Why We Recommend and Use “The R.G.C.C. Cancer Test” 08.29.13

We have been using this test for about 9.5 years. We were the first clinic in the US and Canada to start looking at a better more Personalized Patient-Centered Cancer Care to help those with cancer. This has been in place in Europe for over 10 years. This is not "The Greece Cancer Cure" from Dr. Hariton-Tzannis Alivizatos of Athens, Greece. We do not profess to cure cancer.

Over the last 10 years this test has emerged to be one of the most accurate and complete test of its kind we have seen to date. The test is performed in Greece by Ioannis Papasotiriou, M.D., PhD, medical director of RGCC-Ltd. It was good in the beginning and has consistently improved over the years to a great test, in my opinion and the opinion of many other physicians throughout the world. The use of a simple blood sample with RGCC-Ltd works with ALL cancers (solid tumors, blood cancers, sarcomas, etc.) except brain and central nervous system primary tumors (glioblastomas, astrocytoma, meningioma etc.).

The field of oncology has become highly competitive over the past 2-3 years, due to a beginning paradigm shift, based on long standing lack of good predictable results. Mass General, Sloan Kettering, University of Texas M.D. Anderson Cancer Center in Houston, and Dana-Faber Cancer Institute of Boston have all started using and developing similar test in the last 2 years. They estimated it may start being used in about 5-9 years. At this point, none of these centers or any others we have looked at can do what RGCC-labs of Greece can do from a simple blood test.

We know that cancer has been metastasizing [spreading and with a vengeance] in most all cancers patients for many, many years with little or no change. Up until recently no one knew for sure how or why this happened, just that it happened with great frequency. Now many scientist throughout the world and saying, it is due to the circulating tumor and cancer stem cells (CTC’s/CSC’s). This is rapidly becoming the focus of much cancer research, how to stop these peripheral CTC’s and CSC’s from causing metastatic tumors which is responsible for at least 90% of all cancer related deaths. Furthermore, the CTC’s and CSC’s are suspected by many scientist to be the cause of almost if not all the metastasizes that do occur. With this new information what should be one of the main targets by oncologists? Both the tumor and circulating CTC’s and CSC’s for each individual.

The primary cancer tumor is bad enough, but the CTC’s and CSC’s are the real problem. These cells allow the metastasis and return of this chronic, systemic disease. After 42 years and well into the trillions of dollars spent on cancer research and treatment since the war on cancer was declared in 1971, there has been between 2.1-7.5% increase in the 5 yr. survival rate (see page 5, #1 for source and details). All this time, money, patient suffering and death, in my opinion, is not something one would be proud of, and definitely not a good return on your investment.

The personalized cancer test from RGCC-Labs in Greece is known as an ex vivo test. Ex vivo (Latin: "out of the living") means that which takes place outside an organism. In science, ex vivo refers to experimentations or measurements done in or on tissues (or in this case CTC’s and CSC’s) in an artificial environment outside the organism with the minimum alteration of natural conditions. Ex vivo conditions allow experimentation under more controlled conditions than is possible for in-vivo experiments (in the intact organism), at the expense of altering the "natural" environment. RGCC has developed a way to not change any of the genetics (genotype and phenotype) and more important to not change the epigenetics of the CTC’s and CSC’s. this is very important.

In vivo (Latin: "within the living") is experimentation using a whole, living organism as opposed to a partial or dead organism, or an in vitro ("within the glass", i.e., in a test tube or petri dish) controlled environment. Animal testing and clinical trials are two forms of in vivo research. In vivo testing is often employed over in vitro because it is better suited for observing the overall effects of an experiment on a living subject. In microbiology in vivo is often used to refer to experimentations done in live isolated cells rather than in a whole organism, for example, cultured cells derived from biopsies. In this situation, the more specific term is ex vivo. Once cells are disrupted and individual parts are tested or analyzed, this is known as in vitro.

In microbiology in vivo is often used to refer to experimentations done in live isolated cells rather than in a whole organism, for example, cultured cells derived from biopsies or from the peripheral blood test (the RGCC Test).
In vitro (Latin: “within glass”) refers to studies in experimental biology that are conducted using components of an organism that have been isolated from their usual biological context in order to permit a more detailed or more convenient analysis than can be done with whole organisms. Colloquially, these experiments are commonly referred to as “test tube experiments”.

Why use the blood since only a small number of CTC’s and CSC’s are found in the blood?

