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RGCC: A Leading Company in Analysis of CSCs as Progenitors of All Cancer Relapses

RGCC Ltd is a leading company in analysis of circulating tumour cells (CTCs) as well as cancer stem cells (CSCs). Through their analysis, RGCC Ltd is able to offer services in the clinical field as well as in R&D in the pharmaceutical industry. By using the most advanced and innovative technologies of molecular and cellular biology, RGCC Ltd manages to overpass several restrictions and difficulties that the analysis of CTCs and CSCs involves. Through such an approach a massive amount of information and data has been generated in order to be used for identifying new «druggable» targets as well as offering methods in clinical practice like new and precise assays, risk scale and classification of cancer patients.

By answering the question: “Which is the best pool of data harvested from tumours”, RGCC Ltd was able to develop a target technology in order to generate the best options and pure data which will reflect clinical reality, and at the same time these data will include most of the relevant information about the risk of relapse and repeatable patterns of gene expression. Specifically, it is well known that in a primary tumour there are two major classes of cells. The first one is the stroma, which includes normal cells like endothelial cells, monocytes, fibroblast etc., and they support the existence and feeding of the tumour. The second group of cells includes the malignant cells. However, this last group of cells is NOT homogenous. It is composed of several subpopulations with different genotypes and phenotypes, with different behaviour and abilities due to the genetic instability of cancer cells. Only very few subpopulations of those cells have metastatic features which they can enter from an epithelial to mesenchymal transition (EMT). These cells will invade and enter into the circulation and they will become circulating tumor cells (CTCs). These cells include the progenitor of

every micro-metastasis. These cells are known as cancer stem cells (CSCs). Hence, CTCs and CSCs have all the necessary information for colonisation and engraftment to distant organs as micro-metastases, causing relapse of the disease.

RGCC Ltd has developed an innovative method in order to identify, isolate and sort these cells from the most appropriate sample (mainly blood). By using flow cytometric methods as well as powerful sorters it is possible to identify, enumerate and isolate the CTCs and CSCs.

But even from CTCs, only those who have CSC phenotypes have the ability to engraft and generate distant micro-metastases. Hence, by using negative and positive selection, RGCC Ltd has developed assays in order to identify and isolate CTCs. Sequential to that, an additional innovative method has been generated in order to expand the CSC from the CTCs. The risk of changing the genotype of the cultivated cells has been minimised by using the appropriate media and by performing this method for a short time window.

These cells are expanded and they enter into an exponential phase of growth. Then the cells are analysed in an all-genome gene expression profile in order to:

- Analyse the up and down regulation of genes;
- Identify stable patterns of aberrant expressed genes which may become «druggable» targets.

These «druggable» targets are validated by RGCC Ltd through knock-down methods like antisense or RNAi. Additionally, more protein-based methods have been used in order to down-regulate the expression level of protein.

The kind of genes that RGCC Ltd is interested in are related to the cell

cycle, metastases, neoangiogenesis, apoptosis etc.

Parallel to that, RGCC Ltd has developed several viability and cytotoxicity assays in order to assess and validate a candidate drug against cancer cell lines. By that method the candidate drug is validated in order to proceed further in trials and gain a license for daily clinical use.

RGCC Ltd has generated several human cancer cell lines and also CSC cell lines in order to generate a huge cell line bank that can be used for identifying patterns, as well as for using the different cell lines for viability assays, in order to establish whether a candidate drug is effective.

Finally, RGCC Ltd has developed a repeatable and comparative analysis in order to compare the expression profile on time. Specifically, a comparison analysis between samples from the same patient provides us with an advantage in preventing relapse.

In a few words, RGCC Ltd, as a clinical company and a CRO, has generated new assays and methods in order to help clinicians to deal easily with difficult cases. The methods that RGCC includes and performs in its facilities are:

- PCRs (endpoint, gradient and qPCR)
- Flow cytometry-sorting
- Micro-array gene expression analysis
- Cell culturing
- Blotting
- Viability-cytotoxicity assays (MTT, CVE, SRB, etc)
- Spectroscopy
- Microscopy

All these issues make RGCC Ltd a leading CRO, as well as a company providing clinical services. The expertise of this company is expanding, with branches and distributors in Europe, Asia, Africa, and the USA, as well as in Oceania. Additionally, RGCC Ltd has

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developed strong cooperation and collaboration with local and foreign universities and companies in order to participate in larger projects and R&D programmes.

RGCC Ltd is a company you can choose as a CRO in order to validate «druggable» targets, to assess candidate drugs, or to perform high-throughput screening of a substance when it is exposed to cell lines in order to verify the possible effect.

For all these reasons RGCC Ltd has become the most effective CRO in order to generate data and validate candidate drugs in the field of oncology ■

Ioannis Papatiriou

I was born in Germany in 1973 and after years I return in childhood in Greece where I studied in Medical school of Thessaloniki and I specialized in Human Genetics in Switzerland. Two master degree rewards have been obtained in molecular biology in Medicine from the Westminster University (UK) and in oncology from the University of Nottingham (UK). A promotion have been performed (MD) in MLU in Germany under the field of evaluation of TKIs in human cancer cell lines. Since 2004 I am the director and founder of RGCC Ltd which is activated in both areas of services (Research and Clinical).

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