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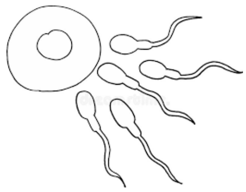
BIOLOGY OF GAMETES

Reproductive Biotechnologies Course



AA 2025-2026

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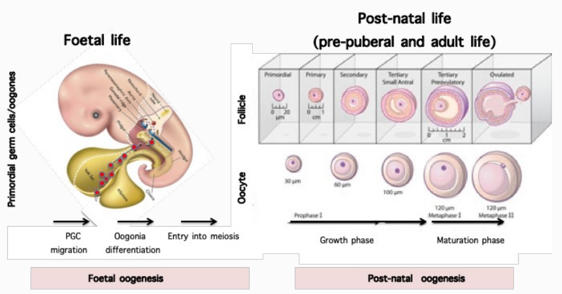
BIOLOGY OF GAMETES: OBJECTIVES



OVERVIEW ON THE OOGENESIS

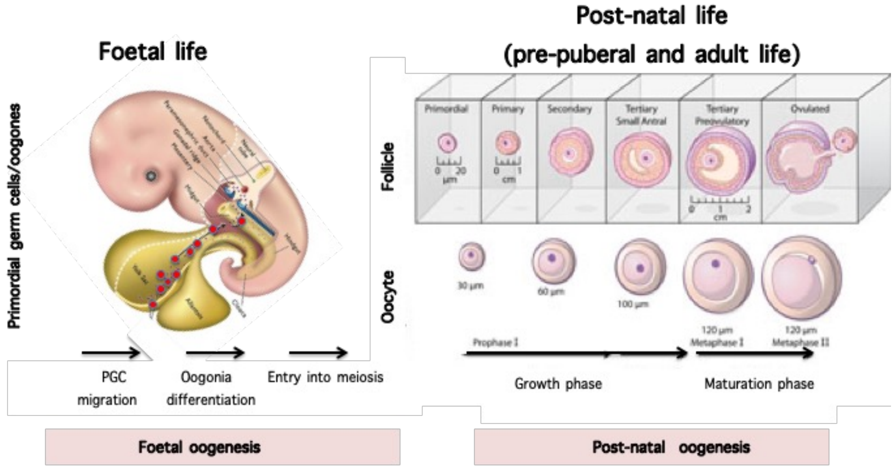
Structural and biochemical modifications during oogenesis

TIMIMG
When modifications occur?

To what extent the various phases of oogenesis affect female fertility by influencing the ultimate events of fertilization and blastocyst formation?