It is well known and widely accepted by the scientific community that the primary tumor consists of stroma (fibroblast, monocytes, lymphocytes, vessels, etc.) and the malignant cells which are heterogeneous (not all cells are the same) since they are composed from different subgroups and subclones with different features and abilities. These are known as circulating tumor cells (CTC’s). A portion of these CTC’s are actually cancer stem cells (CSC’s). Only very few of this population will develop metastatic ability which will allow them to invade the surrounding tissue, pass into the circulation and perform the epithelial to mesenchymal transition (EMT) creating the CSC’s. These cells now have all the information and ability to form micro colonization and micrometastases and often will later develop into potent micrometastases. This is why cancer returns. This is also why we see these CSC’s still in the blood long (I know for certain a minimum of 34 years) after the patients primary tumor is not detectable by PET/CT, MRI, CT, standard blood markers (CA 125, CA 19-9 etc.) or any other standard traditional measurements. As we have said many times before, the CSC’s are the real trouble makers. Remember these CSC’s are immortal (they have no Hayflick limit for cell division) and can divide as long as they live. They are circulating in your blood stream 24/7/365 days a year just waiting for the right opportunity (when your internal micro-environment is not “up to par”) to start another tumor or they may go dormant for up to 30+ years only to raise their ugly heads again. For this reason RGCC has selected blood samples as the most appropriate form for analysis since it includes the circulating cancer cells with the most relevant information for calculating the risk for both a potent metastasis and/or a reoccurrence from a few months to many years later. This is why we feel this is the best way to test, since metastasis is really what will kill most every cancer patient even 30+ years later. That is also why we use this test for regular follow-up testing to see if CTC’s/CSC’s remain, how many and any sudden changes in the number of CTC’s/CSC’s that may occur in the circulation over the months or years. This gives us a good idea, with other standard medical measurements, to find reoccurrences (if any) much earlier. We do not limit our test to any one test. The standard medical test and biopsies are still recommended and used as well. This gives us the best and most comprehensive way to evaluate the patient individually.

How does RGCC assure the purity of the CTC’s harvested from your blood?

RGCC-Ltd uses powerful sorters and flow cytometers as well as negative selection based interrogation. They are able to actually isolate the relevant CTC’s/CSC’s and not enrich them (not change your cancer cells in any way). Hence, they manage to have a pure sample of CTC’s/CSC’s and simultaneously harvest from a single blood sample.

How do we analyze the harvested cells and use them to show risk of cancer relapse in clinical reality?

This is done by appropriate expansion of the CTC’s. The CTC’s will expand as the cancer stem cell like cell and then enter into exponential phase of growth which will generate a respectful number of CSC’s in a very short period of time. At the same time we manage to keep intact both the genotype and phenotype of the cells and avoid any changes to the primary CSC’s. Therefore, after the final expansion we have maintained the identical genotype. The key to this exponential (rapid) growth phase is the cell culture. Dr. Papasotiriou has an international [world] patent on this cell culture which does not change the genetics or epigenetics of the original CTC’s/CSC’s as shown by his patent. This is what allows RGCC-Ltd to verify the actual agents as well as the genetics. Most other labs only show results on the genetics of the tumor and what they should be sensitive to. A respectable percentage of the time they do not actually respond. Plus, RGCC results give us an actual percentage of response or resistance.

How does RGCC analyze the gene expression profile for the sensitivity/resistivity of the CSC’s?

The expanded cells will be analyzed for one expression profile in a hall genome micro-array analysis. Hence, we now have all the information concerning epigenetic screening of the CTC’s/CSC’s. This profile will indicate to us which therapy (chemo therapeutics as well as nutritional therapeutics) your CTC’s/CSC’s are sensitive or resistant to and is Personalized for each patient. We have tested 600+ patients with a wide variety of cancers and have never had the same protocol on any 2, even if the cancers were the same. The difference between protocols are 30-60% different even in siblings with the same cancer.
How does RGCC verify that these chemosensitivity/chemoresistance results are really valid?

The information obtained from the gene expression analysis will be validated in a micro culture where the effect of each substance (chemo drugs) will be tested for 6 (six) days and plotting a graph of the total number of your cells that were killed, while maintaining proper osmolality of the cell culture. The natural substances are tested by leaving the herb, vitamin, etc... in contact with your cancer cells for 48 hours, because it takes this long for the natural compound to activate the caspase 3/9 and cytochrome-c pathway to induce apoptosis (cell death) of your cancer cells. These assays overcome the problem of linearity between gene expression and protein expression levels. The RGCC lab does not rely on the genetic assay only, as most other labs do, they actually test each individual chemo and natural substance to see if it really works and how well it works. No one else in the world has this capability. In my opinion, RGCC does this without changing the genetics or epigenetic expression of your cancer cells. This is remarkable and what no one, I know of, can do at this time.

