

What is responsible for the development of the embryo?

The development of embryo in multicellular organisms is regulated by two processes namely cell division and cell differentiation.

Embryonic development is directed by genoms.

Embryonic induction is an interaction between one (inducing) tissue and another (responding) tissue, as a result of which the responding tissue undergoes a change in its direction of differentiation. This is probably the single most important mechanism leading to differences between cells and to the organization of cells into tissues and organs.

SYGNALING PATHWAYS

CELL-CELL INTERACTIONS

INTERCELLULAR COMMUNICATIONS

HEDGEHOG SIGNALING

RETINOIC ACID SIGNALING

TGFbeta SIGNALING

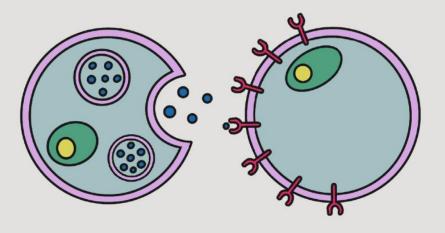
TYROSINE KINASE SIGNALING

WNT SIGNALING

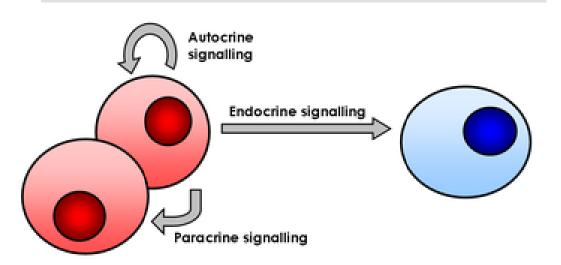
NOTCH SIGNALING

INTEGRIN SIGNALING





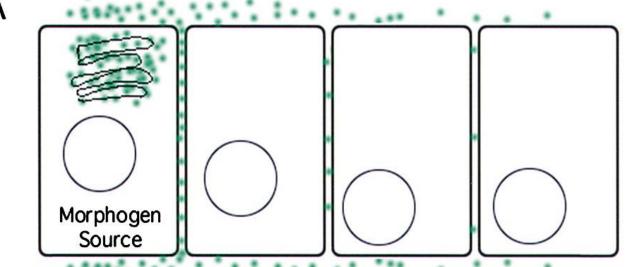
PARACRINE SIGNALING OCCURS OVER A SHORT DISTANCE. HERE, SIGNALING MOLECULES SIMPLY DIFFUSE BETWEEN THE SIGNALING AND RECEPTOR CELLS TO BIND TO RECEPTORS.



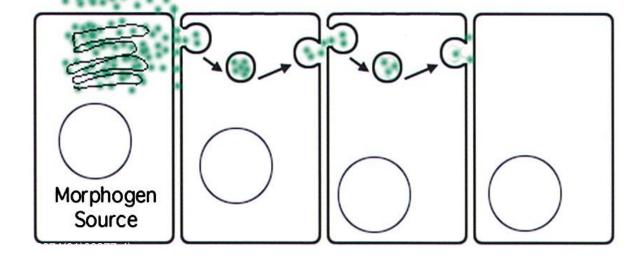
Juxtacrine signaling

Morphogens

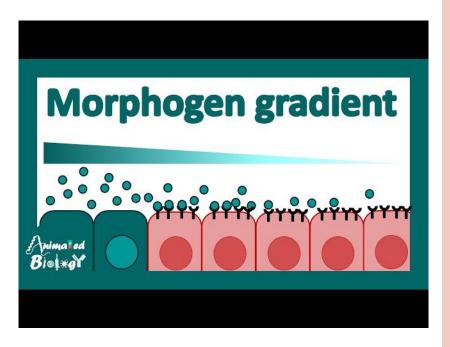
• Diffusible molecules that regulate cell fate determination during development.



B



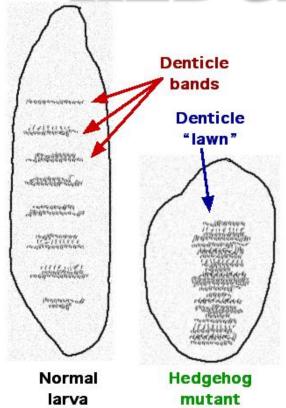




 The formation of morphogen concentration gradients directs the biological responses of surrounding cells. Graded responses occur as a result of morphogens binding to specific cell surface receptors that subsequently activate intracellular signaling pathways and promote or repress gene expression at specific threshold concentrations.

•Activation or inactivation of these signaling pathways provides positional information that ultimately determines cell fate decisions, tissue organization, and morphology.

