

ADVOCACY INVOLVEMENT

A. Advocacy Organization/Advocate(s) Selection and Engagement to Date.

This project will investigate if exposure to compounds used as pesticides can promote breast cancer development and render spontaneously emerging breast cancer lesions more aggressive. With this goal, the proposed research is of high interest for everyone who might develop breast cancer, has had breast cancer or experiences breast cancer progression with metastasis. To ensure that the study design is directly relevant to the 'real-life' situation that we are trying to address, and in case our results indicate a need for public awareness and possibly a push for enhancement of consumer protection, we are closely collaborating with our advocate advisors CJ (Dian) Corneliusen-James, coFounder, and Lori Marx-Rubiner, National Lead of the Ambassador Program of METAvivor.

METAvivor is a non-profit organization dedicated to increasing awareness of metastatic breast cancer and equity in research and patient support. The founders and many members of METAvivor have experienced metastatic disease from breast cancer. While METAvivor as an organization focuses on significantly extending the lives of the already metastasized patient and ultimately finding the treatments that will permanently render their disease a permanently controlled, chronic condition; its members are also very aware of the importance of determining what causes breast cancer to metastasize. Indeed, many members of METAvivor have daughters and sons at risk for metastasis; they want nothing more than to prevent this potentiality.

While preparing this project plan, I connected with CJ, my friend and advisor of many years, to help me identify the most critical issues relevant for someone who has had metastatic breast cancer and very actively works with women who are going through this experience. CJ has the great gift of pin-pointing which aspects of research are important for the overall goal of reducing the mortality to breast cancer. Since 2008, when we first met, CJ has given me important directions and challenged my views of how to focus mechanistic studies. For this project, she connected me with Lori, because Lori lives close to us and will be able to interact and support us personally during the course of the project. Lori is a 10-year breast cancer survivor with metastases and a very strong interest in supporting research dedicated to finding causes of metastatic disease and ways of interfering with and preventing this process. She has been super helpful during the preparation of this project and pointed out the importance of distinct levels of exposure to pesticides that need to be considered.

B. Advocate(s) Role in Proposed Research.

CJ and Lori will work actively with us to maintain a discussion on the clinical relevance of the experiments and to digest the results together. If the planned study indeed finds a cause-and-effect relationship between exposure to pesticides and breast cancer development or progression, a serious discussion will ensue that can have wide ranging ramifications for the use of such compounds. Such results will spur further detailed analyses at the epidemiological level but also at the biochemistry, cell biology and pathology levels to interrogate risk association between exposure to pesticides and breast cancer development and progression in conjunction with genetic predisposition to breast cancer and sporadic breast cancer development. CJ and Lori will work to disseminate the results and help to spur a discussion toward protecting consumers from pesticide exposure as well as invite searches for alternative means to ensure crop protection and agricultural and economical needs.

C. Meeting and Payment Plans.

I will organize and participate in quarterly meetings with Lori and keep up regular e-mail and phone communications with Lori and CJ throughout the study. In most cases, we will try to arrange for Lori to visit our lab for our face-to-face meetings, but I will also travel to Los Angeles to meet with her in cases where that is more convenient for her. I will solicit input from Lori and CJ during the planning and execution phases of the study and make adjustments according to their recommendations. We will very actively work together throughout the project, and I will particularly seek their advice and rely on their unique ability to disseminate results within the advocacy community and the public, once the results have passed the rigor of peer review.

From the grant budget, I will compensate Lori and reimburse her for her expenses associated with travels to my lab, as well as for her attendance of the CBCRP Symposium. I am planning on going to that meeting as well because it will give us an excellent opportunity to assess our team efforts in the context of the CBCRP program, as well as reach out together to colleagues to share our results and get input and support from the greater breast cancer research and advocacy communities.

Letter of Commitment

Advocate(s)

Lori Marx-Rubinar & CJ (Dian) Corneliusen-James
METAvivor
Los Angeles, CA & Annapolis, MD

Principle Investigator

Brunie Felding
The Scripps Research Institute
La Jolla, CA

We are writing this letter in support of Brunie Felding's grant application titled: "Pesticides in breast cancer development and progression". *This project aims to investigate if exposure to compounds used as pesticides can promote breast cancer development and render spontaneously emerging breast cancer lesions more aggressive.* The study will analyze the impact of pesticides on mitochondria of breast epithelial cells and breast cancer cells and analyze if damaged mitochondrial functions synergize with genetic alterations to cause breast cancer and breast cancer progression to metastatic disease.

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I, CJ (Dian) Corneliusen-James, first met Brunie at a Special Conference of the Metastatic Research Society in 2008. We have maintained a friendship and discussion of directions and new findings in metastasis research ever since. I have been privileged to be able to visit Brunie's group at Scripps multiple times, had a chance to get updated on new research in her group and have discussed with her findings in the field to evaluate progress toward effective treatments of breast cancer metastasis. My interest is not only as co-founder of *METAvivor* but also as a metastatic breast cancer patient myself. I cannot speak highly enough of Brunie's longstanding dedication to research for my disease.

