genetic Cancer Centre

**R.G.C.C. International GmbH** is a leading company in analysis of circulating tumor cells as well as Cancer Stem Cells.

Through their analysis, is able to offer services in clinical field as well as in R&D in pharmaceutical industry.

By using the most advanced and innovative technologies of molecular and cellular biology, **R.G.C.C. International GmbH** manages to overpass several restrictions and difficulties that the analysis of CTCs (Circulating Tumor Cells) and CSCs (Circulating Stem Cells) involves.

Hence, through such an approach a massive amount of information and data has been generated in order to be used for identifying new drugable» targets as well as offering methods in clinical practice like new and precise assays, risk scale and classification of cancer patients.



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**Where can i get these tests?**