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Inside Story

Are COVID-19 Vaccines Safe for Mothers and their Newborn Babies?

It has been some time since the vaccines passed the clinical trials and have been administered to the public, yet there are still speculations about its safety for pregnant women and its effect on newborn children. Recently, a study titled "COVID-19

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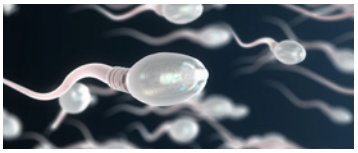

Modifying Sperm Genome Structure Affects Fertility

In a study spearheaded by Dr Aurora Ruiz-Hererra of the Universitat Autònoma de Barcelona, it was observed that changes to the three-dimensional structure of sperm chromosomes throughout sperm development can affect fertility in mice.

According to this research, the dynamics of the genome assembly during the gametes formation and recombination is impacted by the presence of chromosomal rearrangements; thus, affecting sperm viability.

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IVF-Born Babies, No Growth Dissimilarities

With the growing number of babies born via assisted reproductive technologies (ART) through the years, several studies have been keen on doing a follow up on these children and assess if they have preeminent health risks compared to their naturally conceived counterpart.

In recent years there has been a lot of interesting researches concerning this field. A particular study of interest is one that was published in the journal Fertility and Sterility wherein the researchers examined the differences in DNA

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Are COVID-19 Vaccines Safe for Mothers and their Newborn Babies?

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vaccine response n pregnant and lactating women: a cohort study" was published in the American Journal of Obstetrics and Gynecology (AJOG) by researchers from Brigham and Women's Hospital, Massachusetts General Hospital (MGH), Ragon Institute of MGH, Harvard and MIT was made to analyse the effectiveness of mRNA-based vaccines (Pfizer-BioNTech and Moderna) to produce antibodies against COVID-19 virus in pregnant and lactating women.

Currently being the largest study of this kind, it was able to quantify, evaluate and compare the vaccine-induced antibody titers among its sample population having 131 vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant). According to the study, "titers were equivalent in pregnant and lactating compared to non-pregnant women (median [IQR] 5.59 [4.68-5.89] pregnant, 5.74 [5.06-6.22] lactating, 5.62 [4.77-5.98] non-pregnant, p=0.24)." These antibodies were also present in the umbilical cord blood and breast milk samples which indicate that COVID-19 immunity can be passed on from pregnant women to their newborn children. The study was also able to conclude that vaccine-induced immune response was significantly greater than the normal body response to natural infection.

Having known these study findings, it is strongly advised and recommended to have pregnant women who are more at risk of COVID-19 infection get vaccinated and pass on the immunity to their children. This study also reaches out to researchers to include this group who displayed the willingness to participate in vaccine research trials which eventually will make the common knowledge of COVID-19 vaccines being dangerous to this group, obsolete.

Modifying Sperm Genome Structure Affects Fertility

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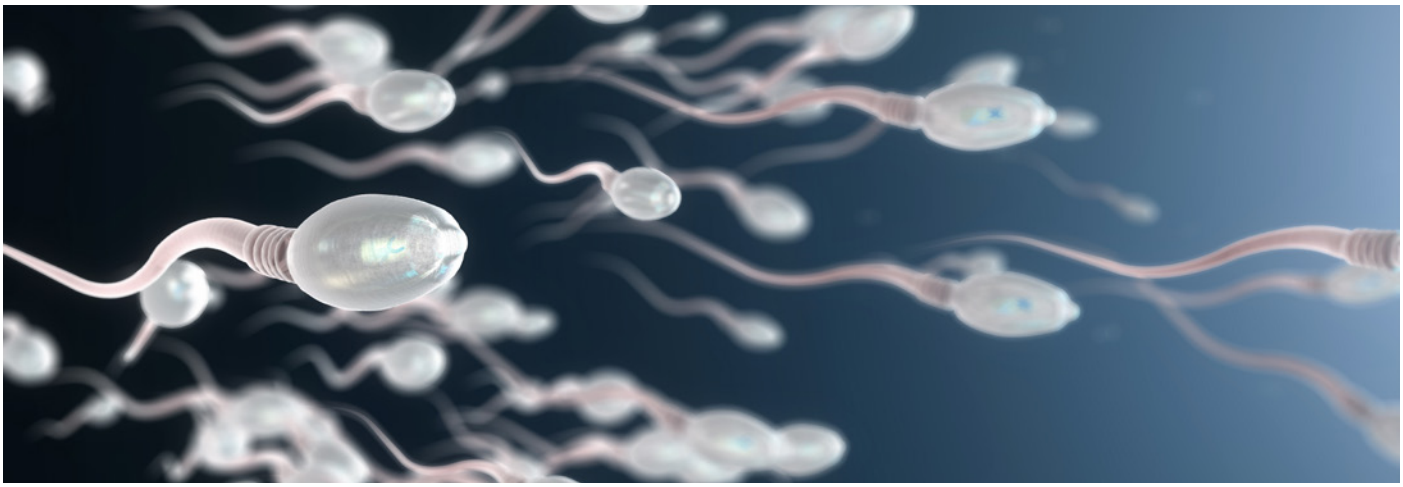

