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MEDIA RELEASE

For Immediate Release

New Epithelial Ovarian Cancer Sub-types Predict Patients' Prognosis

Discovery could pave the way for personalised treatment and new diagnostic tests

SINGAPORE – A clinician-scientist at the National University Hospital has shed new light on the behaviour of epithelial ovarian cancer cells. Dr Ruby Huang, a clinician scientist with the Department of Obstetrics and Gynaecology at the National University Hospital and a senior research fellow with the Cancer Science Institute (CSI) at the National University of Singapore, has identified five new ovarian cancer cellular sub-types that could be used to predict the prognosis of ovarian cancer patients. The discovery was made in collaboration with Prof Jean Paul Thiery and Dr Seiichi Mori from the CSI.

Ovarian cancer is presently the fifth most common cancer among Singaporean women, accounting for 5.5 per cent of all female cancers diagnosed from 2006 to 2010. The rate of this cancer increases greatly after the age of 35. The symptoms of ovarian cancer are bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly and urinary problems such as urgent or frequent urination.

Most ovarian cancers are epithelial in nature, meaning that they occur on the epithelium, the surface of the ovary. Epithelial ovarian cancer (EOC) is heterogeneous, with different invasive behaviours and distinct tissue subtypes. This type of ovarian cancer is characterized by a high degree of genetic damage and multiple genetic alterations caused by different mechanisms.

The study used more than 1,500 gene expression micro-array data to identify five major sub-types of epithelial ovarian cancer using genetic studies. These tumors have varying abilities to undergo epithelial-mesenchymal transition (EMT), where epithelial cells transform into mesenchymal cells that are associated with aggressive, invasive and metastatic cancer. The five identified sub-types were then located on an EMT spectrum which scored cells

according to their epithelial-mesenchymal tendencies. Four of the sub-types were identified as Epithelial A, Epithelial-B, Mesenchymal and Stem-A. The fifth sub-type Stem-B exhibited different behaviour and is the subject of separate research.

Further study showed that ovarian cancer cells with intermediate epithelial and intermediate mesenchymal phenotypes are more migratory, invasive and resistant to programmed cell death (anoikis). They also produce more spheroids, which is a characteristic of malignant cells derived from solid tumours. It is known that patients with epithelial sub-types have better outcomes than those with mesenchymal sub-types. When Dr Huang's team reclassified the 1,500 micro-array samples, they found that the Mesenchymal and Stem-A subtypes had higher mesenchymal scores, supporting the hypothesis that EMT contributes to the aggressiveness of solid tumours. See Figure 1 for a summary of the findings:

Sub-Type	Characteristics	Prevalence in the sampled data	Relative patient outcome
Epithelial A	Enriched in epithelial genes, low EMT score	8.78%	Better
Epithelial B		25.49%	Better
Mesenchymal	More migratory, invasive, resistant to programmed cell death (anoikis) and produce more spheroids Enriched in mesenchymal genes, high EMT score	26.79%	Poorer
Stem-A		20.48%	Poorer
Stem-B (outlier)	Unknown	12.29%	Unknown
Other		6.18%	

Together with Prof Thiery, a renowned expert in EMT, the team is now aiming to use the findings to develop novel treatment strategies to achieve personalised medicine in ovarian cancer.

“Our findings could be used to develop diagnostic kits to identify sub-types, which would give both doctors and patients a better idea of prognosis. We are also trying to find ways to reverse the EMT process. This would make mesenchymal cells less epithelial, rendering them more responsive to chemotherapy or targeted therapy,” said Dr Huang.

“After many years of basic research, an EMT-based therapeutic strategy has been conceived and is currently evaluated in preclinical trials. We hope that ovarian cancer patients not responding to chemotherapy will benefit from this new concept ,” said Prof Thiery.

The research findings were presented at the 2012 Annual Meeting of American Association for Cancer Research (AACR), for which Dr Huang was presented the 2012 AACR-Aflac Incorporated Scholar-in-training Award. She was the only awardee from a non-US institution.

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About the National University Health System (NUHS)

The National University Health System (NUHS) groups the National University Hospital (NUH), the NUS Yong Loo Lin School of Medicine, the NUS Faculty of Dentistry and the Saw Swee Hock School of Public Health under a common governance structure to create synergies to advance health by integrating clinical care, research and education.

The enhanced capabilities and capacity will enable the NUHS to deliver better patient care, train future generations of doctors more effectively and bring innovative treatments to patients through groundbreaking research.

For more information about the NUHS, please visit www.nuhs.edu.sg

About the National University Hospital (NUH)

The NUH is a tertiary specialist hospital and major referral centre for a wide range of medical, surgical and dental specialties including Cardiology, Gastroenterology and Hepatology, Obstetrics and Gynaecology, Oncology, Ophthalmology, Paediatrics and Orthopaedic Surgery.

A member of the National University Health System, it is the principal teaching hospital of the NUS Yong Loo Lin School of Medicine (YLL SoM).

With combined resources from the NUS YLL SoM and Faculty of Dentistry, the NUH is poised to meet the healthcare needs of patients, train future generations of doctors more effectively, and help develop solutions to our healthcare problems through research.

In 2007, the NUH was chosen by the Ministry of Health to develop two new national centres, the National University Cancer Institute, Singapore (NCIS) and the National University Heart Centre, Singapore (NUHCS) to meet the growing needs for cardiac and cancer treatment. The National University Cancer Institute, Singapore (NCIS) offers a broad spectrum of cancer care and management covering both paediatric and adult cancers. The National University Heart Centre, Singapore (NUHCS) brings together cardiac specialists and experts from a multitude of medical and surgical disciplines to provide a comprehensive and holistic approach to the treatment of heart problems.

In 2004, the NUH became the first Singapore hospital to receive Joint Commission International (JCI) Accreditation, an international stamp for excellent clinical practices in patient care and safety.

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