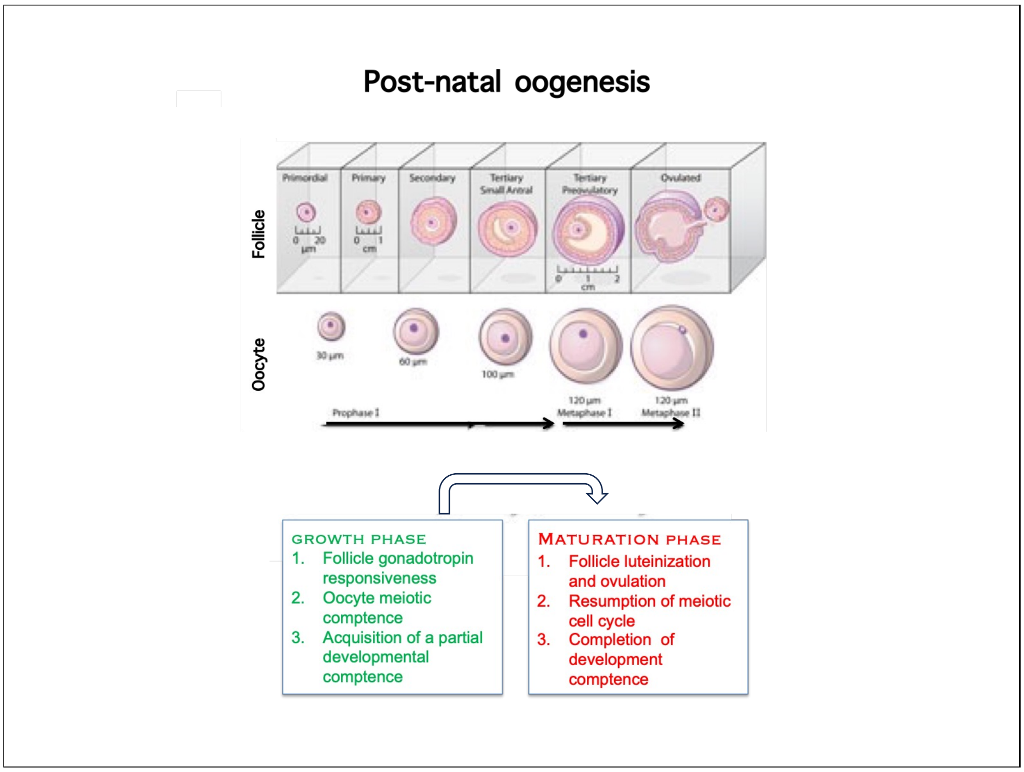
LESSON I

Introduction to oogenesis



Oogenesis is a long process starting early in the foetal life and ending when the last gamete is available inside the ovary in adulthood.

During this long period the female gametes change dramatically by increasing their degree of specialization.



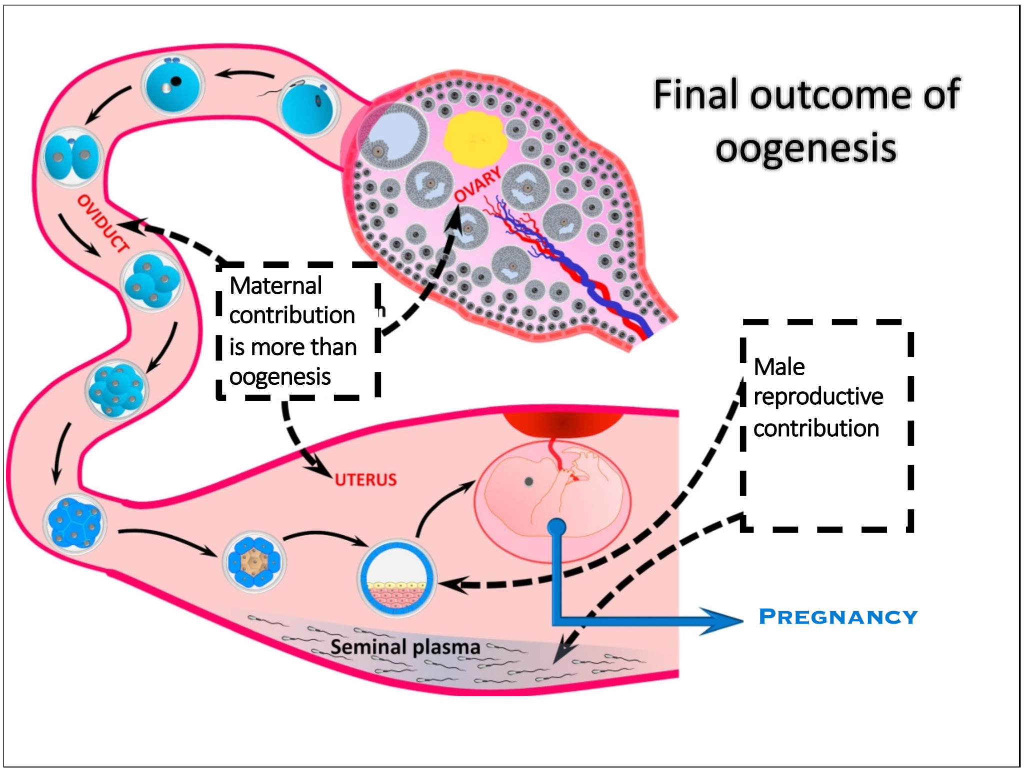
Post-natal oogenesis involves two sequential and cyclic events engaging a pool of oocytes.

1.Initially, oocytes grow in size during the growth phase, alongside their corresponding ovarian follicles, which develop sensitivity to gonadotropins (receptors expression)