The results of the study were published in Nature Communications, wherein the 3D genome organisation in wild population (of house mice) germ cells were described. It is said that the study signifies a momentous progress in researches involving generation and regulation of gamete formation's genome structure and function.

In a nutshell, the process implicates sexually-reproducing organisms producing haploid gametes via two consecutive cell divisions preceded by a one-time round of genome replication. During meiosis, genome organization is strongly regulated to bring about recombination, a vital mechanism that sustains the organism's genetic diversity through the exchange of the progenitors' homologous chromosomes. Simultaneous to this process is letting the resulting chromosomes to be transferred innately, without changes in their number and structure, to the next generation.

The researches see this as a breakthrough since the existence of these fusions could have an emergent and transformative role in uncovering parts of the genome to various regulatory mechanisms. The discovery in this study is a great tool in the understanding of processes impelling fertility and genetic condition in human beings.

**** Original story from Universitat Autònoma de Barcelona*

IVF-Born Babies, No Growth Dissimilarities

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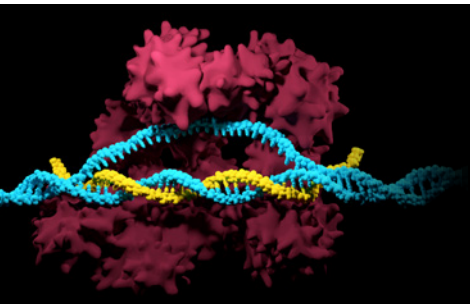
methylation at birth and in early childhood (eight to ten years) in children born in New York State from 2008 to 2010. DNA methylation is a biological mechanism used by cells to control gene expression. In this process, methyl groups are added to the DNA molecule, and as such, it can change the activity of a DNA segment without changing the sequence. Furthermore, the addition of methyl groups to DNA shifts genes off which in turn inhibit protein production. Such addition and removal of methyl groups from DNA occur throughout and individual's lifetime. Noteworthy to mention is the fact that such changes can be prompted by any of the treatments used within the IVF procedures. Such treatments include the use of hormonal therapy, and even the modifications in the culture medium in which the embryos develop.

Study analysis show that there were decreased levels of DNA methylation at certain regions of DNA in newborns conceived via IVF. These observed differences were from 157 newborns conceived via IVF and 520 spontaneously-conceived newborns. Also, they did not observe any differences in DNA methylation in newborns conceived via intrauterine insemination (IUI) or ovulation induction (OI).

In conclusion, Dr Edwina Yeung, the principal author of the research conducted at the Eunice Kennedy Shriver National Institute of Child Health and Human Development in Maryland, mentioned that the study found small differences in DNA methylation at birth and that these were not observed during early childhood. Also, it was noted that there are no differences in children's growth and development – a comforting and reassuring statement for couples who have conceived via ART and to those considering such treatments.

**Original news from https://ivf.net/



Controlling *A. aegypti* Populations using Sterile Insect Technique

Mosquitoes have been present since the early ages and have caused several infections that have been life-threatening to man. One of its species particularly is the *Aedes aegypti* which is commonly known to transmit dengue, yellow fever, Zika, and several other viruses. These species of mosquitoes have a very large population scattered across the world and have proven to be problematic especially during rainy days. Scientists have tried to control the population of *Aedes aegypti* previously by using chemicals and radiation to sterilize the male mosquitoes before they are released into the environment. However, this approach was deemed ineffective because although the technique did make the mosquitoes sterile, it also negatively affected the health of the male mosquitoes to the extent of affecting their capability of mating with their female counterparts.

