

My long-term goal is to initiate a change in the way breast cancer metastasis is viewed and treated today. I envision changing its current state from palliative to curative, where clinicians are encouraged to opt for the latter. This will be possible only if the research arm of metastasis grows stronger where innovative approaches are not limited to primary tumor treatments but also for tested for widely metastatic cancers.

As an independent investigator studying cancer metastasis, my research goal is to understand the unique biology behind metastatic cancers in order to improve the clinical management of the disease and to enhance the quality of life in cancer patients. To achieve this goal, I have joined the Institute For Cancer Genetics at Columbia University investigating basic mechanisms of cancer metastasis and collaborating with our clinical colleagues at the Breast Oncology program at the Herbert Irving Comprehensive Cancer Center at Columbia University. Our recent work in the area of breast cancer metastasis (Acharyya et al., Cell, 2012) has shed new insights and revealed the interplay of metastatic cancer cells with granulocytic immune cells, cells of innate immune system in our body. From our preliminary data, we find that the function of the granulocytic cells changes from tumor-killing to tumor-promoting with metastatic progression. We would like to devise strategies to reprogram the cytotoxic ability of these immune cells to kill metastatic cancer cells, much like the neutrophils that rapidly sense pathogens, are recruited to the infection site and eradicate the attacking pathogens. We need to utilize the natural innate immune system of our body such as granulocytes that sense cancer cells and are mobilized to the tumor milieu. We propose to *capitalize on three features of granulocytic cells* enormous expansion capability over 20-fold in cancer, rapid ability to sense, respond and migrate to metastatic sites and low chances of adaptation and evolving resistance in tumors. As body's natural host defense against pathogens, granulocytic cells possess an arsenal of cytotoxic agents ranging from proteolytic enzymes to superoxides. We need to this cytotoxic strategy of these granulocytic cells to kill metastatic cancer cells. We have proposed a comprehensive strategy involving addressing basic biological questions, preclinical trials with adoptive transfer of granulocytic cells in combination with frontline therapeutic approaches and clinical validation integrating with ongoing clinical trials at Columbia University towards our goal. Such findings will be critical for devising strategies to improve the clinical management of metastatic breast cancer in the long run.