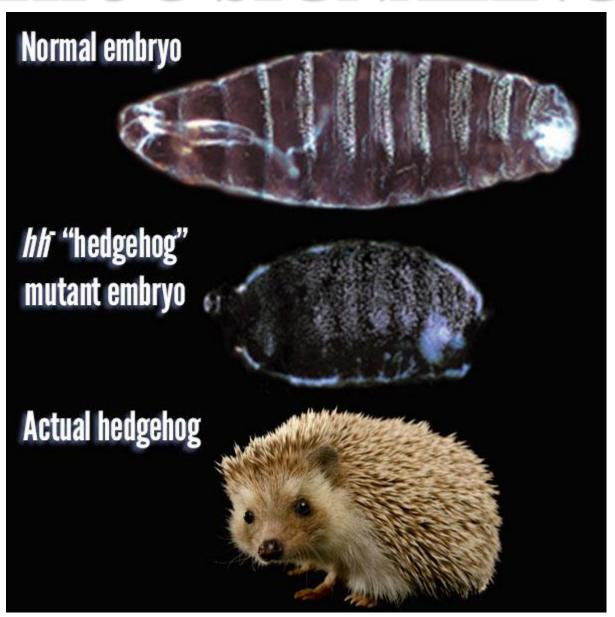
HEDGEHOG SIGNALING



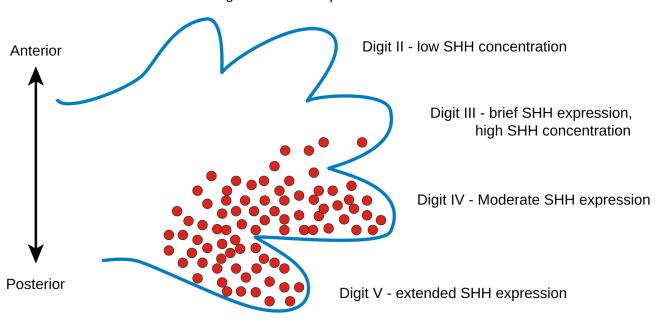


Indian hedgehog

Desert hedgehog



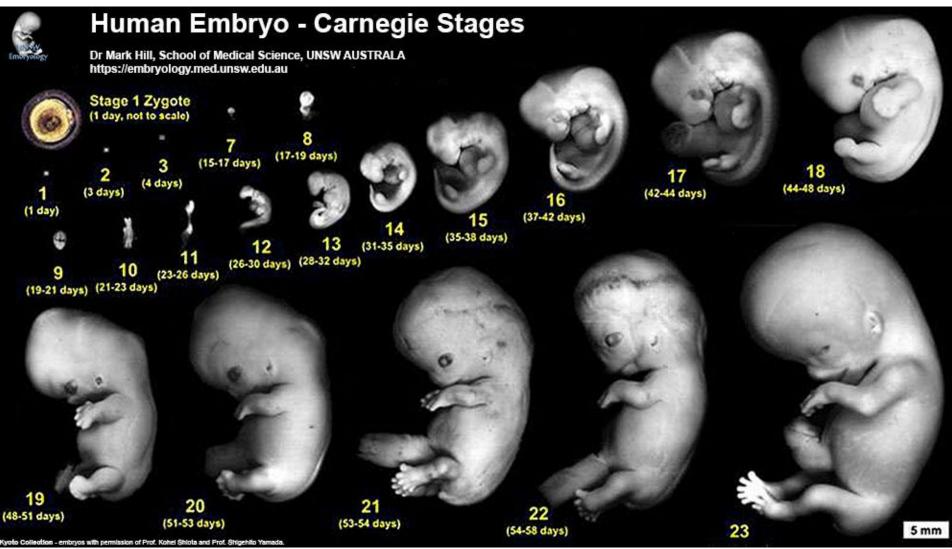
Digit 1 - SHH independent



Descendants of SHH expressing cells



Carnegie stages



Carnegie stages are named after the famous Carnegie Institution of Washington which began collecting and classifying embryos in the early 1900's.

1. PREEMBRYONIC PERIOD

From the fertilization of the ovum to the formation of the embryonic disc with three germ layers (from day 1 to week 3, inclusive)

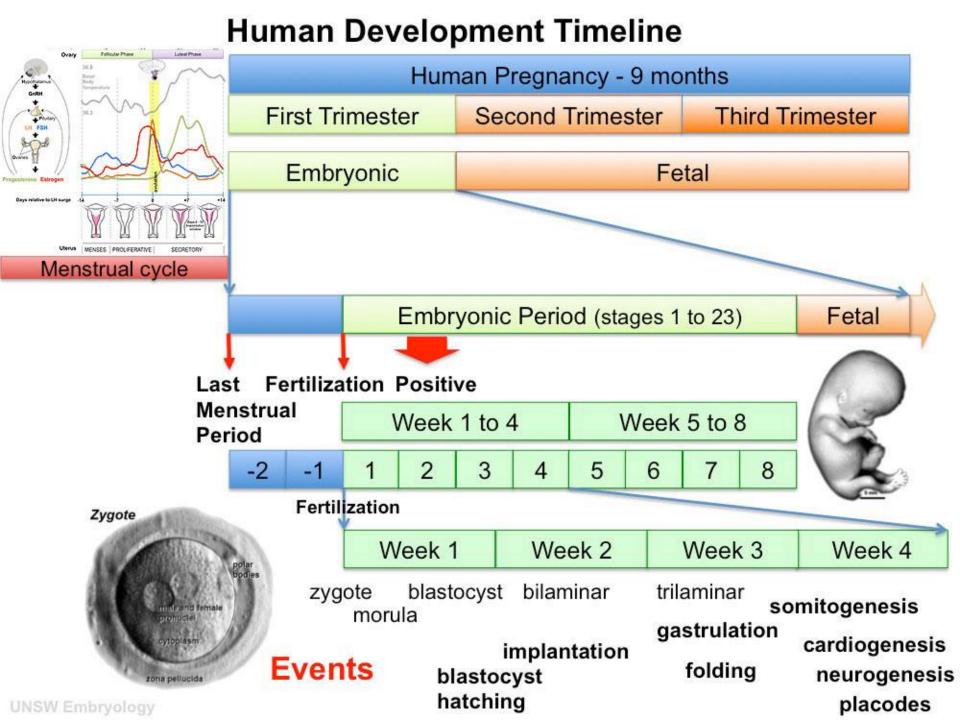
2. EMBRYONIC PERIOD

Rapid growth and differentiation, and formation of all the major organs of the body (from week 4 to week 8, inclusive)

3. FETAL PERIOD

Growth and further development of the organs and systems established during the embryonic period (from week 9 to parturition)

- 1. EMBRYONIC PERIOD from day 1 to week 8, inclusive
- 2. FETAL PERIOD from week 9 to parturition



THE LENGTH OF PREGNANCY

280 DAYS OR 40 WEEKS AFTER THE ONSET OF THE LAST NORMAL MENSTRUAL PERIOD (LNMP)

or

266 DAYS OR 38 WEEKS AFTER FERTILIZATION

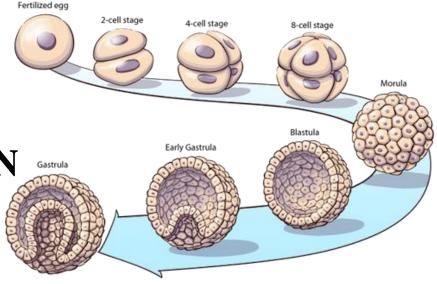
PREEMBRYONIC PERIOD

- FERTILIZATION

- CLEAVAGE

- BLASTOCYST FORMATION

- IMPLANTATION



Cell Cleavage
Process by which the number of cells in a developing embryo is multiplied through cell division.

- FORMATION OF THE EMBRYONIC (GERM) DISC

EMBRYONIC PERIOD

-GASTRULATION (THREE GERM LAYERS FORMATION)

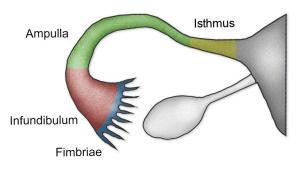
Fertilization is the process in which a new cell (zygote) is formed when two gametes – sperm and ova fuse together.

