

UW College of Agriculture and Natural Resources
Global Perspectives Grant Program
Project Report

1. COVER PAGE

Award Period (e.g. Spring 2012): Spring 2015

Principle Investigator(s) M. Gomelsky

Department: Molecular Biology

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Project Title from Application: Engineering remotely controlled tumor-killing bacteria

Amount spent: \$ 4000

Non-technical summary (max 1500 characters plus spaces): Provide a one paragraph non-technical summary that most people can understand.

Cancer is the second leading cause of mortality in the developed nations. Radiation and chemotherapy, which long have been the mainstream treatment options, are not always effective and have severe side effects. Therefore, the demand for alternative cancer treatments has remained high. The idea of using bacteria in cancer treatment emerged in the late 19th century as a result of clinical observations of spontaneous tumor regression in patients experiencing systemic infections. Some bacteria spontaneously accumulate and propagate inside solid tumors. While growing in the nutrient-rich environment of solid tumors, bacteria destroy them from the inside. Other bacteria elicit strong immune responses against tumors. Currently we lack the means to control bacteria inside the body, which limits applications of bacterial anticancer therapies. The PI's laboratory has been engineering optogenetic systems to control bacteria with near-infrared light, which penetrates deep into mammalian tissues. These optogenetic systems may allow us to control location and anticancer activity of bacterial drones inside patients. The goal of this Global Perspectives grant was to partially support the PI's sabbatical in the Department of Microbiology, Cell and Tumor Biology, Karolinska Institute, Stockholm. This department has world-class experts in microbiology and tumor biology. The PI was expected to learn critical skills (mouse tumor model, whole-animal imaging and genetic manipulations of intracellular bacteria) for implementing the idea of remotely controlled bacterial anticancer therapy and develop collaborative efforts in this area.

2. REPORT: Maximum of two pages of text; please also include **photos**. Must be written in a style understandable by the lay person.

Include:

1. Main results of activities planned in the proposal.

The intracellular pathogen, *Salmonella enterica* Typhimurium, has been described as one of the most promising bacterial species for cancer therapy. The PI has worked with several professors and researchers in the Department of Microbiology, Cell and Tumor Biology, Karolinska Institute (Drs. Ute Römling and Teresa Frisan, experts in *Salmonella* genetics and virulence; Drs. Jonathan Coquet, Maria Issagouliantis and Joanna Zawacka-Pankau, experts in immunology and tumor biology) on genetic engineering of this bacterium and on using the engineered bacteria in a mouse tumor models. We have established the *Salmonella*-based antitumor model and observed bacteria (that have been made luminescent) to accumulate inside tumors. Unexpectedly and contrary to published reports, all experiments with attenuated *Salmonella* resulted in severe infections in mice. This led us to abandoning the *Salmonella*-based antitumor model and refocusing on alternatives. We tested a nonpathogenic bacterium *Rhodobacter sphaeroides*, that has recently been reported to propagate in tumors without causing virulence.

During the sabbatical, the PI presented invited talks in the Department of Microbiology, Cell and Tumor Biology; "After Biofilm" Meeting (Stockholm); International Meeting on Cyclic Dinucleotides (Berlin); Department of Microbiology, National University of Ireland (Galway).

A joint meeting between the PI's and Römling's laboratories has held (via Skype) every 4-6 weeks.

2. Describe any future plans

We are actively pursuing research on remotely controlled anticancer bacteria. Developing such bacteria is the dissertation topic of a Ph.D. student (R. Abrar). The *Rhodobacter* model, as well as an attenuated bacteria *Listeria monocytogenes*, are currently being pursued in the PI's lab in collaboration with researchers from UW (Drs. A. Lyuksyutova; J. Gigley), as well as from Einstein College of Medicine (Dr. C. Gravekamp), Fox Chase Cancer Center (Dr. I. Astsaturov) and Bowling Green University (Dr. J. Zeilstra-Ryalls). See article in UW News:

<http://www.uwyo.edu/uw/news/2015/09/uw-scientists-want-to-develop-bloodstream-bacterial-drones-to-kill-tumors.html>

Several grant proposals have been submitted to expand research on the subject of remotely controlled bacteria as anticancer therapy (to Karolinska Institute, Wanner-Gren Foundation

[Sweden] and NIH). None are funded at present.

A visit by a Ph.D. student from the Dr. Römling's lab (host lab at Karolinska Institute) to the Gomelsky lab is planned for Spring 2017.

3. Outline potential impacts to a) the College of Agriculture and Natural Resources, b) the University of Wyoming, and c) the State of Wyoming

The main impacts of the PI's sabbatical, which was partially supported by the Global Perspectives grant, involve the development at UW of the innovative line of research on remotely controlled bacterial drones as anticancer therapy. As outlined above, this research has attracted attention of scientists from other universities. Several of them have visited UW for mini-sabbaticals (Dr. J. Zeilstra-Ryalls) or with research seminars (Dr. C. Gravekamp). We expect to ultimately attract federal funding and contribute to developing effective anticancer treatments.

The trip partially sponsored by the Global Perspectives grant helped the PI expose audiences in several European countries (via invited talks) to research performed at UW. During these talks, students were made aware of graduate opportunities at UW.

4. Photos—be sure you have necessary permissions to be posted to the AES website.

Photos are attached.

QUESTIONS? Contact Joanne Newcomb in the Agricultural Experiment Station office at aes@uwyo.edu or (307) 766-3667.