With the discovery of CRISPR-Cas9 gene editing, a vast number of studies have been done to explore the limits of its use, one of which includes the Sterile Insect Technique (SIT). A study by Chen, J. et. al. published at Proceedings of the National Academy of Sciences of the United States of America (PNAS) last June 1, 2021, used this very technique to create sterile male *A. aegypti* mosquitoes by creating a null mutation in the *A. aegypti* ß2-*tubulin (B2t)* gene that eliminates male fertility. In this study, they have allowed these *B2t* sterile males to mate with wild-type females and observed that the female did not produce progeny also even after a wild-type male has mated after the *B2t* male. They also simultaneously introduced *B2t* and wild-type males with wild-type females and have found a larger number of the *B2t* males relative to the wild-type males.

By implementing the SIT using the CRISPR-Cas9 gene-editing technology on a larger scale of the population of *A. aegypti*, it gives the possibility of reducing the future generation population of these invasive mosquitoes. As the study suggested, it would be more effective when *B2t* males are repeatedly released to the environment to overpopulate wild-type mosquitoes.

Cervical Cancer and Its Effect on Fertility

According to World Health Organization (WHO), cervical cancer is the fourth most common cancer in women. In the year 2018, around 570 000 women were diagnosed with cervical cancer worldwide and about 311 000 women died from the disease. However, cervical cancer is one of the most successfully treatable forms of cancer if it is diagnosed and managed at early stage. Though, for those patients who were diagnosed in late stage of the cancer can still be treated with proper treatment and palliative care.

What is Cervical Cancer?

Cancer is a type of disease wherein some cells in the body grows in an uncontrollable way and spread to other parts of the body. It happens when there is a mutation in cells that grows out of control forming new abnormal cells. In case of cervical cancer, mutation happened on the woman's cervix, a part that bridges uterus to the vagina. This cancer can metastasize to other parts of the body such us lungs, bladder, liver, vagina and rectum. This cancer is brought about by the virus called Human Papilloma Virus (HPV). There are different strains of HPV, but only HPV-16 and HPV-18 cause cervical cancer.

Risk Factors

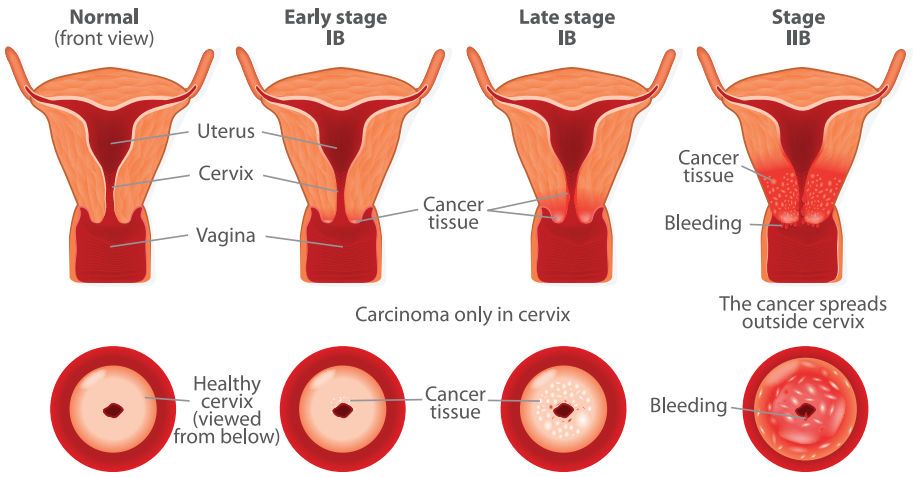
Any woman can be at risk of having a cervical cancer, especially for those women aging 30 years old and above. But here are some of the factors that can heighten the risk of having cervical cancer.

1. Sexual History

Becoming sexually active at young age (18 years old and below) and having multiple sexual partner can increase risk of having cervical cancer.

2. Smoking

Tobacco smoke has different cancer-causing chemicals that are absorbed by the body through lungs then carried in the bloodstream throughout the body. Researchers found tobacco by-products in the cervical mucus of women who smoke. They believed that these substances can damage the DNA of the cells found in cervix and leads to mutation that causes cervical cancer.



3. Long term use of birth control pills

Oral contraceptives might increase the risk of cervical cancer by changing the cervical cells to persistent infection with high-risk HPV types. According to the study, women who have used oral contraceptives for 5 or more years have a higher risk of cervical cancer than those who are not. However, the risk goes back down over the years after the woman stop taking oral contraceptives.

4. Chlamydia infection

This infection is another type of sexually transmitted infection, certain studies show that Chlamydia helps in the growth of HPV in the cervix that increases the risk of cervical cancer.