SECONDARY OOCYTE (arrested in meiotic metaphase II)

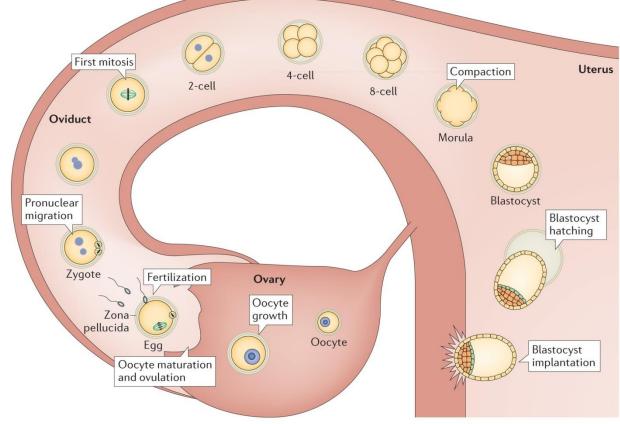
SPERMATOZOA

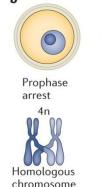






Fertilization most often takes place in the ampulla of the Fallopian tube











extrusion







chromosome recombination

Spindle assembly

Spindle relocation

Homologous chromosome

segregation

arrest



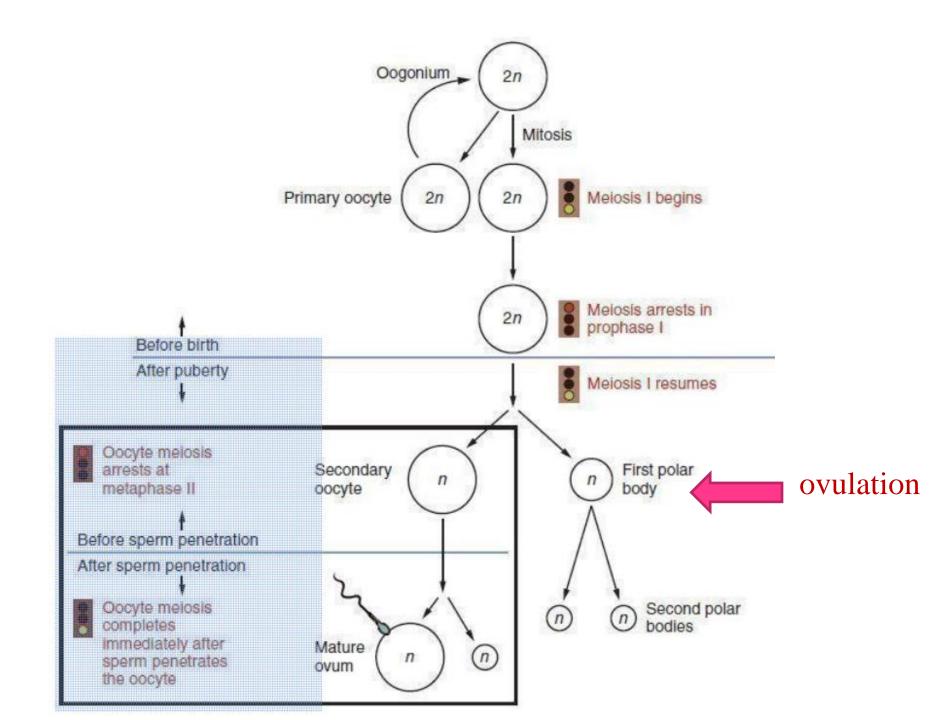


Sister chromatid segregation

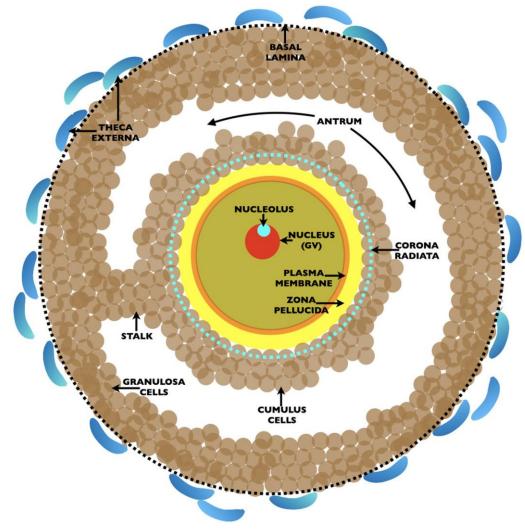
Pronuclei

formation

Haploid pronuclei



Graafian follicle:



Zona pellucida

transparent, porous, glycoprotein coat that surrounds oocyte

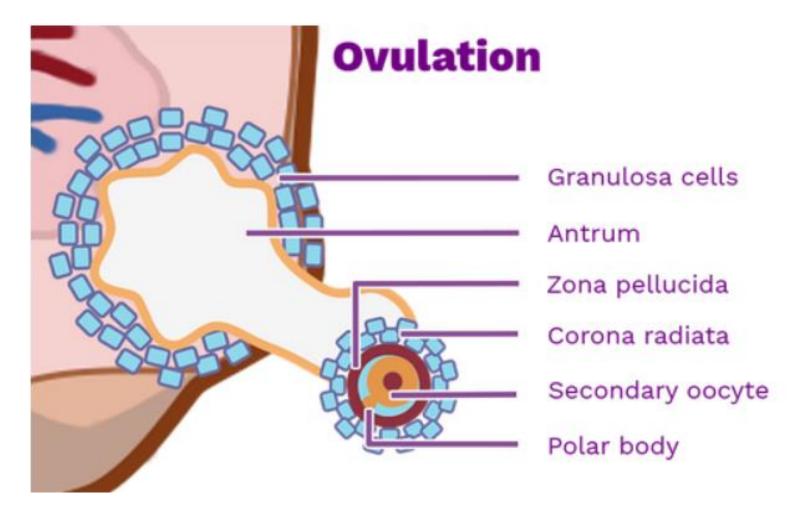
Which of the elements is not subject to ovulation?

