

February 25, 2013

Misrock Foundation
c/o JOERIN Advokatur & Mediation
Schneidergasse 1
CH-4051 Basel
Switzerland

Dear Mr. Joerin,

I hope this letter finds you and your colleagues at the Misrock Foundation well. I am writing to provide a **final report** on the work of the 2012 Misrock Fellows at the Koch Institute at MIT, and to introduce you to the newest Fellows.

You will likely recall from my update to you in December that both 2012 Misrock Fellows, Kris Wood and Tal Danino, have made notable advancements in their research and contributions to the scientific community.

Kris's project, "Sensitizing tumors to targeted inhibitors and nanoparticle therapeutics using miniaturized functional genomics," was focused on refining and validating a screening platform that he developed using melanoma as a test case. The technology helps to identify the genes and pathways that control cancers' sensitivities to targeted inhibitors, as well as the biological mechanisms that control their sensitivities to nanoparticle therapies. Kris's screening tools provide an improved understanding of the 'design rules' for effectively connecting small molecule therapies and nanoparticle delivery systems with signaling pathways and cellular processes.

Additionally, the pathways that Kris identified seem to play a major role in determining patient response to anticancer drugs. He anticipates that testing for the activity of these pathways can predict which patients will respond to drugs, and that using drugs that block these pathways may generate more powerful and more lasting anticancer responses.

A paper describing Kris's work, "MicroSCALE Screening Reveals Genetic Modifiers of Therapeutic Response in Melanoma," was published in *Science Signaling* last year. I have enclosed a copy here along with a personal letter of gratitude from Kris, who is now an assistant Professor in Pharmacology and Cancer Biology at Duke University. There he is beginning to assemble his own research team and to apply his screening system to several other types of cancer.

Tal, you will likely recall, is working on a project to engineer targeted minicells, or nanoparticles produced from aberrant cell divisions in bacteria, for cancer therapeutics. The special promise of minicells is that, because they maintain plasmids, produce energy, and transcribe and translate DNA, they can be engineered as intelligent rather than passive delivery vehicles. Tal's work to produce targeted minicells responsive to external triggers, such as heat, is an essential first step to

achieving this potential and may help to open up a new class of programmable nanotechnological materials.

Enclosed is a research summary that Tal has prepared, along with a copy of a message he has addressed to the Foundation and to Kathy Misrock. (I sent the original to Kathy.) I have also included two papers Tal has published on this research, in which he cites his support from the Misrock Foundation. The papers both appeared in a special issue of the American Chemical Society's journal *Synthetic Biology* devoted to therapeutic applications of engineered microbes. In fact, the work of Tal and his colleagues is highlighted in the edition's cover art, and mentioned twice in the editor's introduction, both of which are also enclosed.

As for the 2013 Misrock Fellows, Tal Danino has been selected for a second term as a fellow and will continue his work, attempting to improve minicell triggering and further refine their targeting. Since you are already familiar with his work as a scientist, I want to tell you about how his talents as a filmmaker enrich our community and our educational outreach programs. Last spring, Tal helped to organize a Bio Flash Mob as part of the Koch Institute's involvement with the Cambridge Science Festival. The Bio Flash Mob brought together 200 Boston-area students, MIT scientists and local community members for a colorful, human-scale demonstration of how nanoparticles destroy cancer cells. Perched atop the roof of the adjacent Biology building, Tal captured the whole event on film and edited it for inclusion in the brief video enclosed here. In fact, Tal is a cofounder and editor of coolsciencevideos.com, an educational website that curates and produces artistic and engaging videos to promote public understanding of science.

More recently, an image of a fluorescing colony of his engineered bacteria was one of 10 chosen from among more than 150 submissions by our selection committee to hang in our public galleries for the coming year. This honor will not be formally announced, nor will the image be installed, until the end of next month, so the image has not been released. However, given the Foundation's special role in supporting Tal's work, we thought it was fitting to use the image as the cover art for the Bio Flash Mob dvd.

The second 2013 Misrock Fellow is Kogularamanan Suntharalingam. Rama, as he is known, is a postdoctoral associate in the laboratory of Koch Institute member Stephen J. Lippard. Rama's project is entitled "How Do Nanoparticle Formulations Mediate the Phenanthriplatin Cellular Response?" He aims to create improved nanoparticle designs for delivering phenanthriplatin, the promising new platinum-based anti-cancer compound identified by the Lippard laboratory. Phenanthriplatin may be familiar to you from reading about the research of 2011 Misrock Fellow Ga Young Park, who designed the initial nanoparticle carrier for the compound.

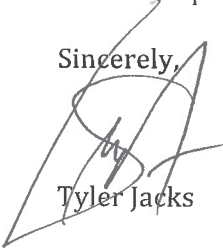
Analysis of this current phenanthriplatin nanoparticle formulation revealed that it induces a completely different cellular response profile than the platinum drugs widely used in the clinic, and a better understanding of the body's reaction will enable important refinements. Specifically, Rama plans to identify how the current nanoparticle carriers for phenanthriplatin are taken up and modified by cancer cells, and to investigate the cellular response to the internalized nanoparticles. The results of these inquiries will allow him to devise new nanoparticle formulations that help to maximize the effectiveness of this powerful compound by offering improved delivery, targeting, stability and imaging potential.

Originally from the United Kingdom, Rama earned his undergraduate and graduate degrees in chemistry from Imperial College London. A copy of his CV is enclosed. When not in the lab, Rama enjoys watching and playing soccer.

Finally, I also want to provide a brief update on Avi Schroeder, the second 2011 Misrock Fellow. Avi is now an Assistant Professor of Chemical Engineering at the Technion in Israel, heading a growing laboratory group whose efforts build on his exceptional work at MIT. I understand additional papers based on his research as a Misrock Fellow are now in press, and we will be sure to pass these along once they are published.

Until then, please know that we remain deeply grateful for the Misrock Foundation's support for our gifted young researchers and the innovative ways in which they are integrating nanotechnology and advanced science to combat cancer. I look forward to keeping you up to date on their continued progress in the months ahead.

Sincerely,

A handwritten signature in black ink, appearing to read 'Tyler Jacks', is written over the word 'Sincerely,'.

Tyler Jacks

Enclosures (8)

CC: Kathy Misrock