5. History of Cancer

Woman in the family that is diagnosed with cervical cancer has more likely to have one. Due to the inherited mutation in genes related to HPV infection making them more susceptible to infection thus increasing the risk of having cervical cancer.

How Cervical Cancer Affects your Fertility?

Having cervical cancer is troublesome, especially for women under "childbearing age". Cancer treatments may require therapies that involves radiation, drugs that will destroy cancer cells such as chemotherapy or surgical operation such as removal of tissues with cancer cells. And by such, those kinds of treatment can damage the patient's reproductive system since the target organ of the cancer is the cervix as well as the target organ of the chosen treatment. It may cause

difficulty in conceiving or worse permanent infertility to the patient being treated.

Chemotherapy

When a patient undergoes chemotherapy, the drugs will kill both cancer cells and healthy cells. There is a possibility that even the egg cells stored in the ovaries could be damaged too. It will put the patient at risk of miscarriage and early menopause.

Radiation Treatment

On the other hand, if the patients choose to use radiation therapy, high energy rays are used to aim the patient's pelvis to kill the cancer cells. This will expose the ovaries to radiation that will damage the egg cells stored in ovaries resulting to premature menopause. Moreover, the risk of miscarriage also increases due to the exposure of patient's uterus to the radiation. Radiation may cause scar to the uterus and reduces blood flow in that area.

Conization

This type of surgery is used for patients with small growths of tumor in their cervix. This procedure removes the cancerous tissues surrounding the cervix. But doing this procedure may scar your cervix and may lead to a higher risk of miscarriage or infertility.

Radical Trachelectomy

This procedure involves taking out some of the surrounding tissues, some portion of upper vagina and nearby lymph nodes. In doing this procedure, there is 70% chance of carrying a pregnancy term. Though the pregnancy will be considered as high-risk and will need to deliver your baby in C section.

But in some condition, chemotherapy, radiation treatment or hysterectomy (removal of uterus or cervix) are the options needed to treat the patient. Chemotherapy and radiation treatment can destroy the eggs and damage the uterus. In order to preserve the patient's fertility, it is recommended to have egg freezing before the procedure takes place. By egg freezing and with the help of assisted reproductive technology called IVF, the patient is still capable of bearing a child either using her own uterus or through surrogacy.

As you can see, cervical cancer can make the patients infertile by damaging some parts of their reproductive organs. But with the help of the innovations in our health technology nowadays, it is still possible to conceive a child. Egg freezing together with in vitro fertilization (IVF), as the most common assisted reproductive technology, can help cancer patients to have their offspring even after doing such procedures.

The Use of Preimplantation Genetic Testing in Improving IVF Cycles

When it comes to pregnancy, the number one priority is the baby's health. Many cases of pregnancy even with a traditional way or with the help of IVF, ended up unsuccessful (miscarriage, stillbirth neonatal infant loss, etc.). Failed pregnancies may occur because of different reasons such as low implantation rate due to abnormal uterine lining, hormonal problem, poor quality of the embryo, ectopic pregnancy, etc. So, when advancement in reproductive technology takes place, another milestone has been discovered that helps in improving the pregnancy success rate, especially when undergoing IVF treatment. This technology is called Preimplantation Genetic Screening (PGS) also known as Preimplantation Genetic Testing for Aneuploidy (PGT-A) and Preimplantation Genetic Diagnosis (PGD).

Preimplantation Genetic Diagnosis (PGD)

Preimplantation Genetic Diagnosis or PGD is typical genetic testing for embryos, the difference is that PGD is a test for specific genetic disease while PGS is a general screening for embryo normalcy. Moreover, PGD is not a general screening test; it is more of an examination of one specific gene for a known potential disorder. This test can be used for testing disorders that would be fatal to the fetus as well as diseases that may not affect the children as they grow older. This is also used to know if there is presence of a genetic defect such as BRCA-1 which can be a carrier of ovarian or breast cancer. It can also aid in diagnosing different single-gene disorders such as cystic fibrosis, sickle cell anemia, hemochromatosis, Tay-Sachs, etc. The main purpose of this test is to know beforehand if there is a heritable disease or genetic problem present and then prevent it from passing to their offspring by only transferring the embryos that don't carry the genes for those diseases.