Brunie also visited the *METAvivor* team and local membership in Annapolis, Maryland in 2011 and shared with us her recent research results on how alterations in breast cancer cell metabolism, and particularly aberrations in mitochondrial functions can determine the aggressiveness of the tumor cells and be an underlying cause of metastatic progression.

For the currently planned project, I facilitated a connection between Brunie and our National Lead of the *METAvivor* Ambassador Program, Lori Marx-Rubiner. Lori lives in Los Angeles and works with *METAvivor* from there. I too will be happy to support the study and provide my input and feed-back primarily via e-mail and phone from Annapolis, while Lori will be able to personally represent *METAvivor* and physically connect with Brunie's group in Southern California.

I, Lori Marx-Rubiner, have a very strong interest in supporting research dedicated to finding causes of metastatic disease and ways of interfering with and preventing this process. I am a 10- year breast cancer survivor and for me, any knowledge toward a better understanding of how breast cancer and metastasis develop and how they can be curbed is of utmost importance. Having the personal experience of breast cancer metastasis and being very aware of a potential environmental involvement in breast cancer development and progression to metastasis very strongly drives me to work with researchers who have dedicated their studies to these issues.

I very much welcome the opportunity to work with Brunie, her group and with CJ, to support the planned project and advise from the stand point of the person who has the experience and first-hand knowledge of how the diagnosis of metastatic disease, additional treatments and thoughts of the future impact one's life.

The planned project not only seeks to analyze if and how effects of organophosphates and organochlorines impact mitochondrial functions of normal human epithelial cells, but also to assess if these compounds can make already transformed breast cancer cells more aggressive and hasten the development of metastasis.

Based on the results from Brunie's group, it is very likely that active compounds in pesticides damage mitochondrial functions and may have the dangerous effect that Brunie is postulating and will analyze.

Both CJ and I will work closely with Brunie and her group, maintain a discussion on the clinical relevance of the experiments and digest the results together. If the planned study indeed finds a cause-and-effect relationship between exposure to pesticides and breast cancer development and progression, a serious discussion will ensue that can have wide ranging ramifications for the use of such compounds. Such results will spur further detailed analyses at the epidemiological level but also at the biochemistry, cell biology and pathology levels to interrogate risk association between exposure to pesticides and breast cancer development and progression in conjunction with genetic predisposition to breast cancer and sporadic breast cancer development.

We will work to disseminate the results and help to spur a discussion toward protecting consumers from pesticide exposure and invite searches for alternative means to ensure crop protection and agricultural and economical implications.

We have agreed to the following expectations, roles, and duties below.

We, CJ (Dian) Corneliussen-James and Lori Marx-Rubiner will:

- Participate in quarterly meetings (Lori) and e-mail and phone communications (Lori and CJ) with Brunie and her research team
- We will directly communicate relevant results and considerations of the study plan with the METAvivor organization and the advocacy community.
- We will help disseminate the results at the time when they are published in scientific journals to maximize access by the public and advocacy community. We will work actively with Brunie on press releases, and use our status as advocates of the breast cancer survivor community to raise awareness of the research findings, particularly representing the interest of persons with metastatic breast cancer experience.
- I, Lori Marx-Rubiner, will attend the CBCRP Research Symposium with Brunie and I, CJ (Dian) Corneliussen-James, will meet up with Brunie at other research conference(s) that we both attend. We will keep each other in the loop of our plans to participate in meetings and will specifically schedule to meet up in person and directly discuss the study.

I, Brunie Felding, will:

- Organize and participate in quarterly meetings with Lori and keep up regular e-mail and phone communications with Lori and CJ throughout the study.
- Solicit input from Lori and CJ during the planning and execution phases of the study and make adjustments according to their recommendations. We will very actively work together throughout the project and I will particularly seek their advice and rely on their unique ability to disseminate results within the advocacy community and the public, once the results have passed the rigor of peer review.
- From the grant budget, I will compensate Lori and reimburse her for her expenses associated with travels to my lab, as well as for her attendance of the CBCRP Symposium.
- We will acknowledge Lori and CJ as contributors to our studies.

We all very much welcome this opportunity of working together to evaluate if exposure to pesticides can be an enhancing or causing factor in the development of breast cancer and its progression to metastasis. This study may have very high impact on our understanding of environmental impact in breast cancer and lead to a serious discussion that could result in changes in public exposure to compounds widely used in agriculture and landscaping.

Sincerely,

Lori Marx-Rubiner

*Natl. Lead for the METAvivor
Ambassador Program*

CJ (Dian) Corneliussen-James
*Co-Founder and Director of
Advocacy for METAvivor*

Brunie Felding
Researcher