**What All Is Tested with the TU-Profile Plus Test?**

The absolute beauty of this test is the ability to test what your cancer responds to without having any idea of where the primary tumor is located or even the type cancer it is. The lab will test 52 common chemo drugs and 49 natural substances and are not limited because of location or the type cancer which most other labs are limited to the approved drug list.

RGCC, Ltd. will test 49 natural substances covering cytotoxic agents; immunostimulants/immunomodulators, cytokines; and increase of PBMC & NK, growth factor inhibitors of EGFr, IGFr, VEGFr, PDGFr, FGFr, and signal transduction pathways. The results shows in %, the effectiveness of each individual agent to induce apoptosis (cell death) of your cancer cells, i.e. ex-vivo. The test also includes 52 chemotherapeutic agents. These include 21 alkylating agents, 1 epothilone, 3 inhibitors topoisomerase 1, 9 inhibitors topoisomerase 2, 5 nucleus spindle stabilizer 1, 3 nucleus spindle stabilizer 2, and 10 nucleoside analogues. You will also receive 4 resistance factors (MDR1, MRP, LRP, GST). The results shows, in %, the effectiveness of each individual agent tested. In other words which chemotherapy works best for your cancer cells.

You also receive results on 62 tumor related genes (this is very important): 22 genes related to growth factors and proliferation stimuli; 11 genes related to self repair and stimuli; 5 genes for angiogenesis; 6 genes for cell cycle regulation and immortalization/apoptosis; 4 genes covering angiogenesis-metastasis; 11 genes concerned with drug metabolism and targets; and 2 markers. You receive these results in % of over or under control, very exact. This will give your health care provider more detailed information about your cancer and their ability to grow and metastasize faster, their ability to resist certain drugs, the tendency to become immortal and much more. This is the true beauty of detailed Personalized Patient-Centered Cancer Care. I know of no other testing like it in the world.

**How Do We Use All This To Personalize Support For Those With Cancer?**

Our first goal is to decrease the tumor burden and the CTC’s/CSC’s. This severely stresses your immune system everyday all day. There are several ways of doing this. First, surgery early on will work 50% of the time for the primary tumor (not necessarily the CTC’s/CSC’s). Second, is chemo therapy which can be used in conjunction with surgery. Third is radiation and this can be used in combination with any of the previous. However, this is up to your oncologist to decide. In regard to the natural substances, our goal is to help support the immune system, help improve lifestyle, and support the physiological and biochemical processes of the human body by offering the integration of various nutritional support systems. This is also done using the test results to develop a personalized program for each individual patient. Generally we will re-test (onco-count or onco-trail, not the entire test as in the beginning) every 3-4 months to measure the actual circulating tumor and/or stem cell like cell numbers. We also recommend you follow your oncologist schedule of ongoing PET/CT, MRI etc. testing. Since cancer is a systemic, chronic disease our goal is to help you live a quality and productive life, for as long as you should, and then leave this earth with the cancer NOT from the cancer.

I have included a number of quotes and publications below that may be helpful for you to in making a truly informed decision of which lab you want testing your circulating cancer tumor and stem cells to see which chemotherapeutics and natural substances can cause the decrease of your tumor burden. While keeping in mind, the circulating CTC’s/CSC’s are the real ongoing, long term trouble makers for over 90% of cancer patients. May you be blessed in all you do.

If you have any questions please let us know so we can clear up any concerns, also visit our website.

We offer referrals for health care providers throughout the United States, Canada, and North Central America

*This test will NOT DETECT cancers of the brain or other cancers that have been “encapsulated” by the body, not releasing circulating tumor or stem cells (CTC, CSC) into the blood stream or if any of these cells are dormant. We still recommend the use of biopsy, blood markers and/or various scans with this test when cancer is suspected or known to exist. No test is 100% accurate.