- A. Secondary oocyte
- B. First polar body
- C. Corona radiata
- D. Zona pellucida
- E. Cumulus oophorus

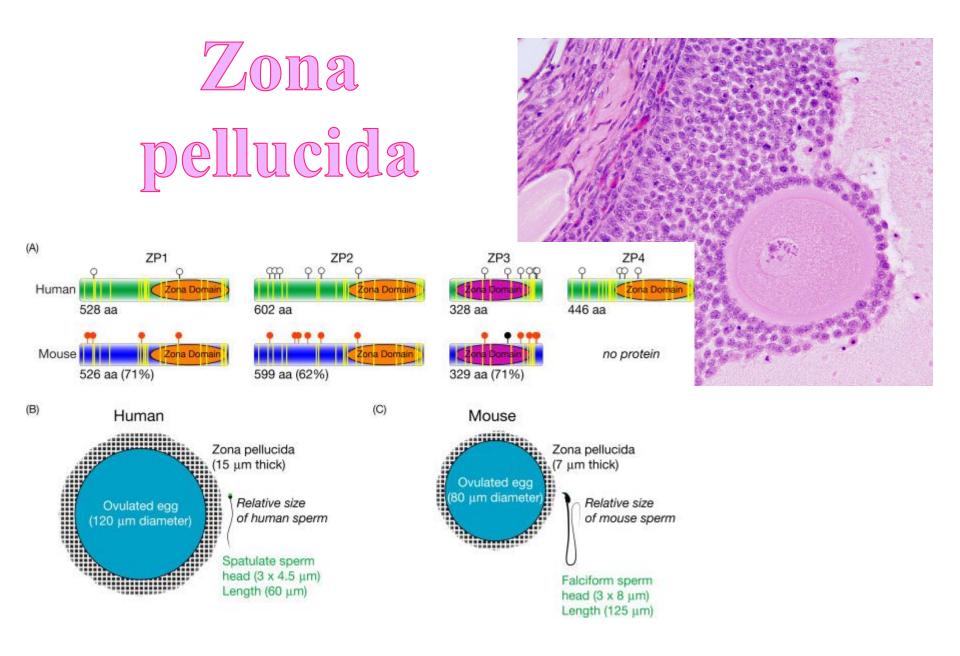
Which of the elements is not subject to ovulation?

- A. Secondary oocyte
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- C. Corona radiata
- D. Zona pellucida
- E. Cumulus oophorus

During ovulation, the ovary releases:

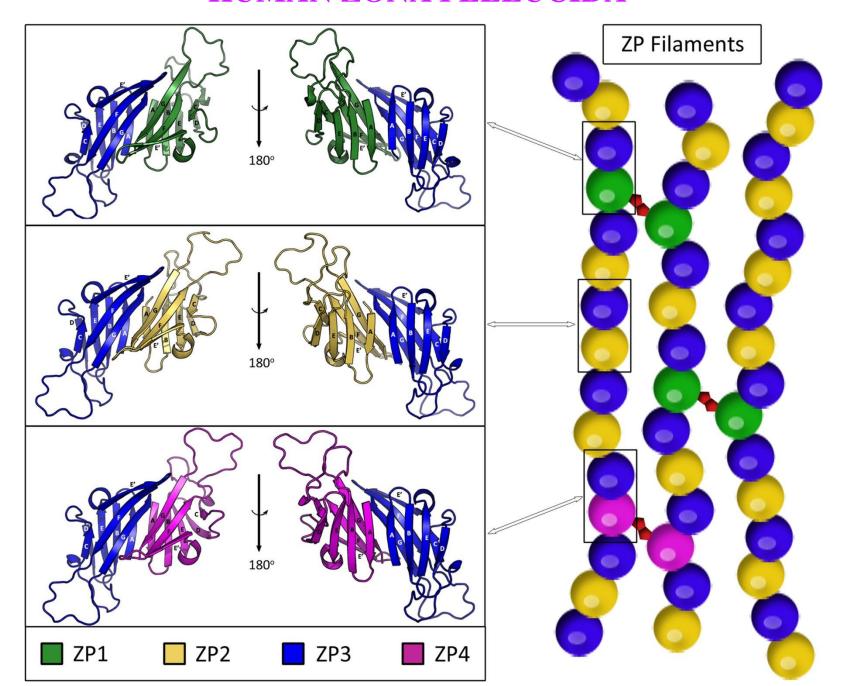


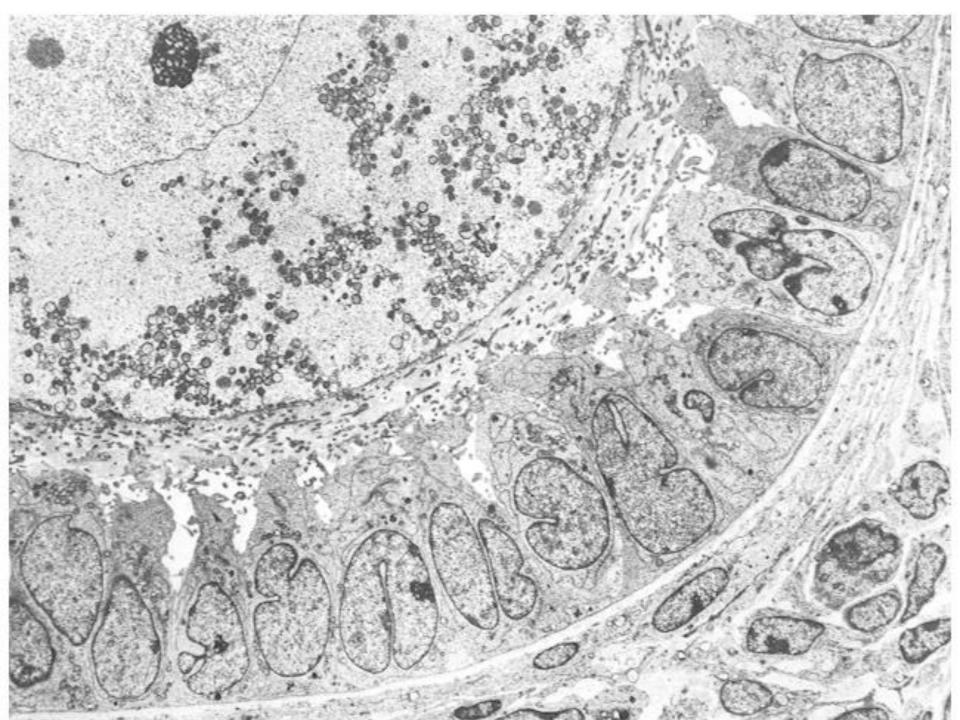
The granulosa cells that are ovulated with the secondary oocyte are known as the corona radiata



Zona pellucida is formed by growing oocytes. ZP are sulfated glycoproteins

HUMAN ZONA PELLUCIDA





OVUM

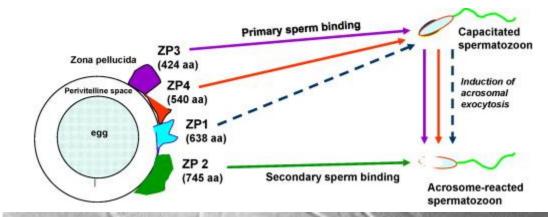
- CORTICAL GRANULES
- ZONA PELLUCIDA
- -ZONA PROTEIN 1, 2, 3, 4 (GLYCOPROTEINS)



