Details of the Project sanctioned under the Human Resource Development scheme of Department of Health Research

1. **Project Title:** Screening for a universal "invasive" molecular signature of metastatic tumorigenic stem cells in breast cancer.
2. **Category of fellowship:** DHR Women Scientist- Category A (non-medical)
3. **PI (Name & Address):** Dr. Vinitha Richard, Rajiv Gandhi Centre for Biotechnology, Bio-Innovation Campus (RGCB-BIC), Kinfra Film and Video Park, Near Sainik School, Kazhakuttam, Thiruvananthapuram - 695585.
4. **Qualifications:** PhD Biotechnology
5. **Mentor or Co.PI (Name & Address):** Dr. T. R. Santhosh Kumar, Ph.D., Scientist E-II, Cancer Research Program, Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram.
6. **Duration of the project:** 3 years
7. **Broad area of Research:** Genomics

   7.1 Sub Area: Tumor stem cell biology
8. **Summary of the Project:** (Give in about 300 words)

   Cancer is a disease affecting multiple tissue types portraying common pathological stages despite different tissue specific gene mutations. Since the disease condition progresses from the reversible pre-malignant stage to the malignant metastatic stage, the crucial turning point in the life cycle of a tumor cell is its transition to a tumor- promoting stem-like cell which still eludes our current understanding. Even though several experiments have identified stages preceding this transition and rationalized it to expression of specific transcription factors such as snail, slug, twist etc, we are insistently in pursuit of additional factors that decide which cancer cell amidst the pool of similar genetically altered cells is the disease-purveyor destined to be the successor. Albeit there are multiple subtypes, the pathobiology is the same for all types of breast cancer. So a successful identification of a common molecular imprint hallmarking the threshold of invasiveness across all BrCa subtypes might turn out to be an ideal target documented so far. The aim of this project is to characterize the Indian population of breast cancer patients irrespective of varying aspects of cell proliferation, various biochemical pathways and thereby define tumor-initiation potential in terms of cellular and molecular regulatory networks that reveal the point of transit to a malignant stem-like cell.
9. **Objectives of the Proposal:**

   • To accomplish a meticulous molecular and functional definition of metastatic stem cell-like subpopulations across different subtypes of breast epithelial tumors.

- To pursue a detailed study of the regulatory networks involved in the homeostasis of metastatic breast cancer stem cells (BrCa-CSCs) isolated from different breast tumor subtypes and correlate with tumorigenic and drug resistance potentials.
- Screen for a universal molecular signature (mRNA) regulating the transient shift of non-invasive to invasive BrCa-stem-like cells in all BrCa subtypes and validate the crucial molecular events determining the malignant transformation to an invasive and migratory cell type.
- Evaluate the role of cell cycle stage in acquired tumorigenicity and initiation of metastasis?

10. Innovations in the project: (Give in about 100 words)

Cancer stem cells (CSCs) have been identified in certain subtypes of breast cancer based on expression of stemness associated cell surface markers. Whole genome analyses of these CSCs have also been undertaken by many laboratories. Ironically the identification of this small fraction fails to explain the imminent stages of metastasis and recurrence of breast cancer across the aggressive subtypes. This is one of a kind study wherein we intend to overlook the difference in subtypes and achieve an universal molecular signature to denote the CSCs with the highest metastatic potential in all subtypes of breast cancer.

11. Significance of the outcome of the project: (Give in about 150 words)

This is a different approach wherein the entire genomic signature from just those breast cancer stem cells of the patient's tumor that can regenerate the cancer and cause metastatic spread will be analysed. Any contributions in this aspect would improve our early understanding of the processes of intercellular communication between tumor stem cells and the microenvironment and how the disease spreads. This research has the potential to lead to improved diagnostic tools, identify novel targets and also facilitate the development of innovative cancer therapies that prevent tumor manipulation of immune surveillance mechanism and recruitment of immune cells, as a result, impair a cancer's ability to metastasize.

12. Relevance in Public Health:

Elucidation of a common gene signature for all metastatic breast cancer stem cells, would pave way for a more targeted treatment regimen that could eliminate toxic side effects with the desired anti-tumor activity across all breast cancer subtypes irrespective of presence or absence of hormone receptor proteins.

Vinitha R 1/4/16

Signature of the Fellow /Faculty