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Hong Kong Sanatorium & Hospital

**For Immediate Release**

## **HKSH's IVF Centre - First in Hong Kong to Apply Next Generation Sequencing (NGS) to Pre-implantation Genetic Testing – Helps Infertile Couples Enhance Pregnancy Rate and Reduces the Chance of Transmitting Genetic Abnormality from Parents to Their Offspring**

(27 July 2016, Hong Kong) The IVF Centre of Hong Kong Sanatorium & Hospital (“the Hospital”) has always been at the technological forefront to assist couples with infertility issues since the birth of Hong Kong’s first *in vitro* fertilization (IVF) baby at the Centre in 1986. In its latest initiative, the Centre has applied advanced genomic technology, Next Generation Sequencing (NGS), to pre-implantation genetic testing. Pre-implantation Genetic Screening (PGS) and Pre-implantation Genetic Diagnosis (PGD) with sophisticated NGS technology facilitate embryo selection, which in turn help enhance pregnancy rate and decrease the potential hazard of transmitting a genetic abnormality or disease from parents to their offspring.

The first NGS-PGS baby, born in the Hospital in April 2016, has marked a new milestone in local IVF history and brought new hope to couples in need. **Dr. Joseph CHAN Woon Tong, Deputy Medical Superintendent and Head of Department of Women's Health and Obstetrics of HKSH**, said that the Hospital was the first facility in Hong Kong to have applied NGS technology to IVF service. Since service introduction in January last year, a total of 25 couples have undertaken PGS and PGD with NGS, resulting in 15 implantations conducted and 11 pregnancies reported, including the NGS-PGS baby born this April. The new service is particularly beneficial to couples having genetic diseases, repeated IVF implantation failures and recurrent miscarriages.

Dr. CHAN noted that IVF service demand has risen over the past 30 years. “There is an overall increase in service demand in different age groups but growth is particularly prominent among

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香港養和醫院有限公司  
Hong Kong Sanatorium & Hospital Limited

香港跑馬地山村道2號  
2 Village Road, Happy Valley, Hong Kong

[www.hksh-hospital.com](http://www.hksh-hospital.com)

電話 Tel : (852) 2572 0211  
傳真 Fax : (852) 2838 5186  
電郵 Email : [hospital@hksh.com](mailto:hospital@hksh.com)



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women aged 40 or above. The number of IVF cases in this particular group has jumped from about 300 cases in 1986-1995 to 1,800 in the past 10 years,” Dr. CHAN said.

He said it is believed to be related to the rising maternal age of Hong Kong women and the city’s stressful lifestyle. Government statistics show that the median age of women in Hong Kong having their first baby has increased from 26.6 in 1986 to 31.3 in 2014.

At present, infertility is affecting one out of six local couples for reasons such as ovulatory problems, tubal obstruction or adhesions, endometriosis, semen abnormality, or other unknown reasons.

To help couples tackle infertility, the IVF Centre has introduced a range of cutting-edge technologies over the past 30 years, including Intracytoplasmic Sperm Injection (ICSI), Ultrarapid Vitrification of embryos and oocytes (female’s eggs) and *In Vitro* Maturation of Oocytes. IVF treatment has a success rate of 40% in recent years whereby uterus and embryo (including eggs, sperms, and fertilized eggs) are two main reasons affecting the outcome. Studies in recent years have also shown that about 50% of embryo-related infertility problems are related to chromosomal abnormalities.

**Dr. TANG Oi Shan, Specialist in Reproductive Medicine of the Hospital** said, “Pre-implantation Genetic Diagnosis (PGD) is a technique that combines IVF and genetic testing on the embryos to avoid transmission of a genetic abnormality or disease, for example, Thalassaemia or unbalanced translocation of chromosomes. Detection of genetic abnormality of the embryos before implantation can also allow the transfer of genetically normal embryos, thus avoiding the need for termination of pregnancy and its associated physical and psychological damage. Besides, the same technique of genetic testing can be used in Pre-implantation Genetic Screening (PGS) to select embryos with normal number of chromosomes for transfer. This will improve the success rate of IVF, reduce miscarriage rate and fetal anomaly due to aneuploidy (abnormal number of





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chromosomes) which is commonly found in women with recurrent miscarriages, repeated IVF failures and at advanced age.”