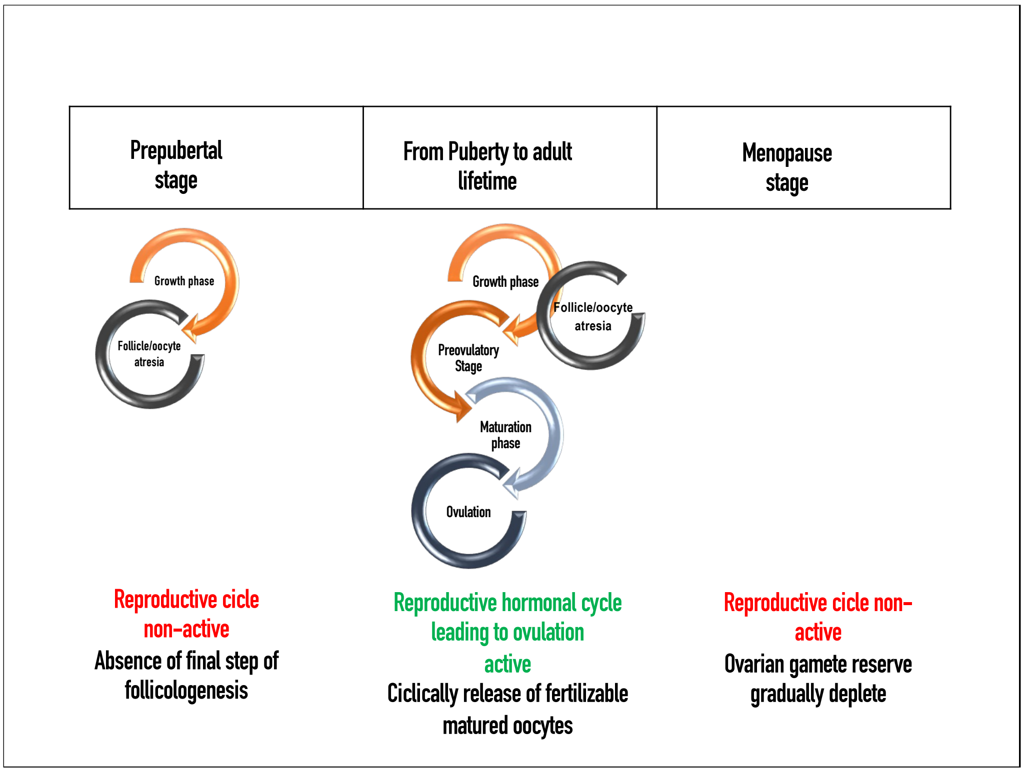
Upon reaching full size, oocytes is ready to attain meiotic resumption (to acquire meiotic competence). An event that occurs into an oocyte enclosed in a preovulatory follicle which is stimulated by an appropriate gonadotropin levels (maturation phase).

2. This maturation phase concludes oogenesis by enabling pregnancy through (1) ovarian follicle luteinization and (2) ovulation.

preparing the female gamete for embryo development post-fertilization, thereby achieving developmental competence.



At the end of the long-term process of oogenesis, one or more matured oocytes may cyclically be released into female genital tract ready to be fertilized in order to start a pregnancy (*female reproductive outcome*).

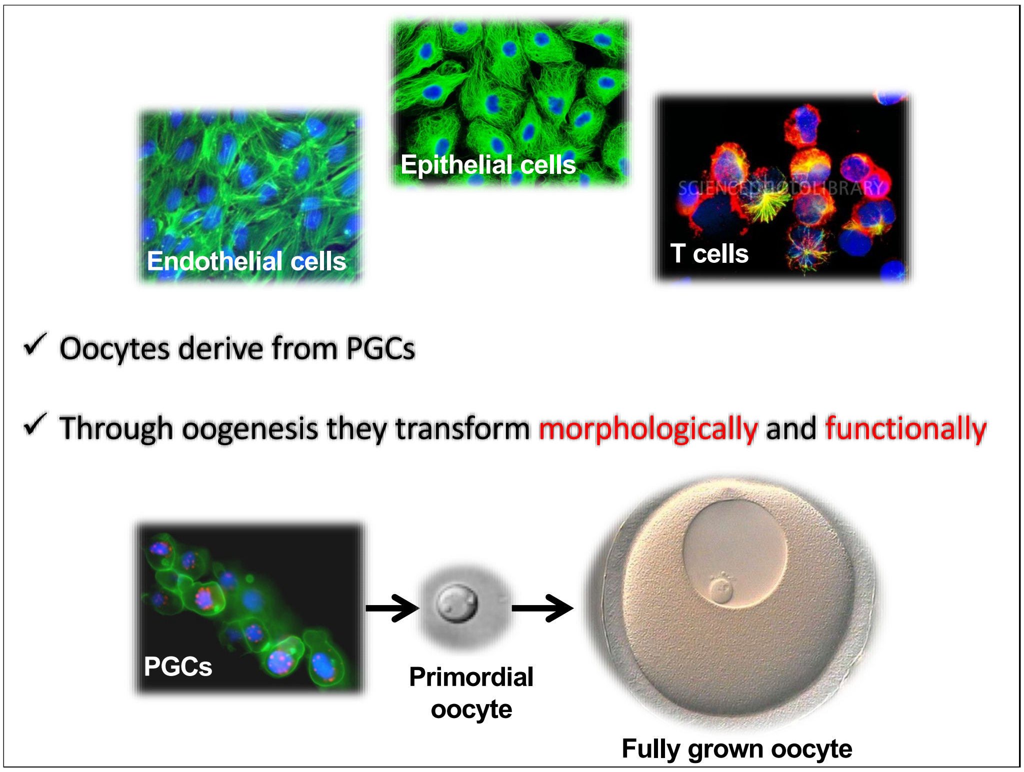


Post-natal oogenesis enables pregnancy only in adult or pubertal females, as a full reproductive hormonal cycle leading to ovulation occurs only after puberty when the hypothalamus-pituitary-ovary axis becomes functional.