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MEMBER OF TEXAS HEALTH CARE ENTITIES (A PRIVATE MEMBERSHIP MEDICAL ASSOCIATION)
EXCITING NEWS FOR RGCC, Ltd OF GREECE 04.23.12

We are in the pleasant position to announce that we have passed the assessment and validation from the National Organism of Accreditation and they have accredited our lab with the ISO 17025:2008 for the following methods:

1. CTC/CSC isolation and immunophenotyping
2. Cancer cell culture viability/cytotoxicity assays after exposure to substances
3. Gene expression assays (mainly related with cancer stemness)

I hope that this will help our physicians their patients and other clients understand our level of commitment to quality and remove any doubts that may have existed concerning the validity of the assays since this accreditation includes inter-laboratory validation (performance of the assays from different labs which we have no interest or relation).

We will utilize such tools as often as needed to promote the quality and sincerity of our work.

ISO 17025 identifies the high technical competence and management system requirements that guarantee your test results and calibrations are consistently accurate.

This accreditation is recognized and accepted throughout the international scientific and laboratory communities as the standard of excellence.
For adjuvant chemotherapy (chemotherapy given in addition usually to surgery and/or radiation) the success for 5 yr. survival rate for the 5 major types of malignancy (breast, colon, lung, prostate, skin) varies from 2.1% to 2.3%.

Royal North Shore Hospital Clin Oncol (R Coll Radiol) 2005 jun;17 (4):294

For the curative stage of disease the success rate varies between 5-7.5% for the same 5 types of malignancies.

The overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was estimated to be 2.3% in Australia and 2.1% in the USA.


The next 3 quotes come from the above book:

"Evidence for the existence of biologically distinct CSC's, first demonstrated in a hematological malignancy and in the past 5 years in several solid tumors, has shaped a new paradigm of human cancer as a hierarchical disease whose growth is sustained by a population of CSC's. This conceptual shift has important implications not only for researchers seeking to understand mechanisms of tumor initiation and progression, but also for the development and evaluation of effective anticancer therapies".

"Thus, research must be directed at the relevant cell populations as identified through functional assays, the ultimate goal being the rational development of therapies that interfere with the oncogenic program within the CSC’s."

"In contrast, the CSC model postulates that with an appropriate purification strategy, the CSC’s with the capacity to initiate and sustain tumor growth in vivo can be identified and isolated from the bulk cells that do not have tumor-initiating activity.”

"Here we show that a small population of cancer stem cells is critical for metastatic colonization, that is, the initial expansion of cancer cells at the secondary site, and that stromal niche signals are crucial to this expansion process”.


"Cancer lethality is mainly due to the onset of distant metastases and refractoriness to chemotherapy. Growing evidence indicates that a cellular subpopulation with stem cell-like features, commonly referred to as cancer stem cells (CSC’s), is critical for tumor generation and maintenance”.


...most primary solid tumors probably go through a prolonged state of avascular, and apparently dormant, growth in which the maximum size attainable is ~1–2 mm in diameter. Up to this size, tumor cells can obtain the necessary oxygen and nutrient supplies they require for growth and survival by simple passive diffusion; (ii) these microscopic tumor masses can, in some way, eventually switch on angiogenesis by recruiting surrounding mature host blood vessels to begin sprouting new blood vessel capillaries which grow toward, and eventually infiltrate the tumor mass, thus setting in motion the potential for relentless expansion of the tumor mass and hematogenous metastatic spread as well...


"All truth passes through three stages:
First: it is ridiculed
Second: it is violently opposed
Third: it is accepted as being self-evident”

Schopenhauer
“When health is absent, wisdom cannot reveal itself, art cannot manifest, strength cannot fight, wealth becomes useless and joy cannot be felt.” **Herophilus**

“The doctor cannot overcome what the patient will not do.” **Unknown** *This is the reason for Patient-Centered Cancer Care*

"Discovery consists of seeing what everyone has seen and thinking what nobody else has thought."

Albert Szent-Gyorgyi

Stress is definitely just a decrease of happiness, joy, peace, and calmness, always things are decreased as a result of stress. There is virtually nothing that stress does not effect on a physiological level in every person. Remember it is the “fight or flight” that keeps you alive on one hand and can even kill you on the other hand, with many negatives between these 2 extremes.

“**Ignaz Philipp Semmelweis** (July 1, 1818 – August 13, 1865) (born Ignác Fülöp Semmelweis) was a Hungarian physician of German extraction now known as an early pioneer of antiseptic procedures. Despite various publications of results where hand-washing reduced mortality to below 1%, Semmelweis’s observations conflicted with the established scientific and medical opinions of the time and his ideas were rejected by the medical community. Some doctors were offended at the suggestion that they should wash their hands and Semmelweis could offer no acceptable scientific explanation for his findings. Semmelweis’s practice earned widespread acceptance only years after his death...”