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The Use of Preimplantation Genetic Testing in Improving IVF Cycles

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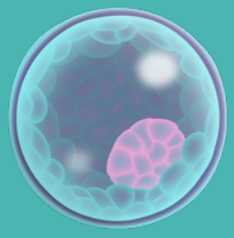
Preimplantation Genetic Screening (PGS)

Preimplantation Genetic Screening or PGS is a genetic testing done on the embryos which are produced with the help of in vitro fertilization. This test is used to evaluate the embryo's health by testing the presence or absence of normal number of chromosomes (46 chromosomes are the normal number in humans). A small number of cells are taken from the embryo through biopsy then the genetic makeup of these cells is tested and analyzed in a genetic laboratory. This test is used to choose which of the embryos is genetically normal and healthy that can be transferred to the uterus for a potential pregnancy. This genetic screening increases the pregnancy rate in an IVF cycle as well as lowers the chance of miscarriage by ensuring that only genetically healthy and able to develop embryos are being transferred. PGS is useful especially for those older women who have lower egg quality which are prone to producing embryos with genetic problems.

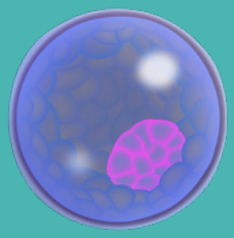
PGS Results

Since this test is screening whether the embryo contains a normal or abnormal number of chromosomes, the results are reported as:



• **Normal or Euploid**

This means that the embryo has the right number of chromosomes and has a higher chance of survival rate during the implantation procedure.

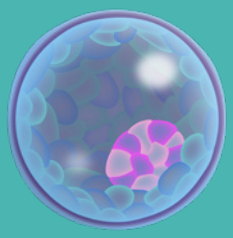


• **Abnormal or Aneuploid**

Aneuploid means that the cells retrieved from the embryos contains the wrong number of chromosomes, either it has missing pair or having extra pair of chromosomes. Aneuploid embryos most likely failed to develop due to some genetic defect and one of the most common causes of miscarriage, however, some aneuploids can luckily survive but then will manifest a genetic condition (most common is Down Syndrome caused by trisomy in chromosome 21).

Aneuploidy can be classified as:

a. **Nullisomy** – if one entire chromosome pair is missing
b. **Disomy** – if there is an extra copy of one entire chromosome
c. **Monosomy** – if there's only one pair of chromosomes
d. **Trisomy** – if there's an extra copy of one in a pair of chromosomes

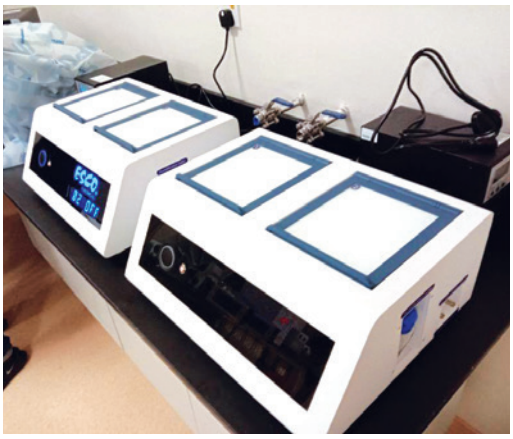


• **Mosaic**

Mosaic is also a type of chromosome abnormality wherein there were some normal and abnormal cells present in the embryo. Mosaic embryos may have about 20% – 80% abnormal cells and these embryos have a much lower chance of surviving rate which is around 15%.

Preimplantation genetic diagnosis and screening can be included as part of in vitro fertilization. But these tests are optional and not automatically performed every IVF treatment. Moreover, it is important to know that are only used to detect some defects on the embryos and not to produce "designer babies" or genetically engineered babies. PGS and PGD may indeed allow the parents to know the sex of their offspring but it can't determine the embryo's features like the color of the hair, the eye or the possible child's height, or anything other than the presence of an abnormal number of the chromosome or specific genetic defect.

Events Highlights 2nd Quarter of 2021



Product Installation in Malaysia (April 05, 2021)

Two units of Mini MIRI® Humidity incubators were installed at the Hospital Raja Permaisuri Bainun (HRPB) in Ipoh, Malaysia. Currently the third largest Ministry of Health Hospital in the entire Malaysia, HRPB continues to provide fertility treatment to couples wanting to have a baby. IVF procedure was first made available at the Raja Permaisuri Bainun Hospital in 2008.

Esco Malaysia TL technology and embryo culture management webinar (April 21, 2021)

As part of Esco Medical's intention of continuously providing educational learning experiences to IVF professionals across the globe, the Esco Malaysia hosted another webinar for IVF professionals across Malaysia last April 21, 2021. The 2-hour webinar talked about time – lapse (TL) technology, embryo culture management, and an overview of Esco Medical's product portfolio.

