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Next Generation IVF

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It was on the 25th of July 1978 at Oldham General Hospital in Oldham, UK, when it all started. The birth of Louise Brown, after the passionate efforts of the "fathers" of contemporary IVF, Sir Robert G. Edwards and Dr Patrick Steptoe, provided us the first tools to create new horizons in modern IVF.

Since then, we have invented the most sophisticated embryo culture incubators employing mixed gases in order to mimic the uterine environment. We have developed culture media that can sustain embryo development to blastocyst stage. We have been able to perform ICSI with all forms of spermatozoa achieving remarkable fertilization and pregnancy rates, while the application of preimplantation genetic diagnosis (PGD) has allowed the prevention of pregnancies affected by genetic disorders.

The application of oocyte and embryo vitrification technique and the manual vitrification protocols developed recently guarantee a 100% post-thaw survival rate. This has revolutionized oocyte and embryo cryopreservation and generally the management of the IVF cycle. Hyperstimulated patients, patients undergoing blastocyst biopsy for PGD purposes or must-cancel embryo transfer cases for other reasons may now have the same, if not increased, live birth chances with the fresh embryo transfer cycles by vitrifying their oocytes or embryos.

And where do all these innovations stop? The scepticists may think that we have reached a limit to the therapeutic applications of IVF. The truth is though that we have just arrived at the doorstep of a new era in human assisted reproduction. The era of "Next Generation IVF", where gamete and embryo manipulation and micromanipulation will play a key role.

The evidence for that has already arrived. It was only recently that Zhang and colleagues [1] announced a polar body transplantation technique in order to restore the developmental potential of oocytes to blastocyst stage in cases of repeated embryo fragmentation. In addition, Zhang and colleagues [2] have reported a pregnancy derived from human zygote pronuclear transfer in a patient who experienced embryo developmental arrest after IVF, while others claim to have achieved the first live births from such techniques. The idea of polar body, pronuclear or spindle transplantation to donated cytoplasts is highly likely to transform the IVF of the future.

Gamete manipulation such as the artificial oocyte activation in order to enhance post-ICSI low fertilization rates has also been reported. In their work, Ebner and Montag [3] have shown that the use of calcium ionophore may salvage total or near total fertilization failures post-ICSI, while

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Economou and colleagues [4] have reported the combination of calcium ionophore A23187 and GM-CSF cytokine to not only artificially activate human unfertilized oocytes 18 hours post-ICSI, but also to enhance their developmental potential to form chromosomally normal blastocysts.

Gamete and embryo modification techniques employing genome editing tools such as the CRISPR/Cas9 system for targeted genome editing, may allow a whole new intervention in future IVF: the genome editing of embryos bearing a genetic defect or an inherited gene disorder and the transformation of these embryos into healthy ones.

The first attempts of in vitro gametogenesis have been made years ago, but recently new discoveries have fuelled the field. The potential of the in vitro development of gamete cells from induced pluripotent stem cells seems closer than ever. This development could be precious for IVF patients whose current treatment alternative is gamete donation.

Considering all the above it is more than obvious that we stand at the dawn of a new amazing era in IVF. Next generation IVF will combine gamete and embryo manipulation and micromanipulation for the benefit of the IVF patient. All these new weapons though have to be used wisely by the clinical embryologist and the reproductive physician. Strict bioethical rules have to be set and followed in order to avoid mistakes that could lead to an unfair misuse of this valuable "arsenal". Only then, may the full benefit of these technologies be transferred to the well-deserved IVF patient.

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