

In Conversation: Research Fellow Junfang Ji, Ph.D.

(Photo: R. Baer)



Junfang Ji, Ph.D.

CCR: Junfang, you work on hepatocellular carcinoma, which is a particularly aggressive cancer, especially in males. What prompted you to take a translational research approach to this cancer?

Junfang: I started working on liver cancer after coming to CCR to work with Xin Wang, Ph.D., in the Laboratory of Human Carcinogenesis. As a Ph.D. student at Peking University Medical College, in Beijing, my work focused on oncogenic function and DNA repair. From there, I kept thinking whether and how our scientific findings could be connected to patient benefits. Translational research is the conduit. It is highly challenging but also rewarding. CCR is a great environment for doing translational research—the questions I must address are more complicated, but there are lots of resources here and opportunities for collaboration.

CCR: What are the overall goals of your investigations here?

Junfang: Liver cancer has tremendous heterogeneity from patient to patient

and also within single tumors. In the big picture, we try to understand the genetics of tumor heterogeneity so we can stratify patients by their gene profiles. We also aim to identify key driver genes for each cancer subgroup. Our hope is that by targeting driver genes, we can increase the survival of patients with liver cancer. This would allow us to maximize treatment efficiency.

CCR: What are you learning about intertumor heterogeneity, or the way tumors differ among individual patients?

Junfang: Males and females have very different liver tumor biology: Females are less likely to develop liver cancer, and when they do, they have better survival. We found that compared to males, females express much higher levels of a microRNA called miR-26, which acts as a tumor suppressor. We also find that miR-26 is reduced in tumor versus nontumor tissues, and that many immune-associated pathways are activated in tumors with low miR-26 expression.

CCR: Do you see translational opportunities for miR-26 in the clinic?

Junfang: Yes. We found that patients with low levels of miR-26 respond to immunomodulating therapy with interferon alpha, while patients with high levels do not. Now we are trying to make a diagnostic—the miR-26 DX test—for use in choosing patients for interferon- α treatment. This could allow for more efficient use of treatment resources.

CCR: What are you learning about intratumor heterogeneity?

Junfang: Some cancer cells in the liver tend to be very hard to treat. Even

after surgery and/or chemotherapy they form new tumors—these are the hepatic cancer stem cells (HepCSC). We isolated HepCSCs using the EpCAM surface marker and found that they have an aggressive phenotype when implanted into immunocompromised mice. We also found that EpCAM-positive HepCSCs highly express a microRNA called miR-181.

CCR: Does that make miR-181 a potential drug target in hepatic cancer stem cells?

Junfang: This is something we are investigating. One problem is that miR-181 is also highly expressed in normal hepatic stem cells. So if we silence it in tumors, we also likely suppress it in these other cells and that is a side effect that we do not want. But recently we discovered another group of microRNAs that seem to be very specifically expressed in hepatic cancer stem cells and we are happy to see that. These data will be published soon.

CCR: What do you hope to do after leaving CCR?

Junfang: I am looking for a faculty position and would like to continue my work on sex-related differences in cancer incidence and mortality. The underlying molecular mechanisms in sex-related carcinogenesis are poorly understood, but our data with microRNAs might be providing important clues. I would like to work on decoding the biological differences between male and female and liver cancers at multiple levels with an overarching goal of developing tools for early diagnosis, prognosis, therapeutic stratification, and effective therapy.