However, this does not mean the ovary is inactive during prepubertal life—oogenesis progresses through the growth phase but cannot complete without entering the maturation phase.

In most mammals, oogenesis continues uninterrupted throughout life, encompassing both growth and maturation phases.

Exceptions include humans and primates, where post-natal oogenesis STOP at menopause—a reproductive halt occurring later in adulthood. This happens because the ovarian reserve of gametes gradually depletes until it is entirely exhausted while the organism remains alive, leading to the cessation of oogenesis and reproductive cycles, allowing life to continue without further reproductive function.



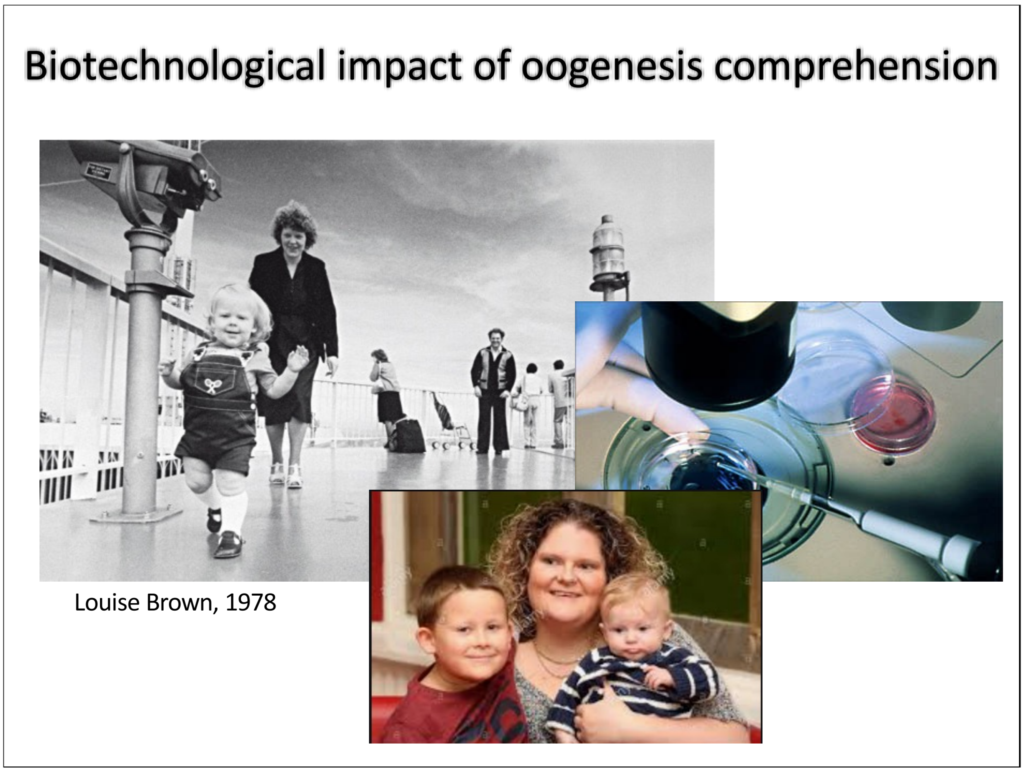
Oocyte derives from primordial germ cells (PGCs) which form in the female gonad during fetal life.

PGCs resemble somatic cells in size (20–30 µm) and undergo mitotic divisions during feotel life.Mitosis allow to increase from a few units to millions.

However, as fetal life ends, female gametes enter meiosis—a reductive cycle that halts the increase in number of gametes but enables genome halving before fertilization.

Upon entering meiosis, oocytes arrest at the diplotene stage of prophase I due to limited size and protein availability for meiotic control. Similar to the G1 phase in mitotic cells, oocytes must complete a growth phase to accumulate molecular components needed to resume meiosis. This is the time to reach the fully growth size as only fully grown oocytes receiving the LH surge proceed to maturation.

