Taking the guesswork out of cancer therapy

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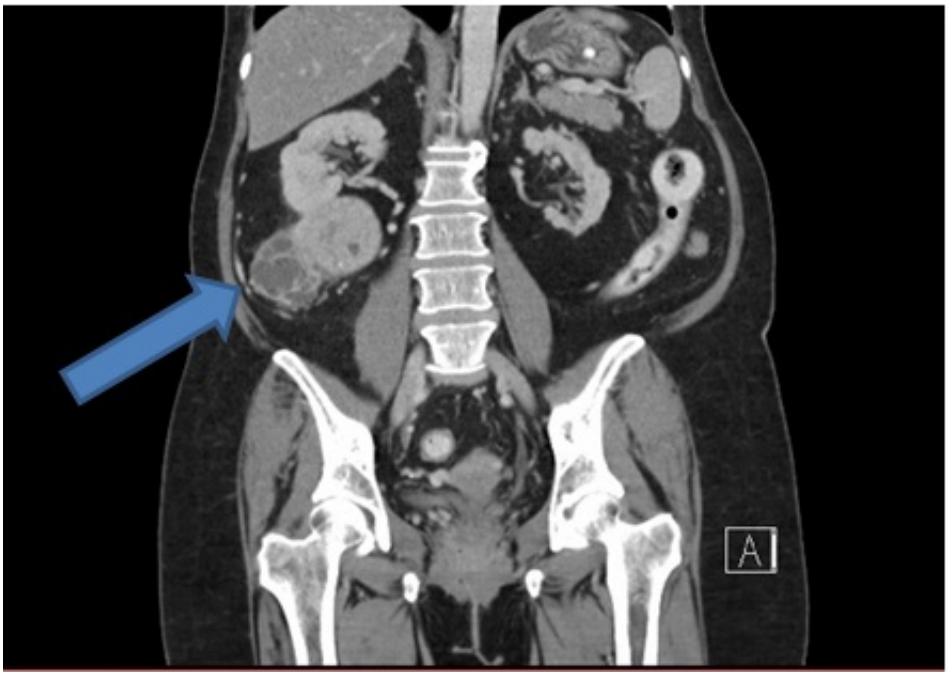


A CT scan with arrow indicating kidney tumor. Credit: IBN

Researchers and doctors at the Institute of Bioengineering and Nanotechnology (IBN), Singapore General Hospital (SGH) and National Cancer Centre Singapore (NCCS) have co-developed the first molecular test kit that can predict treatment and survival outcomes in kidney cancer patients. This breakthrough was recently reported in *European Urology*, the world's top urology journal.

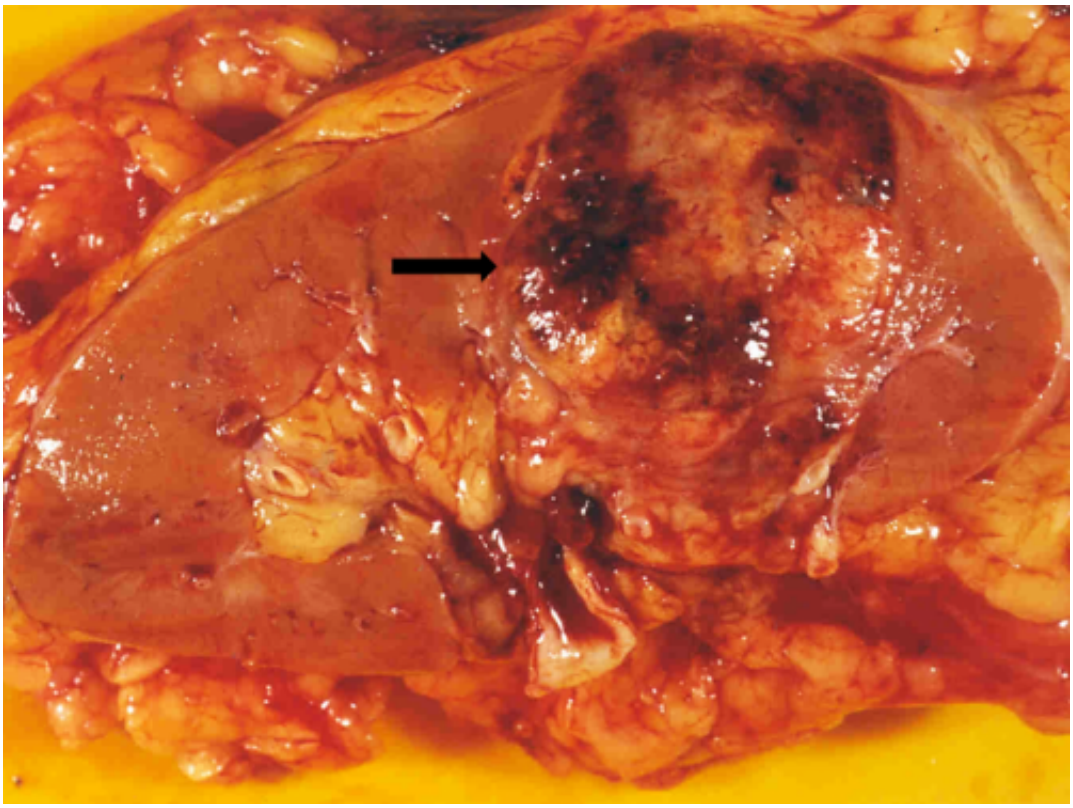
According to IBN Executive Director Professor Jackie Y. Ying, "By combining our expertise in molecular diagnostics and cancer research,

