A. Personal Statement (including developmental objectives and plans)

I began my career by starting my PhD at the Imperial Cancer Research Fund in London, UK, which has since evolved into Cancer UK. I chose to study the process by which tumors spread, or metastasis, that had fascinated me as an undergraduate, and I began my research career by seeking for new genes whose expression changes as tumors become more metastatic. After my PhD, I trained as a post-doc in Toronto, Canada, on aspects of metastasis, therapies for metastatic disease, and tumor resistance to therapy. I now plan to set up a research program that is internationally recognized for pioneering new ideas, and for generating models to help translate laboratory findings into the clinic - by developing new metastatic tumor models, and by refining those I have already established. I have developed the first model of spontaneously metastatic Her-2 positive breast cancer that can be monitored as mice bearing the disease are treated with clinically relevant anti-Her-2 strategies (Francia et al MCT 2008, and CCR 2009). The impact of this work has subsequently led to three editorials (Francia et al Cancer Cell 2009, Nat Rev Cancer 2011, and Francia and Kerbel Nat. Biotech 2010) where I put forward the hypothesis that testing laboratory models of metastatic disease is essential to identify mechanisms by which tumors respond to current therapies in the clinic, and by which they develop resistance to current treatments. I now want to test my hypothesis by developing two new models of human breast cancer that endogenously over-express Her-2. One such model, termed BT474V3, I have now selected for spontaneous metastatic capacity in immunodeficient mice.

The research I propose to carry out is central to the further development of my academic career. The generation of new preclinical models of spontaneously metastatic breast cancer will allow me to establish collaborations (as has been the case with the models I have thus far generated), with basic researchers, translational cancer researchers (i.e. surgeons, oncologists and pathologists), as well as with industry – namely those companies interested in the use of advanced disease models to test investigational new drugs. Thus, for example, current collaborations include those with researchers interested in tumor imaging, in the use of ultrasound to facilitate the delivery of tumor targeting drugs to metastatic deposits in the brain, and in the in vivo evaluation of a new small molecule inhibitor of Her-2 for the treatment of Her-2 positive breast cancer. These scientific interactions will be important to establish my credentials, and my reputation, as an established investigator in the field of experimental therapeutics for metastatic breast cancer.

The new Her-2 positive models will also produce a number of publications in peer-reviewed journals, as well as opportunities to present the work at scientific meetings, in which my lab will describe the development of the models, or their application to identify new therapeutic concepts, or their use to uncover mechanisms by which tumors develop resistance to current therapies. The collaborations initiated, the scientific presentations
at meetings, and the manuscript published, will altogether form an important part of my successful application for tenure at UTEP. They will also be critical in allowing me to seek additional funding; that will ensure that I can place my program at the forefront of our research to understand how metastases emerge and develop, and to the identification of new therapies for metastatic breast cancer.

This SC1 proposal builds on exciting recent results and proposes to develop additional models of Her-2 breast cancer to include tumors from the Hispanic population (which is not represented in the available panel of Her-2 positive breast cancer cell lines). We will use the new models, together with those already developed, to both optimize chemotherapy regimens and Her-2 targeting strategies, since current clinical protocols combine chemotherapy with anti-Her-2 drugs to treat metastatic disease. I have the necessary expertise to complete the work proposed. In addition, to assist me I have sought the collaboration of Dr. Mark Uhlik of Eli Lilly and Company, who will continue to make available a new oral gemcitabine. This drug has produced promising anti-tumor responses in my ongoing experiments, and it is currently being evaluated in clinical trials. With regards to publications, I plan to submit a manuscript on the two new Her-2 models I have derived by the beginning of year 2 of the proposal. The development of cell lines from fresh patient tumors from the El Paso region will be published in year 3 of this proposal, and 2 more peer reviewed publications will be submitted by year 4. Those will deal with the response of the new models to Her-2 targeting therapy, the mechanisms by which the models can become drug resistant, and on new protocols that should be evaluated in clinical trials for the treatment of Her-2 positive breast cancer. The data gathered will be used to submit for an NIH R01 grant by year 4 of this proposal.

B. Positions, Honors

Positions and Employment

1998-2011  Post-doctoral Fellow, Sunnybrook Research Institute, University of Toronto, Canada.
Jan 2012- Tenure-Track Assistant Professor, Department of Biological Sciences, University of Texas at El Paso, El Paso, TX

Other Experience and Professional Memberships

2003-present  Associate Member, American Association for Cancer Research

Honors:

1994-1998  Imperial Cancer Research Fund (ICRF) Studentship
1998-2001  Sunnybrook Health Sciences Centre Post-Doctoral Fellowship, Canada.
2012  2012 ASCB MAC Junior Faculty and Postdoctoral Fellows Career Development Workshop Travel Award
2012  NIH Early Career Reviewer, Tumor Progression and Metastasis study section

C. Selected Peer-reviewed Publications

Most relevant to the current application


### Additional publications of importance to the fields of metastasis and cancer therapeutics


### Additional selected peer-reviewed publications (Selected from 31 peer-reviewed research papers, in chronological order)


### D. Research Support

#### Other Support

**UTEP Startup funding (Total = $ 256,000)**

Francia (PI) 1/1/12 – 1/1/14

Development of new preclinical metastasis models to study cancer therapeutics

The goal of this project is to develop new models of metastatic human cancer in mice, and to use those models
Program Director/Principal Investigator (Last, First, Middle): Kirken, Robert A.

to identify new anti-cancer treatments.