

June 14, 2018

Mr. Jean-Marc Joerin  
c/o JOERIN Advokatur & Mediation  
Schneidergasse 1  
Basel CH-4051  
Switzerland

Dear Mr. Joerin,

I hope this letter finds you and your colleagues well. I am writing to update you on the work of last year's Misrock Fellows, and to announce the 2018 Fellows.

The 2017 Misrock Fellows, as you may recall, were Pedro Pires Goulart Guimarães and Yulia Rybakova, members of the Koch Institute's Langer and Anderson laboratories, respectively. Both have been developing nanoparticle vehicles for RNAi delivery, but to advance different therapeutic strategies. Pedro aimed to shut down a signaling molecule that helps drive multiple myeloma, while Yulia sought to combine RNAs with chemotherapy to make liver cancer more sensitive to therapy.

Pedro has made strong progress toward all three aims of his project, developing and refining a nanoparticle delivery system that shuttles its siRNA cargo to target cells and potently silences the target gene. Working with collaborators at Boston's Dana-Farber Cancer Institute, Pedro and his colleagues showed *in vivo* in pre-clinical models that the nanoparticles, used in combination with another drug, reduce multiple myeloma progression and extend survival. His findings were published recently in *ACS Nano*. Pedro enclosed a copy of the manuscript—in which the Foundation's support is acknowledged—along with his report and a letter summarizing his progress and expressing his gratitude.

Yulia has also made notable advances in her research, conducting a great deal of screening and analytical work that ultimately identified three RNAs with great potential for use in her approach against liver cancer. During the past year, she has presented her work at a conference, and prepared an IP disclosure that will be helpful as her work continues to progress. She has also included a letter along with her report, both of which are enclosed here.

The 2018 Misrock Fellows, Jason Chang and Lei Miao, began their terms at the start of 2018 and have since been hard at work.

Jason is a member of the laboratory of Koch Institute faculty member Darrell Irvine, and is working to adapt a microneedle technology developed by the Irvine group for use in monitoring patients with triple negative breast cancer. Triple negative breast cancer is an aggressive tumor, shows limited response to current therapies, and carries a high risk of early recurrence. However, the only way to detect tumor recurrence currently is by invasive tissue biopsies. Jason is developing a platform that uses the microneedles—essentially a patch with painless, microscopic needles on one side—as a basis for sampling and sensing circulating microRNAs, or fragments of genetic information, associated with triple negative breast cancer. Expression patterns of these cell-free circulating microRNAs are emerging as a way to provide valuable insight regarding disease progression and responsiveness to treatment therapies. His strategy aims to overcome major challenges in other systems for detecting tumor-associated microRNAs, and could enable

minimally-invasive longitudinal monitoring of triple negative breast cancer's progression toward metastasis and its response to therapies.

Jason conducted his doctoral studies in bioengineering at Imperial College London. An image from one of his earlier research projects—a nanoparticle vaccine to jumpstart the immune system against HIV—was selected as a winner of the 2018 Koch Institute Image Awards; it currently hangs in our public galleries and is featured online, along with a video of Jason describing the image, at [ki-galleries.mit.edu/2018/chang-1](http://ki-galleries.mit.edu/2018/chang-1).

A postdoctoral researcher in the laboratory of Koch Institute faculty member Daniel Anderson, Lei is working to develop and test new, lipid-like materials to more effectively deliver therapeutic messenger RNAs, or mRNAs.

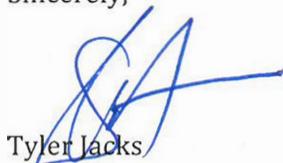
mRNAs hold a great deal of promise for treating many diseases including cancer, where several mRNA properties make it ideal for use in developing new immunotherapies and inducing strong anti-tumor immune responses. However, a few key challenges remain to getting mRNA-based therapies into the clinic. First, mRNAs need to be protected to avoid being broken down in circulation, and second, even when mRNAs are successfully delivered they sometimes can't mount a strong enough response. The Anderson lab has a great deal of expertise in developing lipid-like delivery materials that can help protect and target therapeutic cargo. Building on this expertise and, aided by a materials synthesis innovation she devised, Lei is taking a systematic approach to developing and testing a library of materials that can both potently deliver mRNA into cells and, by nature of their physical structure, boost immune response. Lei holds a doctoral degree in pharmaceutical studies from the University of North Carolina Chapel Hill.

Before I close, I do want to update you on our plan for allocating the remaining balance in the S. Leslie Misrock (1949) Fund for Cancer Nanotechnology, following the generous final tranche of support provided by the Foundation this past fall. Our plan is to combine this gift with a small remaining balance in the fund, and to continue awarding two fellowships per year. Thus, we have awarded two fellowships for 2018, and will award the last two for 2019.

As I hope you can see from the projects that the current and former Fellows are working on, a new era of cancer therapy, and whole new classes of cancer medicines, are on the not-too-distant horizon. Their development is being hastened by a new generation of cancer researchers that are conversant in multiple disciplines, and who work in focused and collaborative ways to overcome specific challenges in diagnosis, treatment and monitoring.

We in MIT's cancer research community are deeply grateful to have been the beneficiaries of the Misrock Foundation's—and especially the Misrock family's—support, and efforts to continue Mr. Misrock's legacy of investing generously in people and in science. I send my best wishes to you and your colleagues for a wonderful summer, and look forward to updating you again early next year.

Sincerely,



Tyler Jacks

CC: Victoria Misrock-Stein

Kathy Misrock

Enclosures (2)