Thus, oogenesis drives both morphological differentiation and functional transformation

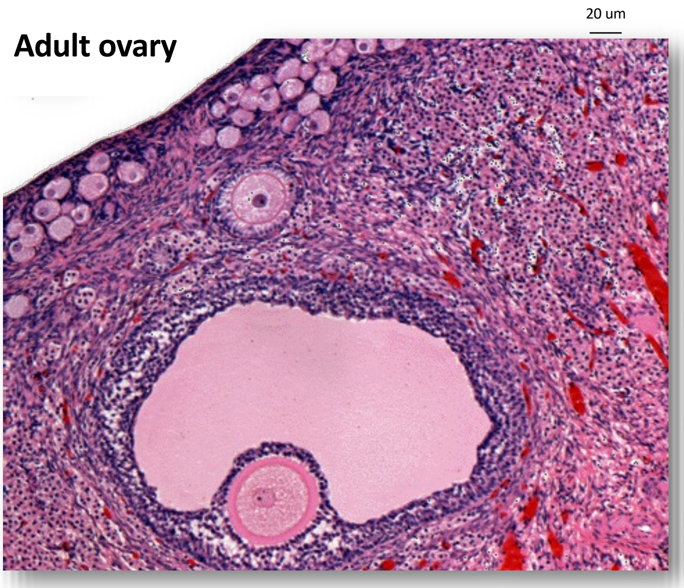


Over the past 40 years, advances in reproductive biotechnologies have been driven BY a deeper understanding of oogenesis mechanisms.

While assisted reproductive technologies (ART) have led to significant successes—starting with Louise Brown, the first of over 6 million ART-conceived babies worldwide—many challenges remain.

Currently, we can replicate certain reproductive events outside the body, such as oocyte maturation (in some species), sperm capacitation, fertilization, and early embryo development. However, crucial aspects like oocyte growth are still beyond our ability to fully mimic.

Adult ovary



Despite the vast number of oocytes in an ovary, current ART can only utilize fully grown oocytes, limiting reproductive potential.

This highlights the urgence to advance reproductive knowledge.

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Adult ovary
1
2
3
20 um
ART enhables us to use 1 of 31 oocyte
20 um

PNR 2021-2027
Programma nazionale per la ricerca

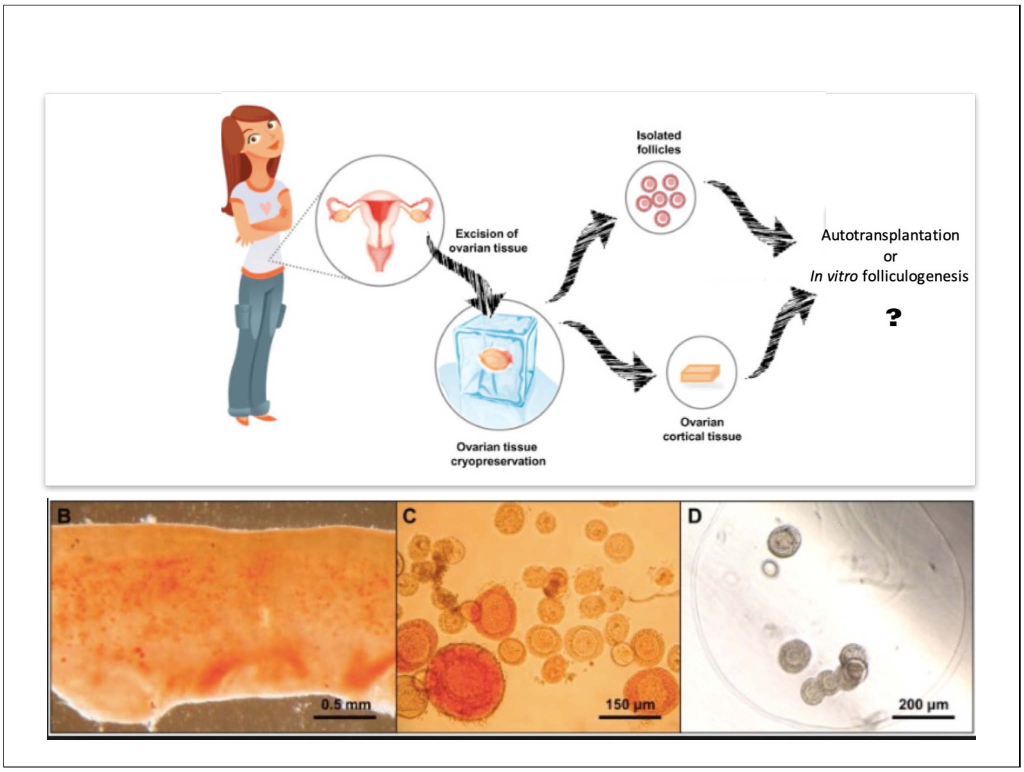
SALUTE	CULTURA UMANISTICA, CREATIVITÀ, TRASFORMAZIONI SOCIALI, SOCIETÀ DELL'INCLUSIONE	SICUREZZA PER I SISTEMI SOCIALI	DIGITALE, INDUSTRIA, AEROSPAZIO	CLIMA, ENERGIA, MOBILITÀ SOSTENIBILE	PRODOTTI ALIMENTARI, BIOECONOMIA, RISORSE NATURALI, AGRICOLTURA, AMBIENTE
Temi Generali	Patrimonio culturale	Sicurezza delle strutture, infrastrutture e reti	Transizione digitale - I4.0	Mobilità sostenibile	Green technologies
Tecnologie farmaceutiche e farmacologiche	Discipline storico, letterarie e artistiche	Sicurezza sistemi naturali	High performance computing e big data	Cambiamento climatico, mitigazione e adattamento	Tecnologie alimentari
Biotecnologie	Antichistica	Cybersecurity	Intelligenza Artificiale	Energetica industriale	Bioindustria per la Bioeconomia
Tecnologie per la salute	Creatività, design e made in Italy		Robotica	Energetica ambientale	Conoscenza e gestione sostenibile dei sistemi agricoli e forestali
	Trasformazioni sociali e società dell'inclusione		Tecnologie quantistiche		Conoscenza, innovazione tecnologica e gestione sostenibile degli ecosistemi marini
			Innovazione per l'industria manifatturiera		
			Aerospazio		