“The service of PGS and PGD was introduced in 2008 at the IVF Centre of HKSH. Currently, pre-implantation testing on embryos has become an important part of our IVF service as aneuploidy of the embryos is well recognized as an important factor for miscarriage, IVF failure and fetal anomaly. In addition, the advance in genetic testing technology such as NGS is also essential,” said Dr. TANG.

**(Please refer to *Supplementary Information* for details of Pre-implantation Genetic Screening (PGS) and Pre-implantation Genetic Diagnosis (PGD) )**

**Dr. Edmond MA Shiu Kwan, Director of Clinical Pathology & Molecular Pathology Division and Specialist in Haematology of the Hospital,** pointed out that clarity and flexibility are the two major benefits of using NGS technology for PGS or PGD. “With NGS technology, DNA-based screening and diagnosis of inherited gene mutations or chromosomal abnormalities can be conducted in one go. Compared with conventional testing methods for PGS and PGD, namely Fluorescence *in-situ* hybridization (FISH) and Array Comparative Genomic Hybridization (aCGH), NGS has outperformed the two in providing results with higher sensitivity, readability and signal-to-noise ratio,” Dr. MA noted.

As the first private hospital in Hong Kong to provide genomics-enabled clinical diagnostic service supported by NGS technology, the Hospital has since 2011 adopted this advanced technology in genetic screening of hereditary breast cancers, and has now extended its application to pre-implantation genetic testing.



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“NGS technology also allows massively parallel gene sequencing to be done, thus enabling the detection of all gene mutations and simultaneous analysis of multiple samples within a shorter timeframe, while also requiring only a minute amount of cells for testing.”

“NGS analysis provides detailed information to help embryologists and the medical team to pick the most suitable embryos for implantation. This will improve pregnancy rate, lower the risk of miscarriage and/or passing on hereditary diseases from parents to their offspring. It is expected that genetic testing prior to implantation using NGS technology will be more commonly applied clinically in the near future,” Dr. MA added.

The doctor responsible for Hong Kong’s first NGS-PGS baby, **Dr. Ingrid LOK Hung, Specialist in Reproductive Medicine of the Hospital**, said that among the first batch of 25 couples receiving PGS and PGD with NGS technology, the pregnancy rate of NGS-PGS and NGS-PGD is 67% and 83% respectively. “It is evident that applying NGS for PGS and PGD is beneficial to embryo selection for implantation and therefore enhances the implantation and pregnancy rate and reduces miscarriage rate associated with abnormal embryos,” Dr. LOK said.

She however reminded that while pre-implantation genetic testing facilitates careful choice of embryos for implantation, the technology is not without limitations. “Though minimal, there is a potential risk that an embryo might be damaged when one or a few cells are removed from it during embryo biopsy. Another limitation of genetic testing is that while it is useful for embryo selection, the procedure cannot rectify genetic abnormalities. Furthermore, test results may have discrepancies and therefore proper prenatal diagnosis for pregnant mothers with PGS/PGD babies is still recommended.”

Looking ahead, Dr. Joseph CHAN said the Hospital’s IVF Centre will continue to provide patient-centered and comprehensive IVF service through a team approach. “Apart from gynaecologists/reproductive specialists, urologists, endocrinologists, haematologists/pathologists,





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embryologists, molecular geneticists, clinical psychologists and professional nurses, our service has recently been further strengthened with a clinical geneticist coming on board in July who will provide genetic counselling and diagnosis service to couples in need,” Dr. CHAN added.