**Epigenetics:** Epigenetics has also played roles in evolution and has served as a molecular driver of mutations. Moreover, the changing environment is currently reshaping the evolution of many organisms through plastic epigenetic processes. Epidemiological factors such as diet, environmental exposure, microbial infections and drugs are also influencing our daily lives through epigenetics.


The dumbest stomach is much smarter than the smartest doctor. Professor in school. *The wisdom of the body!*

Max Wicha, M.D.
Distinguished Professor of Oncology
Director, University of Michigan
Comprehensive Cancer Center

“The problem is, when we treat cancer cells with chemotherapy, the cancer stem cells are being stimulated to grow too.”

“When we take mesenchymal stem cells and mix them with tumor cells, the tumors grow much more quickly in animals.” Dr. Wicha’s lab has found that inflammatory molecules secreted by *dying tumor cells can hook up with the stem cells* and cause them in effect to come out of hibernation.

- Adult stem cells exist in most tissues, and go into action to repair damage from wounds or infections.
- In cancer, they can mutate and no longer obey normal bodily signals to stop growing, Dr. Wicha said.
- He and other researchers say that even when *chemotherapy and radiation cause tumors to shrink dramatically, these stem cells can stay alive*, living under the radar until they are once again spurred into action.
- They also believe *stem cells are probably the ones that break away from an original tumor* and cause cancer to spread elsewhere in the body.
- Chemo and radiation kill off the fastest-growing cells in the body, which applies to most cancer cells, but the cancer stem cells that create those rapidly dividing tumor cells actually grow much more slowly themselves, and are less susceptible to those therapies, he said.
- One tactic to address this problem is to kill off both types of cancer cells at once, Dr. Wicha said.
A recent experimental trial with advanced breast cancer patients at the University of Michigan, Baylor University in Texas and the Dana-Farber Cancer Institute at Harvard University used standard chemotherapy along with a substance designed to block one of the biochemical pathways of stem cells.

The approach killed off more than 90 percent of the cancer stem cells, Dr. Wicha said, and researchers now hope to expand the treatment to a much larger group of patients.

Ultimately, he hopes cancer treatments can avoid general chemo altogether, with its debilitating side effects, and just use targeted therapies against the stem cells.

There is still a long road ahead, he said, and “my feeling is, to really knock these stem cells out, we’re probably going to have to use multiple inhibitors.”


NOW read the Public “retraction”....

“Cancer patients, follow recommended care!

An article published by the Post-Gazette claimed that our research suggests cancer treatments "not only often fail to eradicate cancer, but can make it worse" This statement has been misinterpreted by patients currently receiving radiation or chemotherapy treatments. I have been contacted by both my own patients and Pittsburgh-area patients who have questioned whether they should continue with their chemotherapy. In fact, these treatments are lifesaving for many patients.

Our work does suggest that the resistance of a small population of tumor cells to these treatments may account for some of their limitations. Based on this, we are working to develop new approaches to target this specific cell population — treatments that could augment chemotherapy and radiation therapy. New treatments based on this theory are in their early testing stages. Only through the conduct of rigorous clinical trials will we be able to determine whether addition of these new therapies improves the outcome for patients with cancer.

In the meantime, patients diagnosed with cancer need to follow their doctors' recommendations for treatment according to the current standards of care and inquire whether they are eligible for a clinical trial.

MAX WICHA, M.D.
Distinguished Professor of Oncology
Director, University of Michigan Comprehensive Cancer Center Ann Arbor, Mich.

Dr Bruce Zetter Professor of Cancer Biology in the Department of Surgery, Boston Children’s Hospital

"As many as 90% of all cancer deaths can be attributed to metastatic disease. Cells from the primary tumor, after travel to regional or distant sites, cause failure of essential organs including the lungs, liver, brain and bone marrow. Significant advances in the field make this an exciting time for the study of metastasis. Genetic signatures in primary tumors as well as circulating tumor cells and oligonucleotide or protein biomarkers hold the promise of predicting cancer outcomes and allowing selection of optimal drug candidates. The isolation of circulating tumor cells has further improved our ability to analyze the tumor genotype. The ability to metastasize is influenced by the invasive potential of cells in the primary tumor and particularly by self-renewing tumor cells that have properties of cancer stem cells".