we have developed the first genetic test to help doctors prescribe the appropriate treatment for kidney cancer patients based on their tumor profile."

Dr. Min-Han Tan, who is IBN Team Leader and Principal Research Scientist and a visiting consultant at the Division of Medical Oncology NCCS, shared his motivation, "As a practicing oncologist, I have cared for many patients with kidney cancer. I see the high costs of cancer care, the unpredictable outcomes and occasional futility of even the best available drugs. This experience inspired our development of this assay to improve all these for patients."

The study was conducted retrospectively with tissue samples collected from close to 280 clear cell renal cell carcinoma (ccRCC) patients who underwent surgery at SGH between 1999 and 2012.

"High quality tissue samples are crucial in achieving significant findings in biomedical research. As an Academic Medical Center, we wish to promote the translation of research into advances in healthcare and personalized medicine. The development of this test kit for patient care, utilizing the robust tissue archive that we have at SGH, is a good example of this," said Professor Tan Puay Hoon, Head and Senior Consultant, Department of Pathology, SGH.



This is a nephrectomy specimen showing a renal cell carcinoma composed of a tumor mass with yellowish and hemorrhagic areas (arrow). Credit: IBN

Kidney cancer is among the ten most frequent cancers affecting men in Singapore, according to The Singapore Cancer Registry (2009-2013). The most common type of kidney cancer is clear cell renal cell carcinoma. Treatment options include surgery, ablation or removal of the tumor, or targeted therapy to shrink or slow the growth of the cancer. The latter works by blocking the growth of new blood vessels (angiogenesis) or important proteins in cancer cells (tyrosine kinase) that nourish the tumors and help them survive.

According to Dr. Min-Han Tan, there are currently about 250 new patients diagnosed with kidney cancer per year in Singapore. "Outcomes can be very different. Some patients can be observed for years on end,

some benefit from immediate treatment including surgery or targeted therapy, and for some patients, treatment can be futile. Experience is required in making the right judgment for patients. We hope our assay will play a role in helping that judgment."

Targeted drugs are prescribed routinely for cancer patients. Revenues from anti-angiogenic drugs, such as Sutent® and NexavarTM, are estimated at several billion dollars annually.

Such drugs, however, are not only expensive but may cause side effects in patients, including fatigue, loss of appetite, nausea, diarrhea, pain, high blood pressure, bleeding and heart problems. Due to genetic variations, individual patients respond differently to these drugs and have different survival outcomes.

Pharmaceutical companies and academic institutions have invested heavily in seeking out tools and biomarkers to predict personalized outcomes with these therapies, and the development of a reliable anti-angiogenic predictor would be of significant interest to them.

Extensive molecular characterization of ccRCC by the team and other researchers worldwide in recent studies has suggested the existence of specific subtypes with different survival outcomes. The researchers therefore set out to discover reliable biomarkers that could improve the prognostic prediction, and identify patients who would be likely to benefit from one type of treatment.

For this purpose, the team designed a practical assay for studying/diagnosing real-world tumor samples from ccRCC patients. The assay was able to distinguish patients into groups of different survival and treatment outcomes. This is one of the first assays capable of predicting outcomes of anti-angiogenic therapy, a key goal for cancer care and industry.

Dr. Tan added, "Our diagnostic assay successfully classified ccRCC into groups correlating to different survival and treatment outcomes. This allows patients and doctors to make more educated choices in their treatment options. Additionally, the development of such assays in Singapore demonstrates the highest levels of research, care and expertise that are available to our patients here."

This test has been validated at the Singapore General Hospital and National Cancer Centre Singapore.

More information: Y. Choudhury, X. Wei, Y.-H. Chu, L. G. Ng, H. S. Tan, V. Koh, A. A. Thike, E. Poon, Q. S. Ng, C. K. Toh, R. Kanesvaran, P. H. Tan and M.-H. Tan, "A Multigene Assay Identifying Distinct Prognostic Subtypes of Clear Cell Renal Cell Carcinoma with Differential Response to Tyrosine Kinase Inhibition," *European Urology*, (2014) DOI: 10.1016/j.eururo.2014.06.041.

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