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## Supplementary Information

### Pre-implantation Genetic Screening (PGS)

#### **Technology :**

Pre-implantation Genetic Screening (PGS) is a comprehensive chromosome screening as part of IVF to examine **the number of chromosomes in the embryos** before implantation to the uterus. PGS is recommended for couples with:

1. Advanced maternal age
2. Recurrent miscarriages
3. Repeated IVF failures

Some implantation failures are due to the incorrect number of chromosomes in the embryos. PGS aims to determine if the embryos contain the correct number of chromosomes, i.e. 46 chromosomes, to avoid transplanting embryos with chromosomal abnormalities into the uterus. PGS thereby helps improve the implantation and pregnancy rates, reduce the risk of miscarriage and reduce the potential hazards of delivering a baby with chromosomal abnormalities, e.g. Down syndrome, Edwards syndrome and Turner syndrome.

#### **Procedure:**

To perform PGS, an embryo biopsy on Day 5 will be conducted to extract 3 to 6 cells (Trophectoderm) from a blastocyst with 200 to 300 cells. The embryos after biopsy will be frozen individually for later use. NGS is performed to examine the number of chromosomes on the embryos and identify those with normal number of chromosomes for implantation. PGS test result will be ready in around two weeks.



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## **Pre-implantation Genetic Diagnosis (PGD)**

### **Technology :**

Pre-implantation Genetic Diagnosis (PGD) is used to test for a specific genetic disease when **one or both of the couple has/have a known genetic abnormality**. PGD is recommended if either one of the couple has:

1. A serious genetic disease themselves or is a carrier of that particular disease
2. A family history of a serious genetic disease
3. A child with a serious genetic disease

PGD is beneficial to the above couples as it targets specific inherited gene mutations or chromosomal defects in embryos. PGD reduces the chance for the transmission of serious genetic abnormalities or genetic diseases from parents to their offspring. Such genetic abnormalities include Thalassemia and unbalanced translocations. It can also avoid the traumatic experience related to termination of pregnancy.

### **Procedure:**

Similar to PGS, an embryo biopsy of extracting 3 to 6 cells from the embryo will be conducted in performing PGD. The embryos after biopsy will be frozen individually for later use. In addition, blood samples from the couple and even semen specimen from the husband may also be collected for genetic analysis. NGS is performed to examine specific single gene related to the genetic diseases and balanced translocations. PGD result will be ready in about one month.

As the genetic conditions or inherited diseases may vary in individual cases, in-depth consultation, examination and assessment will be performed by specialists in reproductive medicine and clinical geneticists to conduct a customized genetic and chromosome analysis and diagnosis before any testing or procedures will be provided.





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## **Case Sharing**

### **Case 1: The first PGS baby using NGS technology to screen normal embryo for implantation in Hong Kong**

Mrs. A is about 40 years old. She has failed to get pregnant in the past ten years despite various treatment attempts including repeated *in vitro* fertilization cycles. She and her husband visited HKSH's IVF Centre in early 2015. Detailed examination concluded that the implantation failure in the past was likely to be associated with chromosomal abnormalities in embryos due to advanced maternal age. Mrs. A was advised to undertake PGS as part of IVF treatment to help select embryos with normal chromosomes for transfer.

“We obtained 4 blastocysts for screening following Mrs. A's first IVF treatment in mid-2015. Only two blastocysts contained normal chromosome copy numbers, while another 2 blastocysts had wrong number of chromosomes, or aneuploidy, Trisomy 16, Trisomy 16 & 20 which likely would fail to implant or result in miscarriage,” explained Dr. LOK.

After assessment, one normal embryo was selected for implantation. Mrs. A was successfully pregnant and gave birth to a healthy baby girl in April 2016, the first NGS-PGS baby in Hong Kong.

### **Case 2: Simultaneous genetic testing of PGS and PGD**

Mrs. C, aged 31, had two miscarriages after natural pregnancy since 2007. The couple visited HKSH's IVF Centre in late 2015. The result of genetic test revealed that Mrs. C's chromosomes were normal, but her husband was found to have chromosomal abnormalities.