Public investment in reproductive biotechnology research remains crucial and is a top priority within the health pillar of both the Italian and European research and development framework.

Articolazione 1. Prima infanzia, malattie rare e medicina della riproduzione

Priorità di ricerca: identificazione di marcatori e target molecolari per la cura delle malattie di origine sconosciuta della prima infanzia, delle malattie rare, delle neoplasie anche attraverso lo sviluppo di modelli non clinici rappresentativi e di potenziale applicazione su larga scala. Introduzione di tecnologie genomiche per screening su larga scala per geni malattia nei neonati. Formazione di reti, registri, biobanche coordinati e omogenei a livello nazionale e implementazione di una strategia nazionale per le scienze omiche. Migliore comprensione dei fattori di rischio e strategie di prevenzione e sviluppo di metodologie diagnostiche e nuovi approcci terapeutici per ridurre l'infertilità e l'onco-infertilità. Identificazione e applicazione di approcci sanitari ed educazionali innovativi per favorire accesso alle cure e per l'educazione sulle nuove tecnologie degli operatori medici. Studi sull'impatto delle nuove tecnologie digitali sullo sviluppo neurocognitivo nell'infanzia e nell'adolescenza per identificare i fattori di rischio e sviluppare possibili strategie di intervento/prevenzione.

Impatto atteso[72]. L'attività di ricerca sviluppata avrà impatto sui seguenti aspetti: diagnostica prenatale e diagnosi precoce di patologie dell'infanzia e di malattie rare a etiologia sconosciuta (cfr. impatti attesi di Horizon Europe n. 1, 3); nuove tecniche di riproduzione assistita e diagnosi genetica pre-impianto (cfr. impatti attesi di Horizon Europe n. 5, 6); gestione della salute riproduttiva e riduzione delle disparità dovute a fattori economico-sociali o culturali (cfr. impatti attesi di Horizon Europe n. 2, 3); nuove tecniche di riproduzione assistita (cfr. impatto atteso di Horizon Europe n. 5); nuove tecnologie a supporto dell'onco-fertilità e la preservazione della fertilità (congelamento di gameti e di tessuto ovarico) (cfr. impatti attesi di Horizon Europe n. 5, 6); fattori di rischio di ridotta fertilità per attenuarne l'impatto su fertilità e salute (cfr. impatto atteso di Horizon Europe n.2); meccanismi fisiopatologici e neurocognitivi alla base delle nuove dipendenze legate all'uso della rete in particolare di bambini e adolescenti e relative strategie di intervento (cfr. impatti attesi di Horizon Europe n. 1).



Several research groups worldwide are working on strategies to maximize the use of the ovarian oocyte pool, increasing the number of fertilizable oocytes.