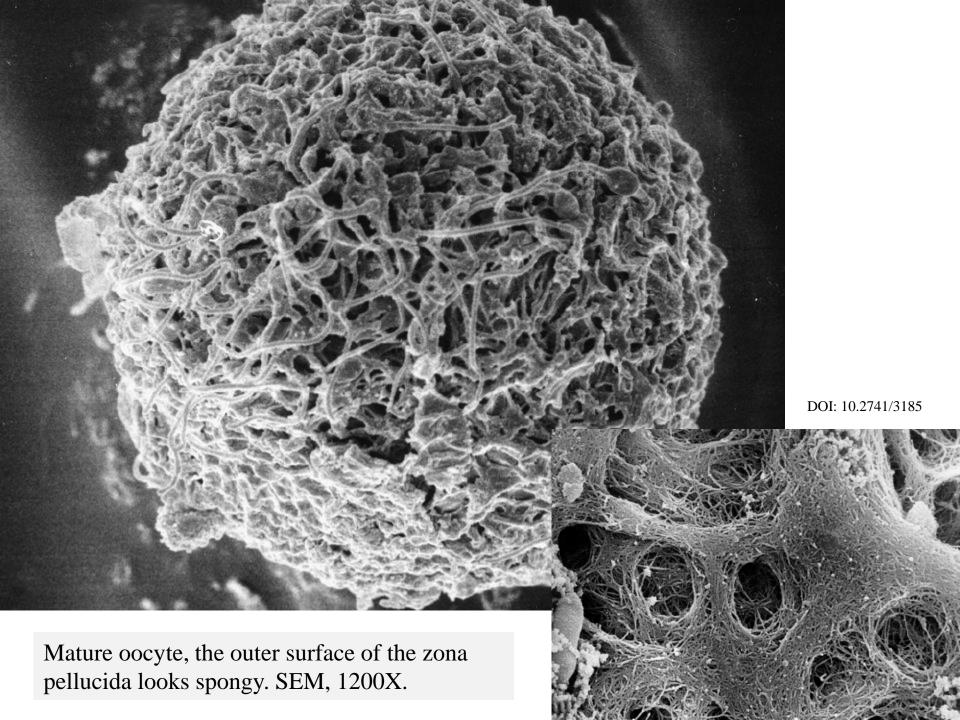
Component of the zona pellucida, an extracellular matrix surrounding oocytes which mediates 1. sperm binding, 2. induction of the acrosome reaction and 3. prevents post-fertilization polyspermy. The zona pellucida is composed of 3 to 4 glycoproteins, ZP1, ZP2, ZP3, and ZP4. ZP4, 3, 2 may act as a sperm receptor. ZP1 - cross-links filaments of ZP1 and ZP3

Mature oocyte. Zona pellucida displays a homogeneous microgranular appearance throughout its thickness and is characterized by an irregular, rough outer margin.

The human egg survival time upon ovulation is limited to 12 hours, after which it disintegrates, if not fertilized in time.





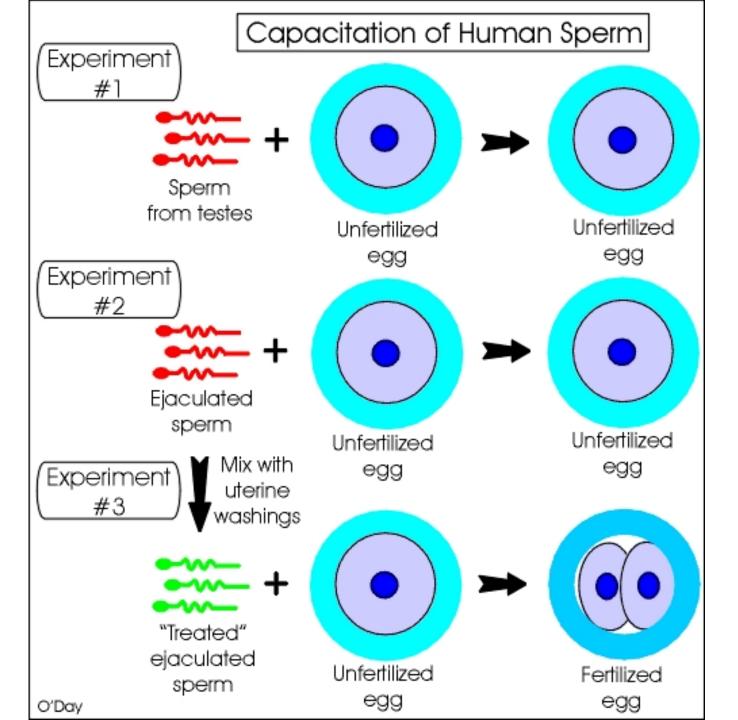


SPERMATOZOON

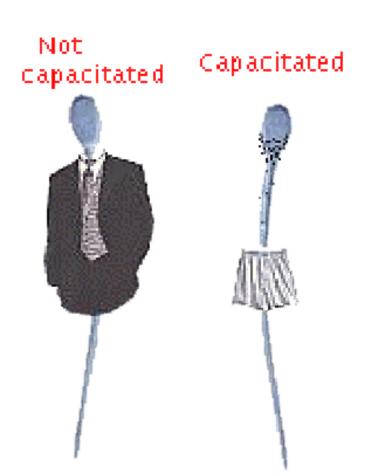
About 300 million human sperm ejaculated during intercourse

Only approx. 200 reach the site of fertilization,

- PENETRATION OF THE FOLLICULAR CELLS (corona radiata)
- BINDING AND PENETRATION THE ZONA PELLUCIDA
- BINDING AND FUSION WITH THE EGG PLASMA MEMBRANE



