

Dr. Jun Yu: biomarkers in pancreatic cancer: recent advances and foreseeable future development

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Expert introduction

Jun Yu (Figure 1), MD, PhD is an Assistant Professor in the Department of Surgery, Division of Hepatobiliary and Pancreas Surgery at the Johns Hopkins University School of Medicine. He is the Chief Scientist of Division of Hepatobiliary and Pancreas Surgery at Johns Hopkins. Dr. Yu received his medical degree from Gannan Medical University in China and a PhD in Surgery and Oncology from Kyushu University School of Medicine in Japan. His research focuses on understanding the biology of pancreatic cancer and cystic neoplasms of the pancreas, and on detecting the actionable mutations/pathways for the patients with pancreatic cancer in a personalized therapeutic strategy. He was trained in the studies of the general surgery and oncology of pancreatic cancer and his work has led to first-author publications in *Journal of Clinical Oncology*, *GUT*, *Annals of Surgery*, and *Clinical Cancer Research* as well as numerous other papers as a first-author or co-author in the field of pancreatic cancer research. He successfully collaborated with other researchers and produced several peer-reviewed publications in some journals with high impact factor, e.g., *Nature*, *Cancer discovery*, *Gastroenterology*, and *Clinical Cancer Research*. Furthermore, he developed several novel sequencing technologies, including digital Next-Generation Sequencing (dNGS) and Single-cell Next-Generation Sequencing (scNGS), which allows pancreatic circulating tumor cells detectable for mutation burden analysis. He is the Principle Investigator of the Pancreatic Cancer Precision Medicine Center of Excellence (PMCoE) at Johns Hopkins. In addition, he serves as a Committee Member of the Clinical Research Review Committee at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Editor's note

The 4th International HBP Surgery Forum was held in Hangzhou, Zhejiang Province on 14–17 June, 2018. The

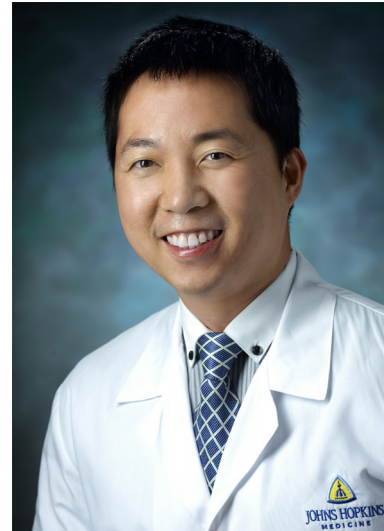


Figure 1 Dr. Jun Yu.

Forum is organized by The Second Affiliated Hospital Zhejiang University School of Medicine (ZUSAH) and the Zhejiang Anti-Cancer Association. The International HBP Surgery Forum, held every two years, has now become a magnificent gathering for the researchers, whom are related to HBP surgery to communicate their work and ideas. The Forum was spilt into several sessions of various events and activities, including operation videos' exchange, MDT discussion on challenging cases, keynote speeches, panel discussion and debate. During the Forum, AME was honored to have invited Dr. Jun Yu, Chief Scientist of Division of Hepatobiliary and Pancreas Surgery at Johns Hopkins, to have an interview with us.

Interview

APC: *Could you please share with us the latest research progress of biomarkers in Pancreatic Cancer?*

Dr. Yu: Although incessant efforts from surgeons,

radiologists, and chemotherapists have been made to improve the overall survival of patients with pancreatic cancer, few steps have been made toward a satisfying clinical outcome. And as advances in exploring the molecular pathology of pancreatic cancer (PC) and developing novel techniques for nucleic acid sequencing, researchers, in the past decades, have conducted numerous studies showing the potential clinical utility of liquid biopsy, such as circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), and circulating tumor exosomes for various cancers, including PC. These promising markers serve as a unique approach for early detection, monitoring and managing disease states. In recent years, noninvasive disease monitoring technology has witnessed an extraordinary explosion of research in the field of liquid biopsy since circulating cell free DNA (cfDNA) was first revealed in body fluids by Mandel and Metais in 1948. Of these, CTCs and ctDNA are what researchers in our institution have been focusing on. By identifying, quantifying, and sequencing CTCs, or by deep -sequencing ctDNA, we can get genetic information specific to the initiation and evolution of PC, which are of great significance for our understanding of PC. Besides, by extracting CTCs and ctDNA in both horizontal and longitudinal ways, obstacles brought about by the heterogeneity of cancer can be partially avoided, which was unlikely by conventional imaging and regular serum markers such as CA19-9 and CEA.

APC: *What do you think will be the next big development regarding the biomarkers in pancreatic cancer?*

Dr. Yu: As we are gaining more insights into the molecular biology of PC, and by taking advantage of ever-accelerated updating of DNA sequencing technologies, I do believe that we can strive to find ctDNA or nucleic acid in CTCs bearing genetic aberrations specific to PC and to map ctDNA characteristics spectrum of PC which will offer completely comprehensive genetic information of PC that we can draw on to conceive personalized medication for individual patients with PC. Besides, by utilizing single-cell sequencing for CTCs, it's promising to reveal the characteristics of PC in the single-cell level.

APC: *Of the research you have been involved with, which piece are you most proud of and why?*

Dr. Yu: I'm most proud of doing conducting clinical trials, especially those that I'm doing currently. Cuz witnessing

what I have concluded by basic experiments and theoretical reasoning is being translated to clinical use is amazing for me. All fundamental research work is doomed to serve the improvements of medication, thus to improve human health in the worldwide. There is nothing bring more relief than the fact of knowing what I have been doing is practically useful for making cancer patients live better.

APC: *How did you become interested in medicine?*

Dr. Yu: I ever dreamt of saving the world like what the Super Man did in the movie when I was a child. I also dreamt of learning the critical realism of Fyodor Dostoyevsky or developing Newton's laws of motion. And as I grow old and realistic, I thought that dream was hard to realize. Then I came across a book named *The Development of Western Medicine*, which was written in Chinese and I already forgot the name of the writer. It sparkled my boring high school life. I still remember the three key words that I wrote in my book: belief, hope, love. And I thought the best place to figure out the meaning of them is the hospital. Being a doctor is sacred not because doctors are themselves gods, but they are playing roles of god with their profession and mercy. That's how I began to be interested in medicine.

APC: *What is the most interesting paper you have come across recently?*

Dr. Yu: It's *Combined circulating tumor DNA and protein biomarker-based liquid biopsy for the earlier detection of pancreatic cancers* written by Cohen JD at The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins Medical Institutions. They combined blood tests for *KRAS* gene mutations with carefully thresholded protein biomarkers to determine whether the combination of these markers was superior to any single marker. And they concluded that the use of *KRAS* in conjunction with four thresholded protein biomarkers increased the sensitivity to 64%. Only one of the 182 plasma samples from the control cohort was positive for any of the DNA or protein biomarkers (99.5% specificity).

APC: *What advice would you give to someone who is just beginning his career in this field?*

Dr. Yu: I do have several pieces of advice to them:

- (I) Be interested: interests bring forth new ideas and are the origin of innovation;

- (II) Be aspirational: know what you are doing is meaningful and be brave to read articles in a critical way;
- (III) Be patient: you have to be aware of the fact that medical research is nothing fast and wealth-inducing; by bearing this in your mind, you'll spring up when you are confronted with failure and fall down to the ground;
- (IV) Be real: the last but the most important. The nature of life and scientific research is revealing the truth of how diseases arise and evolution and then to figure out ways to cure. So, be real to your lab result reports and articles.

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Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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