With a known genetic abnormality, Mrs. C was advised to receive IVF treatment with PGD and PGS at the same time. Among those 7 blastocysts obtained for genetic testing, 5 blastocysts had unbalanced translocation and 1 was aneuploid (Trisomy 22). Only 1 normal blastocyst was suitable for implantation.

The normal blastocyst was implanted in early 2016, and Mrs. C is now in her 23-week pregnancy.





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### **Hong Kong Sanatorium & Hospital**

Hong Kong Sanatorium & Hospital is one of the leading private hospitals in Hong Kong. With the motto “Quality in Service Excellence in Care”, the Hospital is committed to serving the public as well as promoting medical education and research.

### **IVF Centre at Hong Kong Sanatorium & Hospital**

The IVF Centre at Hong Kong Sanatorium & Hospital has been offering excellent patient care and *in vitro* fertilization (IVF) services to infertile patients since 1986. Our dedicated team – gynaecologists / reproductive specialists, urologists, endocrinologists, haematologists/pathologists, embryologists, molecular geneticists, clinical psychologists and professional nurses – is well experienced in the field of assisted reproductive technologies (ART), which have been successfully applied at our centre in treating male and female infertility.

Tel: (852) 2835 8060

Email: [ivf@hksh-hospital.com](mailto:ivf@hksh-hospital.com)

For media enquiries, please contact:

Department of Corporate Affairs, Hong Kong Sanatorium & Hospital

Mandy SO Tel: 3156 8077

Winnie POON Tel: 3156 8071

Email: [media@cad.hksh.com](mailto:media@cad.hksh.com)





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**Photo Captions:**

- 1) Dr. Joseph CHAN Woon Tong, Deputy Medical Superintendent and Head of Department of Women's Health and Obstetrics (second from left), together with Dr. TANG Oi Shan (second from right) and Dr. Ingrid LOK Hung (first from right), Specialists in Reproductive Medicine, Dr. Edmond MA Shiu Kwan, Director of Clinical Pathology & Molecular Pathology Division and Specialist in Haematology, explain that applying Next Generation Sequencing (NGS) for Pre-implantation Genetic Testing (PGS and PGD) is beneficial to embryo selection as part of IVF treatment for implantation which would enhance the implantation and pregnancy rates and reduce risks of miscarriage.





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- 2) (From left) Dr. Edmond MA Shiu Kwan, Director of Clinical Pathology & Molecular Pathology Division and Specialist in Haematology, Dr. Joseph CHAN Woon Tong, Deputy Medical Superintendent and Head of Department of Women's Health and Obstetrics, Dr. Ingrid LOK Hung and Dr. TANG Oi Shan, Specialists in Reproductive Medicine take photo with the first NGS-PGS baby girl in Hong Kong.





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- 3) The dedicated team of the IVF Centre of HKSH has strived to provide patient-centered and comprehensive IVF service to couples with infertility issues over the past 30 years.

(From Left) Ms. LAW Yuen Ching, Coordinator of IVF Centre of HKSH, Dr. Chris CHAN Tsun Leung, Molecular Geneticist, Dr. Stephen LAM Tak Sum, Clinical Geneticist, Dr. Edmond MA Shiu Kwan, Director of Clinical Pathology & Molecular Pathology Division and Specialist in Haematology, Dr. Joseph CHAN Woon Tong, Deputy Medical Superintendent and Head of Department of Women's Health and Obstetrics, Dr. Ingrid LOK Hung and Dr. TANG Oi Shan, Specialists in Reproductive Medicine, Dr. HO Pak Chung and Dr. Joyce CHAI, Specialists in Obstetrics & Gynaecology, Ms. Karen ROCHA, Embryologist and Ms. NG Yuen Yee, Nurse of IVF Centre.