CAPACITATION



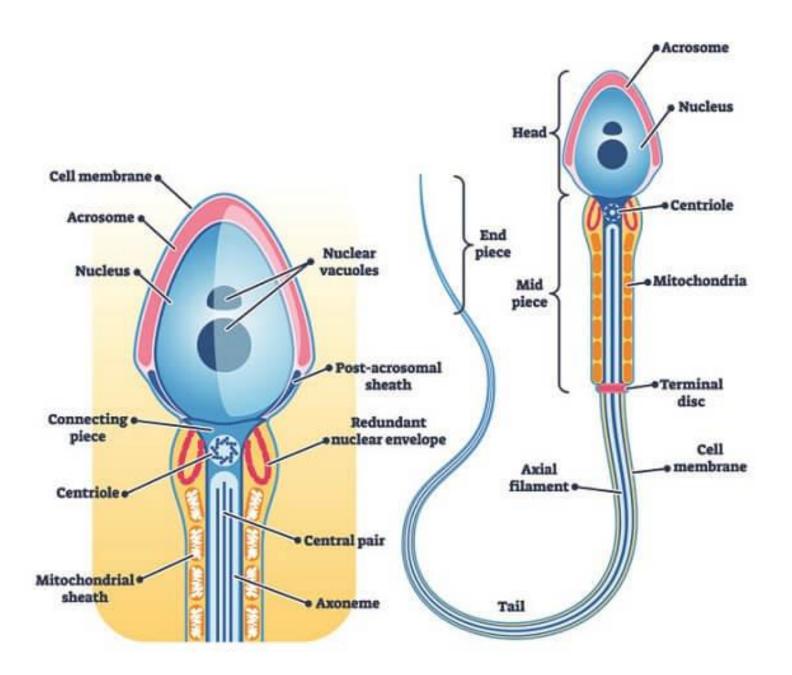
Ejaculated sperm must be modified in the female reproductive tract (capacitation).

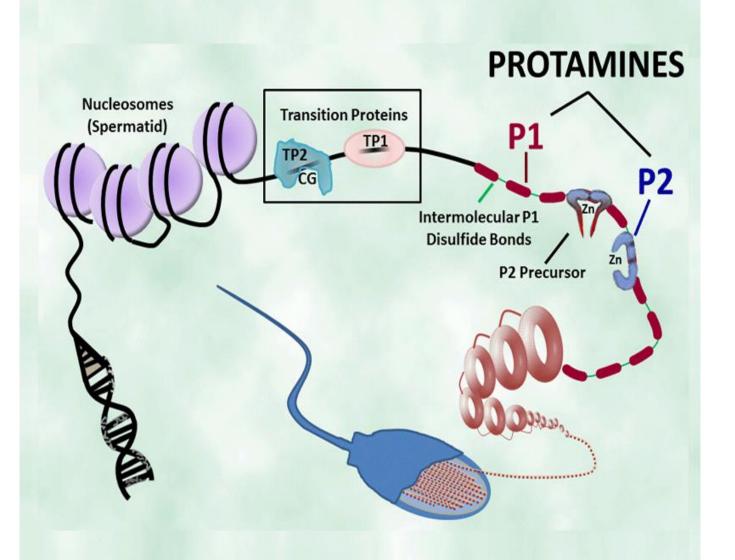
It is triggered by bicarbonate ions in the vagina.

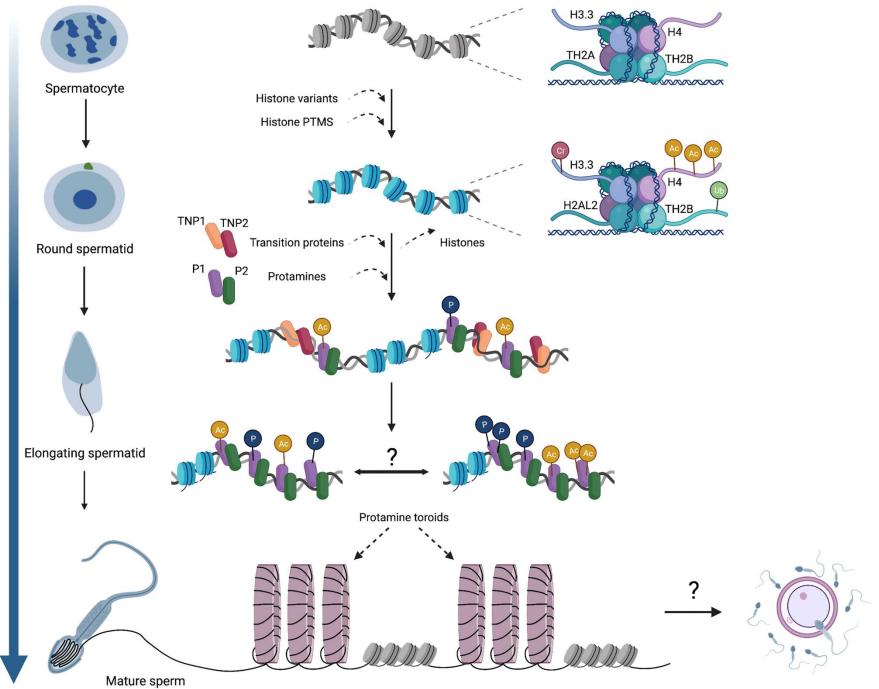
Capacitation alters the lipid and glycoprotein composition of the sperm plasma membrane, increases sperm metabolism and motility.

CAPACITATION

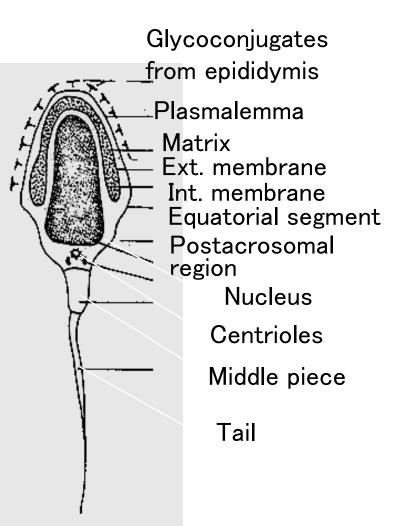
- sperm modification (maturation) in the female reproductive tract
- removal of glycoconjugates (sialoglicoproteins and sulphoglycerolipids) from the sperm plasma membrane that overlies the acrosome (linked in epididymis)
- sperm plasma membrane preparation for adhesion and binding to ZP receptor and to acrosomal reaction
- exposure of sperm plasma membrane ligands (galaktosyltransferase, sp56, sperm receptor kinase SRK or p95) for ZP receptors







Capacitation, cont.