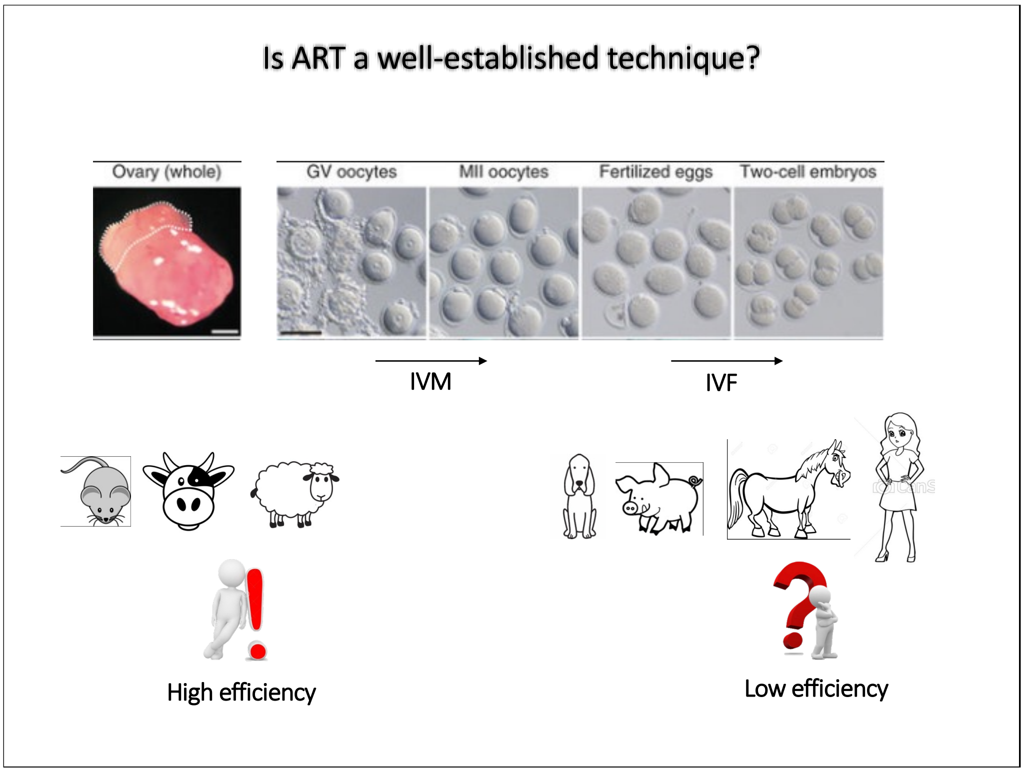
Achieving this requires new technologies to successfully replicate the growth phase of oogenesis, allowing more oocytes to reach full maturity for maturation, IVM, or IVF.

This could particularly benefit young cancer survivors, as chemotherapy often leads to infertility.

Currently, fertility preservation involves cryopreserving ovaries before chemotherapy using advanced freezing techniques. However, restoring fertility later in life remains a challenge. Two main approaches exist:

1. **Ovary Transplantation** – This restores follicle and gamete development but carries a risk of reintroducing cancer cells.
2. **In Vitro Folliculogenesis (ivF)** – Successfully tested in mice, this method grows oocytes in culture until they reach full maturity for use in IVF, eliminating cancer cell risk. However, ivF is not yet viable for humans due to the long and complex process of folliculogenesis, which is difficult to replicate in vitro.

Further advancements are needed to refine ivF for clinical application, making it a promising but still evolving fertility preservation strategy.



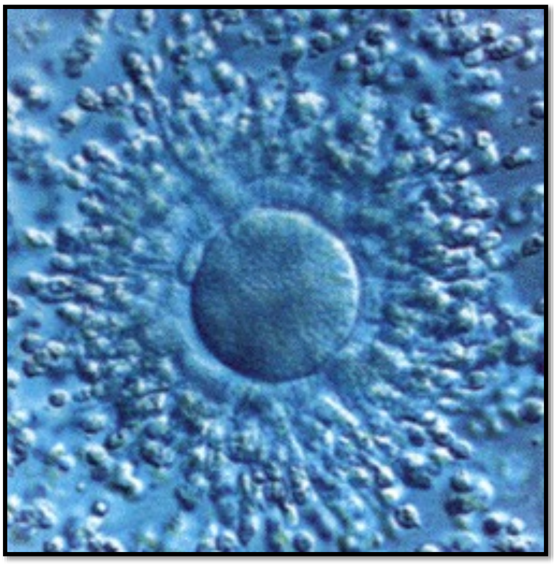
ART (allowing the oocyte to develop life) is often perceived as a well-established technique since it successfully produces offspring in many mammals through IVM/IVF.

However, this is not entirely true.

As an example, for what concern the IVM, this is highly efficient in only a few species, such as mice, sheep, and cows. In contrast, for other species like dogs, pigs, and even humans, IVM is still achieved but with very low efficiency, making it a less reliable reproductive technology.

Why does oogenesis matter?

