KOCH INSTITUTE
for Integrative Cancer Research at MIT

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Mr. Jean-Marc Joerin
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Dear Mr. Joerin,

I am pleased to write to you and your colleagues with news about the cancer researchers supported by the generosity of the Misrock Foundation, both those whose term has just ended and those whose term has just begun. Enclosed first are confidential final reports from the 2014 Misrock Fellows, Drs. **Yi Wen Kong**, **Zhimin Tao**, and **Mark Tibbitt**.

Over the course of her fellowship term, Yi Wen has achieved the stated goals of her project and then some. She has created a nanoparticle that delivers an siRNA inhibitor to silence the MK2 signaling pathway, which helps cancer cells resist the crippling DNA damage caused by chemotherapy, and thus sensitize non small cell lung cancer cells to cisplatin, a standard chemotherapy drug used to treat lung disease. As part of her work, Yi Wen collaborated with members of the laboratory of Paula Hammond, a nanoparticle expert. In addition to targeting a single pathway to enhance chemotherapeutic response, Yi Wen was able to deliver siRNA inhibitors that target both MK2 and another distinct 'chemotherapy bypass' pathway, further enhancing tumor response to cisplatin. Moreover, Yi Wen was able to expand her work to test the siRNA and nanoparticle carrier against ovarian cancer. In fact, she has secured follow-on funding to continue this work.

Zhimin Tao has been developing nanoparticles that are not therapeutic themselves, but that could offer a method for high-throughput screening of traditional, small-molecule drugs for use against certain genetic targets in cancer. Screening these types of drugs for this purpose currently requires much slower and more labor-intensive testing, thus a faster and more efficient system could speed the development of new treatments.

Finally, Mark Tibbitt has been developing a nanogel to attract metastatic cancer cells to a specific location in the body, where information can be relayed to clinicians for diagnosis and staging, and chemotherapy can be administered to those cells. His approach is novel not only in the development of new materials, but also in its strategy of bringing metastatic cells to one location for treatment rather than chasing them throughout the body or into the many biological niches where they can hide.

Over the funding term, Mark has successfully constructed the nanogel. The material can change and reform its shape, it successfully incorporates the desired chemotherapy drugs, and it creates a niche that metastatic cells will find attractive. His findings were published in *Nature Communications* and appeared as the featured story on the MIT homepage last week, an outlet viewed by approximately 500,000 users per month. The development of the gel was also covered by the *Boston Business Journal*. The Misrock Foundation was, of course, credited in all three cases,

which I have enclosed here. Going forward, Mark will work to further develop mechanisms for attracting metastatic cells to the gel, and for relaying information to clinicians. Like Yi Wen, he has also secured follow-on funding.

Finally, I am pleased to announce the two newest Misrock Fellows, **Vikash Chauhan** and **Mohiuddin Quadir**. Originally from Ohio, Vikash came East to earn undergraduate and graduate degrees in chemical and biomolecular engineering at the Johns Hopkins University, and he earned his doctorate in bioengineering from Harvard University. Here at MIT, he is a member of the laboratory of renowned engineer Robert Langer, who was awarded the Queen Elizabeth Prize for Engineering earlier this month.

Vikash's project, "Alleviating hypoxia to reverse suppression of anti-tumor immunity," addresses persistent challenges in using immunotherapies, a very successful new type of cancer treatment, against certain solid tumors. Essentially, he is working to develop a nanoparticle delivery vehicle for recently developed drugs that allow oxygen, and thus immune cells, to permeate the interior of tumors. These agents work synergistically with cancer immunotherapies and, it is hoped, will help immunotherapies to be effective against hard-to-reach tumors and against metastases.

Mohiuddin, better known as 'Mohi,' is a member of Paula Hammond's laboratory. The Hammond laboratory is known for developing customizable nanoparticles that can be produced at industrial scale, that can be adapted inside and out to carry a wide range of therapeutic and targeting components, and that can release cargoes in a controlled way. This enables the nanoparticles to find and fight many types of cancers, delivering therapeutics only at the site of cancer cells, while leaving normal cells alone.