Acrosomal cap

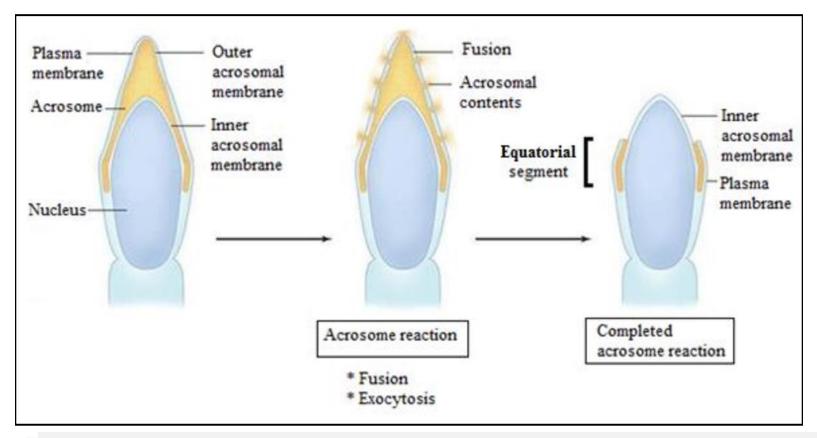
Enzymes

Internal acrosomal membrane

after capacitation after acrosomal

reaction

Acrosome reaction

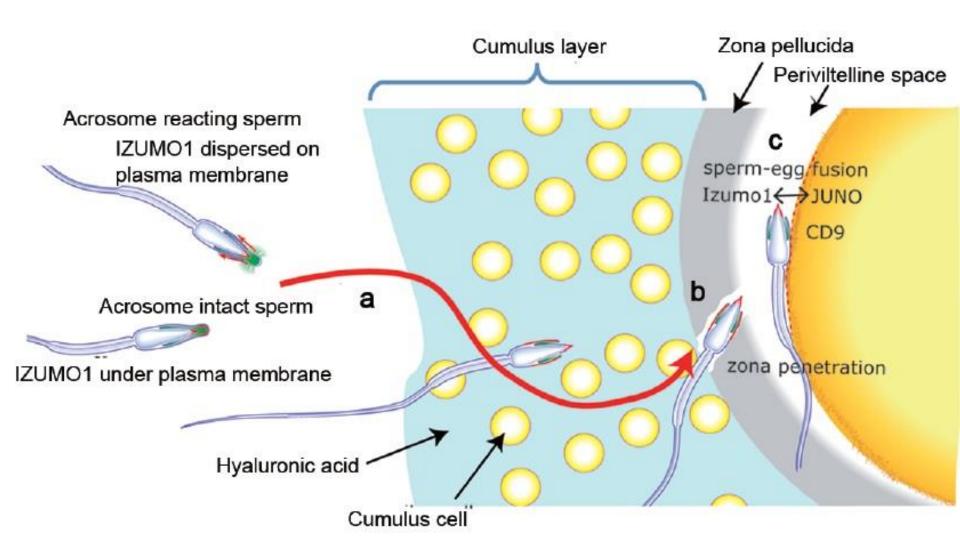


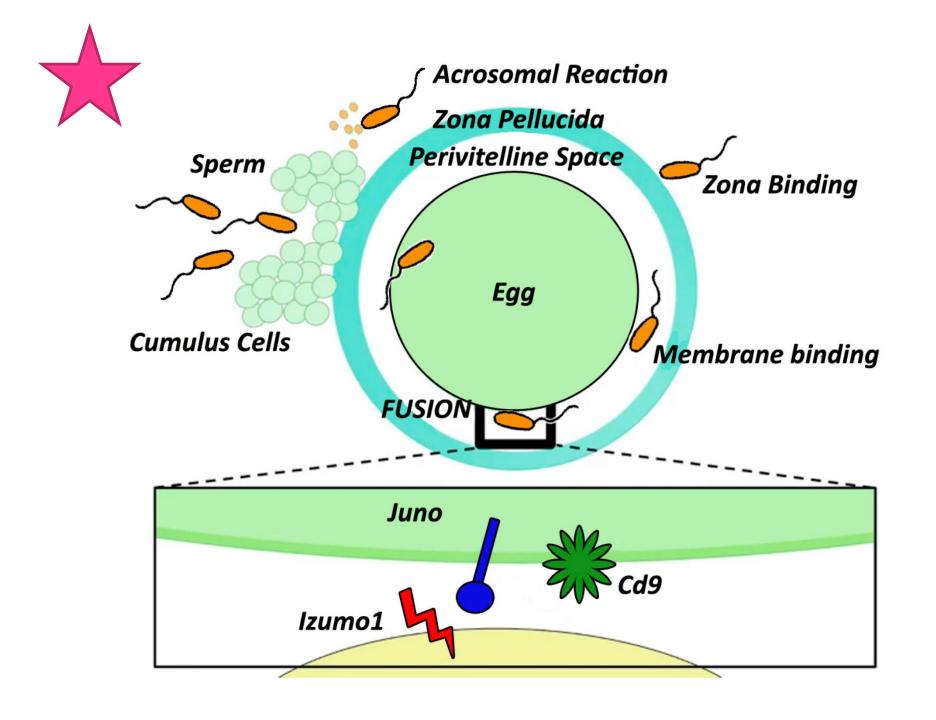
The acrosome contains both instantly and slowly released proteins and its contents are exocytosed during the acrosome reaction in which the sperm plasma membrane (PM) and the OAM fuse in multiple places within the acrosomal cap area.

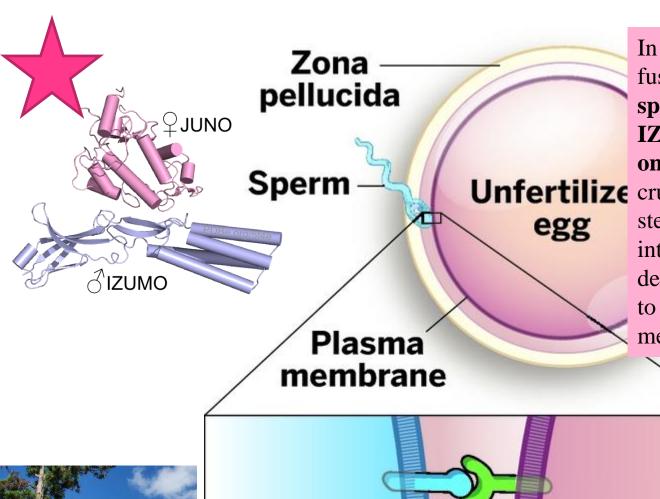
Acrosome reaction

Release of the acrosomal contents: enzymes essential for sperm penetration through ZP (hyaluronidase, acrosin, neuraminidase, proteases)

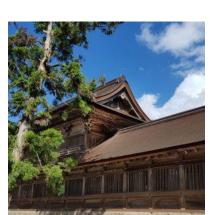
Exposure of inner acrosomal membrane (protein that bind to ZP and proteins that mediates the binding and fusion with egg plasma membrane