John Frederick Manalo (Application Specialist) and Mark Lester Sotelo (Product Specialist) served as the webinar's speakers. During the session, discussion about the benefits of TL technology, essential IVF laboratory practices in managing embryo culture, and the unique design and feature of the MIRI® TL were highlighted. Esco Medical has been conducting several online seminars and trainings as the company's way of keeping customers up-to-date with advancement in the field of reproductive medicine and assisted reproductive technology.

Left: Product Installation in Malaysia

ASPIRE 2021 - Asia Pacific Initiative on Reproduction Congress (April 30 – May 2, May 8 – 9, 2021)

With the challenges posed by the Covid-19 situation since last year, most exhibits and conferences (big or small) were put on hold; others went for the online route. ASPIRE (or the Asia Pacific Initiative on Reproduction) Congress is one of the largest Assisted Reproductive Technology (ART) events in the Asia-Pacific region was supposed to happen in Manila, Philippines last year. Eventually, the organizers pushed it this year and were done virtual.

Esco Medical participated as one of the sponsors at the 10th ASPIRE Congress. With its purpose of promoting awareness of infertility and ART, and improving infertility-related services in the Asia-Pacific region", the virtual congress, was a success as ART professionals and industry personnel from all over the world attended and participated in the various scientific sessions and exhibits.

Scientists in Reproductive Technology (SIRT) Meeting (May 1 – 2, 2021)

The Scientists in Reproductive Technology (SIRT) is a sub-group representing the scientific membership of The Fertility Society of Australia. SIRT holds an annual meeting wherein members come together for updates and promotion of professional excellence amongst the scientists working in the field of assisted reproduction and fertility.

Esco Medical has been a constant partner and support in achieving SIRT's role of promoting education and training of scientists working in reproductive technologies; as well as the promotion of research and dissemination of scientific information within the membership. And despite the virtual staging of the meeting, SIRT this year emerged as a success.

Esco Medical sponsors a CRB-hosted webinar (May 13, 2021)

The College of Reproductive Biology (CRB), a special interest group of the American Association of Bioanalysts (AAB), has been hosting a series of educational webinars. The CRB provides a focused opportunity for andrologists and embryologists to communicate with each other, wherein such professionals are able to share ideas and knowledge, and foster collaborations.

Together with Esco Medical and other IVF companies as sponsors, the webinar on "The Sixth Vital Sign: What Sperm Are Trying to Tell Us and Optimizing Sperm Extraction for ART Success" was successfully held last May 13, 2021. The webinar was presented by Michael L. Eisenberg, M.D. of Stanford University School of Medicine, Stanford, California.

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Egyptian Foundation of Reproductive Medicine and Embryology (EFRE) 2021 (June 2 – 4, 2021)

The first ever Egyptian Foundation of Reproductive Medicine and Embryology (EFRE) Scientific Conference and Expo were held at the Hilton Cairo Heliopolis from June 2-4, 2021. The scientific congress focused on the innovations in reproductive medicine with an intensive and provocative program for its attendees.

Esco Medical, through its exclusive distributor (Egyptian Import Office – EIO), participated at the ERFE Expo by exhibiting two of Esco Medical's top-notch products – the MIRI® TL and the Mini MIRI® with SAFE Sens.

In behalf of the entire Esco Medical team and our partner, EIO, we extend our congratulatory remarks to the organizers of EFRE 2021 for staging a successful event especially in this time of a pandemic. And we thank all of you who dropped by our exhibited products.

Dubai MIRI® TL Workshop 2021 (June 25 – 26, 2021)

Esco Medical – Dubai quarters held a MIRI® TL workshop for its time-lapse incubator customers. The participants had the opportunity to work with the MIRI® TL time-lapse system during a hands-on session at the Conrad Hotel Dubai, United Arab Emirates.

Morten Kristensen, Application Specialist from Esco Denmark, served as the workshop's speaker and facilitator. Kristensen discussed the benefits of choosing time-lapse over conventional incubators, dish handling, embryo loading, starting a time-lapse, embryo annotation and selection.

Kudos to Mehrdad Makky (Business Development Manager, MENA & Africa), and the entire Esco Dubai office for successfully organizing this workshop. We would also like to extend our gratitude to all MIRI® TL customers and professionals who attended the said event.

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Users of Esco Medical products should not hesitate to contact us if there are any unclear points or ambiguities in this newsletter.

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