Mohi's fellowship project is titled, "Multi-compartment, nanoscale platform for combinatorial anticancer therapy." Tumors are usually made up of multiple types of cancer cells, which can have different mutations, different metastatic potential, and different characteristics of other types. Mohi will be working to create a multi-layer nanoparticle that packages together several cancer therapies of various types, and that releases them in the appropriate stages to achieve maximum impact. The aim of this combination is to kill several types of tumor cells, reducing the existing tumor while also fending off drug resistance and metastases.

Mohi holds degrees in pharmacy from the University of Dhaka, in Bangladesh, and earned his doctorate in chemistry at Freie University of Berlin, in Germany.

Over the last five years, funding from the Misrock Foundation has supported some of the Koch Institute's most exciting and innovative cancer research, and some of our most promising trainees. Already, many of these young people are out in the world developing new solutions for the problems of cancer, usually while maintaining active collaborations here at MIT. Highlights include:

- **Avi Schroeder**, who now runs his own nanotechnology laboratory as a faculty member at the Technion, Israel's Institute of Technology. As I wrote to you this past fall, during his fellowship Avi created an orally administered 'nano pill' that he and his colleagues at MIT have continued to develop and that is currently in clinical trials. The device could more easily, effectively and affordably deliver certain types of drugs, including biologics and vaccines, as well as treatments for cancer, diabetes and gastric disorders.

- **Ga Young Park**, who identified a new compound showing significant potential against a broad range of cancers, and created a first-generation nanoparticle carrier for its delivery.

She has since applied her considerable talents at Boston Biomedical, a leading oncology drug research and development company with several agents in advanced clinical trials.

- **Kris Wood**, who is now a faculty member directing his own laboratory at Duke University, and continues research on overcoming therapeutic resistance in cancer. Kris continues to develop and apply the nanotechnology-based screening system he created at MIT to systematically identify signaling pathways that modulate cancer cells' sensitivity to therapy. This work can inform clinical strategies and the use of existing drugs, and highlight targets for the development of new drugs.

- **Tal Danino**, who remains at MIT engineering bacteria to create cancer diagnostics and therapeutics, and has also been appointed a visiting fellow at the Rockefeller University. Outside the lab Tal continues his efforts to engage new audiences with science, technology and cancer research through arts and outreach programs. His work has attracted some high profile attention, particularly collaborations with former MIT visiting artist Vik Muniz, which garnered exhibitions in New York and Sao Paolo, and related works commissioned by the Bill and Melinda Gates Foundation for use in an online health campaign and featured in *The New York Times*, *The Wall Street Journal* and other outlets. Tal was also selected as a 2015 TED Fellow.

- **Kogularamanan (Rama) Suntharalingam**, who now heads an independent research group at King's College London, and pursues his work designing and developing a new and better generation of the metals-based drugs commonly used to fight cancer, and corresponding nanoparticle shells. Rama and collaborators at MIT have secured additional funding to conduct advanced pre-clinical testing of therapeutic nanoparticles, and the promising new compounds they carry, that he developed during his fellowship.

In closing I must tell you that I am, first and foremost, exceedingly grateful for the Misrock Foundation's dedicated support of these promising new talents. Moreover, I am confident that you and your colleagues will agree that your investments in these individuals, and in MIT's cancer research community, have been worthwhile. The tiny injectable, ingestible, illuminating nano-particles, materials and devices created by our researchers are changing the story we all know about cancer - the invasive testing and diagnostics, the debilitating side effects, the prohibitive expense, the decreased quality of life for patients and their loved ones. As nanoparticles and other manifestations of the 'tiny technologies' continue to gain regulatory approval in the U.S. and elsewhere, we will see more and more how they help us not only to fight cancer in new ways, but also to get the most out of existing tools and treatments.

As always, I look forward to keeping you up to date on the progress of the Misrock Fellows, and send my regards to you and to the other members of the Misrock Foundation board and family.

Sincerely,

Tyler Jacks

Enclosures (5)

CC: Victoria Misrock-Stein
Kathy Misrock