JOINT NEWS RELEASE

Singapore, 18 June 2020

NTU Singapore scientists and KKH clinicians develop urine test that identifies pregnancy outcome after threatened miscarriage

Researchers at **Nanyang Technological University, Singapore (NTU Singapore)** and clinicians at **KK Women's and Children's Hospital (KKH)** have developed a urine test that within 30 minutes, can gauge pregnancy outcomes for women presenting with signs of threatened miscarriage.

Threatened miscarriage – characterised by abdominal pain with vaginal bleeding – is one of the most common gynaecological emergencies worldwide.

According to a separate study by Duke-NUS, NTU and KKH[1], one in five pregnancies in Singapore shows signs of threatened miscarriage within the first trimester. Among pregnant women with such symptoms, one in four of them ends up losing their baby within two weeks.

Clinicians do not currently have a way of predicting their risk of miscarriage that is non-invasive. The current lab-based method assesses a pregnant woman's miscarriage risk through a blood test (serum progesterone test) that measures progesterone levels and can take a few hours.

The new test developed by NTU scientists in collaboration with doctors from KKH uses an innovative surface-enhanced Raman scattering (SERS) chip that requires a droplet of urine to screen for urine molecules associated with miscarriage risk. It does this through the chemical 4-mercaptophenylboronic acid (MPBA) which is coated on the chip. MPBA probes and selectively captures the miscarriage-related molecules pregnane and tetrahydrocortisone (THC) from the urine.

In a case-control study of 40 pregnant women who attended the Urgent O&G Centre at KKH with symptoms of threatened miscarriage, the test retrospectively identified accurately the pregnancy outcomes of all participants.

[1] Paper titled "Validation of serum progesterone <35nmol/L as a predictor of miscarriage among women with threatened miscarriage" published in *BMC Pregnancy and Childbirth,* 6 March 2017

Led by **Associate Professor Ling Xing Yi** and **Associate Professor Tan Nguan Soon** from NTU, in collaboration with KKH's **Dr Ku Chee Wai,** the study findings were published in the peer-reviewed journal ACS Nano in February 2020.

The researchers believe their initial success points the way towards a non-invasive, fast, and accurate approach for triaging pregnant women with a threatened miscarriage, identifying those who are at higher risk of a spontaneous miscarriage.

Assoc Prof Ling, of NTU's School of Physical and Mathematical Sciences, said, "Usually molecules associated with miscarriage risk are simply too dilute within the body's fluids and challenging to detect at low concentrations. To solve this problem, our group developed an innovative SERS 'confine and capture' approach and used a chemical 'targeting agent' to isolate miscarriage-related biomarkers from urine, resulting in speedy detection of miscarriage risk."

Assoc Prof Tan, a metabolic disorder expert at NTU's Lee Kong Chian School of Medicine, explained that the unparalleled sensitivity offered by the SERS test and the small sample volume required make it attractive for clinical use.

"This is even more so for cases where large amounts of sample are hard to obtain, such as tear sampling for eye disorders or breath vapour for lung diseases. Our diagnostic platform could revolutionise metabolite detection for medical conditions that are normally challenging to detect and bring testing for them out of the lab and into the clinic," said Assoc Prof Tan,

Fast detection removes undue anxiety for patients presenting with threatened miscarriage in the first trimester

When a woman presents with threatened miscarriage, a reliable and non-invasive diagnostic test would be invaluable for miscarriage risk management say the researchers. However, there is currently no point-of-care test with a quick turnaround time.

Dr Ku Chee Wai, Division of Obstetrics and Gynaecology, KKH, said, "This non-invasive toolkit will enable clinicians to predict risk of a spontaneous miscarriage in women who presents with a threatened miscarriage. Early detection will also allow these pregnant women to receive counselling, medical interventions, or be under close medical management for adverse pregnancy outcomes throughout the rest of their pregnancy. It can also allay the fears and worries of pregnant women who are at low risk of miscarriage and improve their pregnancy experience".

Associate Professor Tan Hak Koon, Chairman, Division of Obstetrics and Gynaecology, KKH, said, "As the largest academic medical centre specialising in women's and children's health in Singapore, KKH has been leading many progesterone and miscarriage-related studies for over a decade. Our research into SERS steered us towards this collaboration with NTU, advancing both KKH and NTU

towards the goal of improving the health outcomes of pregnant women and their babies everywhere in the world."

The NTU team has patented the innovation and is now looking to evaluate the performance of the toolkit in hospital settings, with the aim of commercialising the product in future.

The researchers are also working on adapting the toolkit for use in other types of health conditions.

***

Notes to Editor:

Paper titled "Multiplex Surface-Enhanced Raman Scattering Identification and Quantification of Urine Metabolites in Patient Samples within 30 min", published in *ACS Nano*, 12 Feb 2020.

*** END ***

Media contact:

Ms Junn Loh
Manager, Media Relations
Corporate Communications Office
Nanyang Technological University, Singapore
Email: junn@ntu.edu.sg

Angeline Chen
Assistant Manager
Corporate Communications
KK Women's and Children's Hospital
Email: Media@kkh.com.sg

About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,000 undergraduate and postgraduate students in the Engineering, Business, Science, Humanities, Arts, & Social Sciences, and Graduate colleges. It also has a medical school, the Lee Kong Chian School of Medicine, set up jointly with Imperial College London.

NTU is also home to world-class autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies, Earth Observatory of Singapore, and Singapore Centre for Environmental Life Sciences Engineering –

and various leading research centres such as the Nanyang Environment & Water Research Institute (NEWRI) and Energy Research Institute @ NTU (ERI@N).

Ranked amongst the world's top universities by QS, NTU has been placed the world's top young university for the past six years. The University's main campus is frequently listed among the Top 15 most beautiful university campuses in the world and it has 57 Green Mark-certified (equivalent to LEED-certified) building projects, of which 95% are certified Green Mark Platinum. Apart from its main campus, NTU also has a campus in Novena, Singapore's healthcare district.

For more information, visit www.ntu.edu.sg.

About KK Women's and Children's Hospital

KK Women's and Children's Hospital (KKH) is Singapore's largest tertiary referral centre for Obstetrics, Gynaecology, Paediatrics and Neonatology. Founded in 1858, the academic medical institution specialises in the management of high-risk conditions in women and children. A team of about 500 specialists adopt a compassionate, multi-disciplinary and holistic approach to treatment, and harness medical innovations and technology to deliver the best medical care possible.

Accredited as an Academic Medical Centre, KKH is a major teaching hospital for all three medical schools in Singapore, Duke-NUS Medical School, Yong Loo Lin School of Medicine and Lee Kong Chian School of Medicine. The 830-bed hospital also runs the largest specialist training programme for Obstetrics and Gynaecology and Paediatrics in the country. Both programmes are accredited by the Accreditation Council for Graduate Medical Education International (ACGME-I) and are highly rated for the high quality of clinical teaching and the commitment to translational research.

For more information, please visit www.kkh.com.sg.

###