TOPIC – INNOVATIONS IN EMBRYOLOGY

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INTRODUCTION

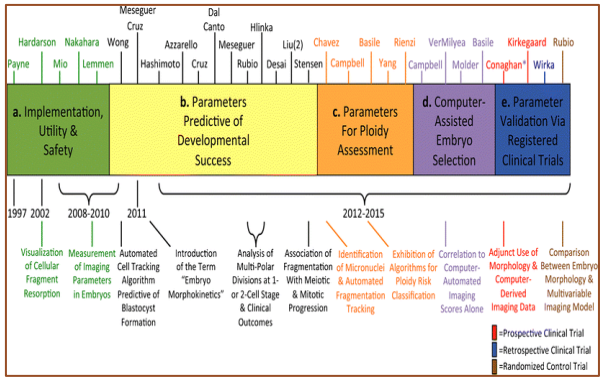
ART involves fertilizing egg with sperm in a laboratory dish and transferring resulting embryo into uterus. Technological innovations being developed and perfected currently hold the potential to change the field of ART in still more dramatic and exciting ways well into future. Such innovation includes: EMBRYOSCOPE (Time lapse imaging), STEM CELL TREATMENT, GEOMETRIC ENGINEERING, LASER ASSISTED HATCHING, CRYOPRESERVATION, PRE IMPLANTATION GENETIC TESTING, MITOCHONDRIAL REPLACEMENT THERAPY, ROBOTIC TECHNOLOGY AND NANOBOTS.

INSIGHTS

❖ AI IN IVF -EMBRYOSCOPE (Time lapse imaging):

A novel technology which enables the integration of more stable embryo culture conditions with embryo assessment through live image tracking at a time interval of 5-20 mins without exposing it to changes in the environment and classifying it using individual time lapse morphokinetic characteristics and constructed algorithms. Future advancements of TL model could predict foetal heart pregnancy with an AUC of 0.93 in all cycles -fresh, frozen, donated [1] .

Evolutionary timeline of time-lapse imaging for embryo assessment



❖ STEM CELL TREATMENT:

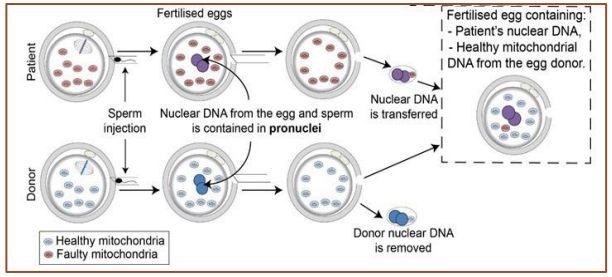
A regenerative medicine promotes repair response of diseased, dysfunctional or injured tissue using stem cells or their derivatives. A recent study that lead to mammalian embryogenesis from embryonic stem cells and extraembryonic stem cells including TS cells, XEN cells and inducible XEN cells invitro that recapitulated the development of whole natural mouse embryo inutero upto day 8.5 post fertilization.

❖ GEOMETRIC ENGINEERING :

An approach that converts single injection of stem cell suspensions to radial arrays of organoids maintained for extended periods without need for passaging. A recent study demonstrated that often manipulating the microenvironment of developing tissues, such as by confining cells into micropatterns (colonies of hESC) or by tuning the 3D matrix can be sufficient to recapitulate complex differentiation events in early development and enhance human embryonic patterning in a highly reproducible manner.

❖ MITOCHONDRIAL REPLACEMENT THERAPY:

It works on a principle of replacing an abnormal mtDNA with healthy mtDNA. Termination of lethal mitochondrial disorders caused due to point mutation. Includes spindle transfer, pronuclear transfer or polar body transfer [2]



❖ LASER ASSISTED HATCHING :

A method used for zona manipulation in case of a thick or dense zona where laser beams delivered through objectives releases energy in ZP and dissolves it with a single laser pulse in a few milliseconds.

❖ CRYOPRESERVATION:

Current application include increased capacity, automatic refilling, integrated alarm system, defogging mechanism. The process of vitrification lead to innovation of cyrodevices- cryotop, cryolock, cryoloop, open pulled straw whose thin surrounding film of vitrification solution and direct contact with LN2 achieve ultra rapid cooling rates. Experimentation continued to understand the role of extracellular stabilizing additives (eg-hyaluronate, hydrocellulose, butylated hydroxytoluene) and polyvinyl polymer.

❖ PGD AND PGS :

PGD includes biopsy of embryos done on D0-1(PB biopsy) or D3(Blastomere biopsy) or D5/D6(Blastocyst biopsy). D3 transport PGD –FISH (chromosome rearrangement screening), D3 or D5/6 transport PGD-PCR based testing(single gene disorder only), D3 or D5/6 transport PGD- SNP array (aneuploidy screening, chromosome rearrangement screening +24 chromosome screening, single gene disorder testing + 24 chr screening, Array CGH transport PGD. PGS includes evaluation of cells from developing embryo for the purpose of identifying aneuploidy.

❖ ROBOTIC TECHNOLOGY & NANOBOTS:

Robotic technology a promising advancement in reproductive surgery and preservation of fertility. A robotic system with embedded open microfluidic chip used for automatic embryo vitrification [3]. Magnetically controlled microrobots are suitable for manipulation in closed space for embryo transfer. Automation of ICSI includes auto injection-transgenics, use of MEMS and micro robotic nano-newton force sensors, servo optical control, RICSI (ongoing human trials)- 720 degree /second, immobilization of sperm in 6-7 seconds (CASA adapted). Spermobikes or spermobots are mini metal motorized helices that just fit around tail of sperm, using rotating magnetic field as joy stick can direct micromotor helices to slip around sperm cell to drive sperm to egg and release sperm for potential fertilization. Spermobot serves as power motor.

❖ OTHER INNOVATIONS :

1) OPTIONS G185 sensortech- pH monitoring
2) G210 Invicell plus- external gas monitoring
3) BT37 –to achieve proper CO2 environment
4) Innovative witnessing system RI for barcoding the samples.
5) Monitoring media pH in incubator- sensor dish using fibre optics.
6) Gavi –Genea biomedx for age of automation
7) OMICS- secretomics and metabolomics to determine optimal embryos for transfer, lipidomics for large scale study of pathways and network of lipids, Proteomics (SELDI-TOF) used to study the modification made to a particular set of proteins.

CONCLUSION

A confluence of advances in biological science and accelerating development of computing, automation and AI is fueling a new wave of innovation in assisted reproductive technology.

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