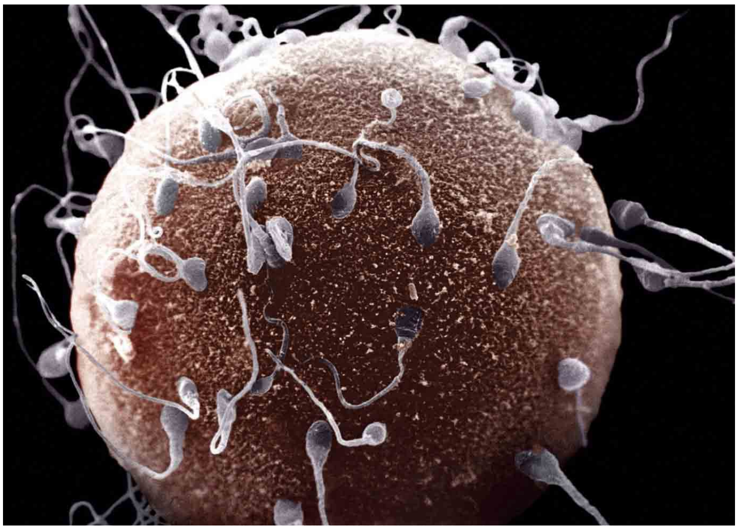
The mature oocyte is the unique cell of the body able to become a totipotent stem cell if properly activated

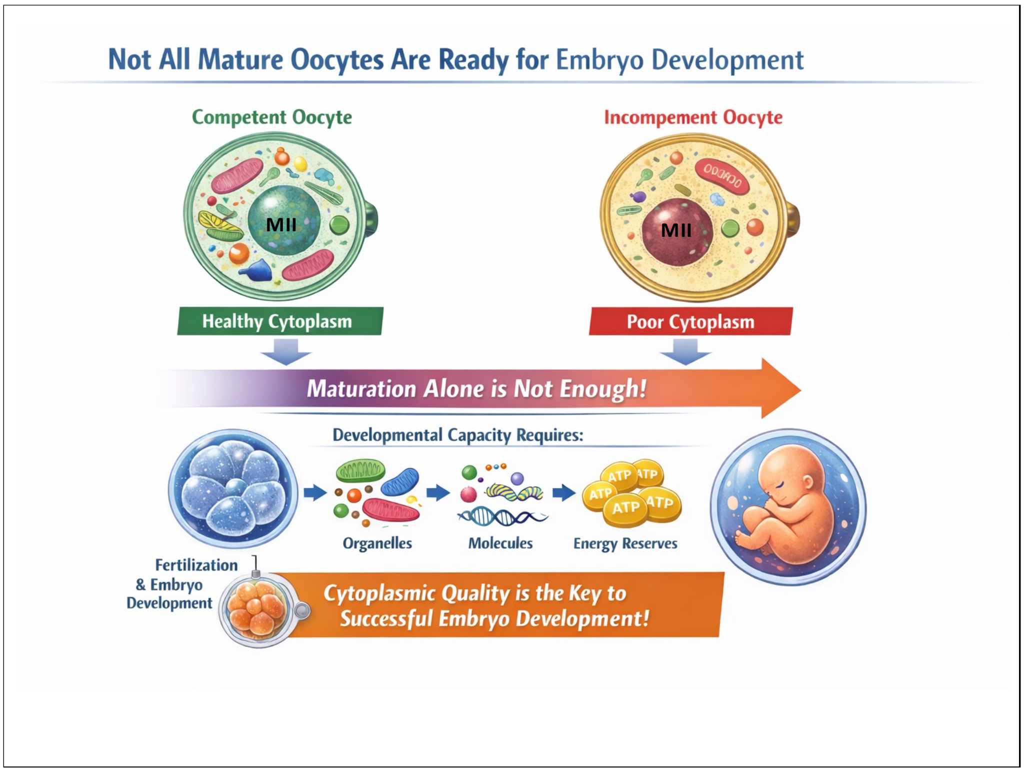


What does totipotency mean?

Totipotency indicate the ability of a stem cells to generate a vital organism through the differentiation of three germ cells layers and in mammals of the extra embryonic annexes both required to sustain embryo and foetal development.

The fertilization is the physiological event able to activate totipotency into a mature oocyte





Not all mature oocytes can support embryo development after fertilization.

Some may be penetrated by sperm without activating the developmental program because they lack the full biochemical machinery for developmental competence.

Successful oogenesis requires not just maturation but also the proper accumulation and distribution of organelles and molecules essential for embryo and fetal development.

Therefore, maturation alone does not guarantee reproductive success—the cytoplasmic quality acquired during oogenesis is the key factor.