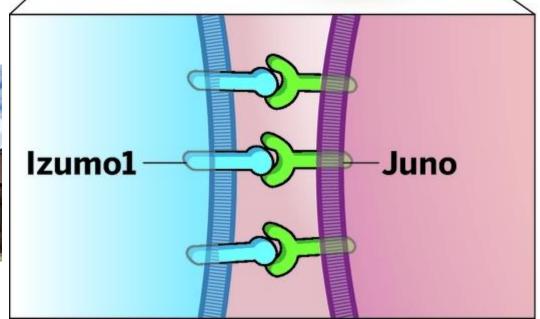




In the steps of sperm-egg
fusion, IZUMO1 on the
spermatozoon and the
IZUMO1 counter-receptor
on the egg, JUNO, play
crucial roles in the very first
step, the formation of an
intercellular bridge, and
deletion of either gene leads
to the failure of gamete
membrane fusion.

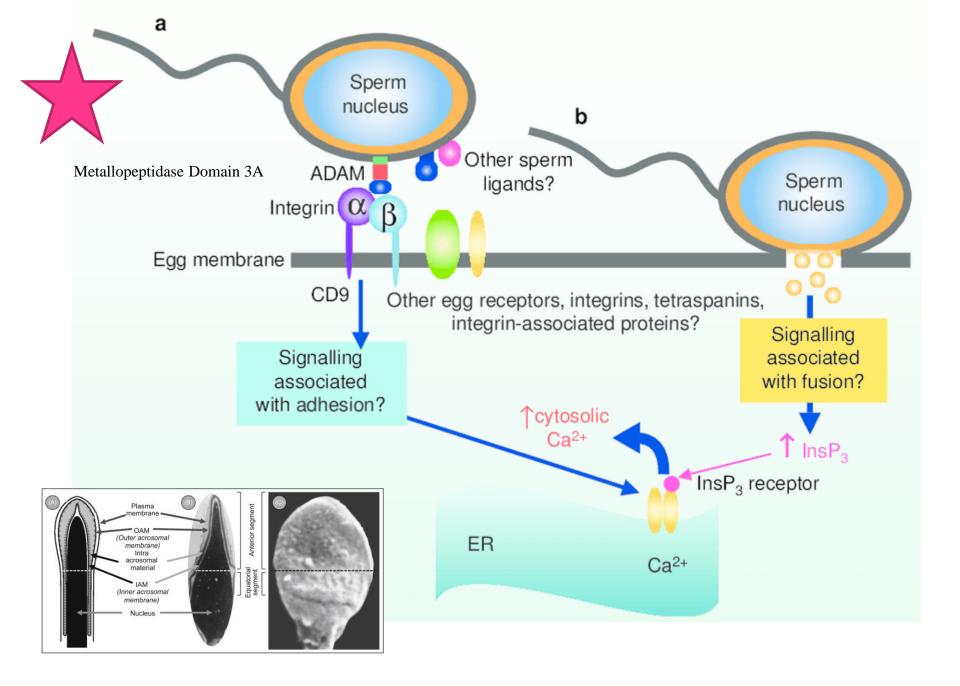


IZUMO Taisha

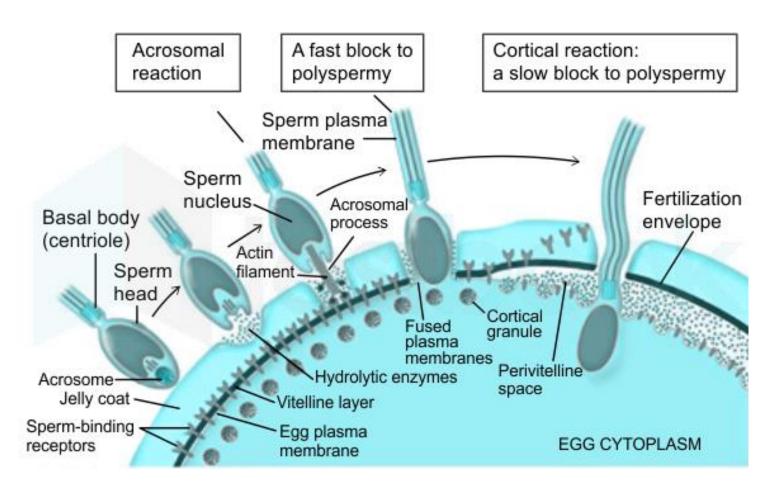




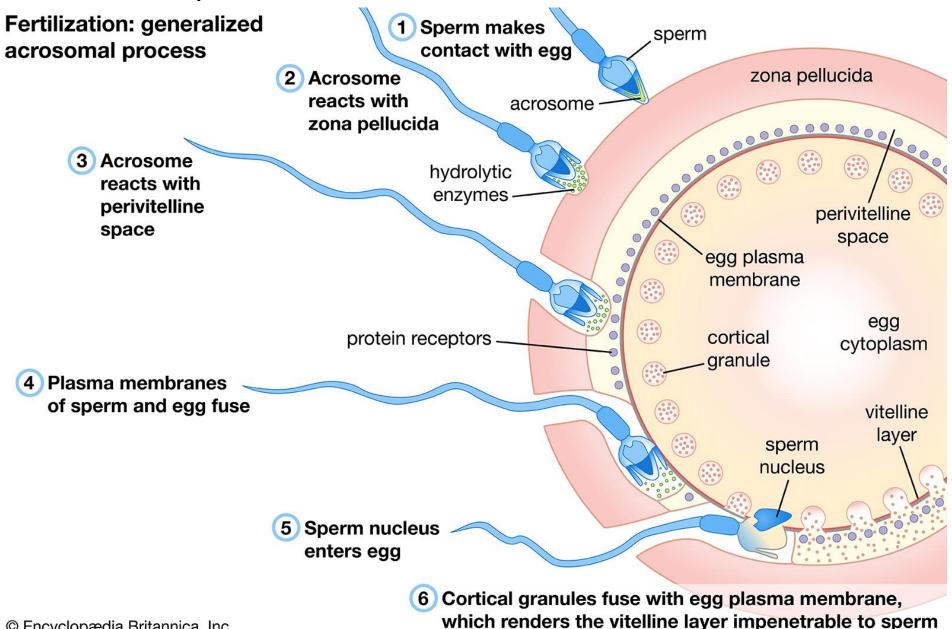
JUNO (Junona)



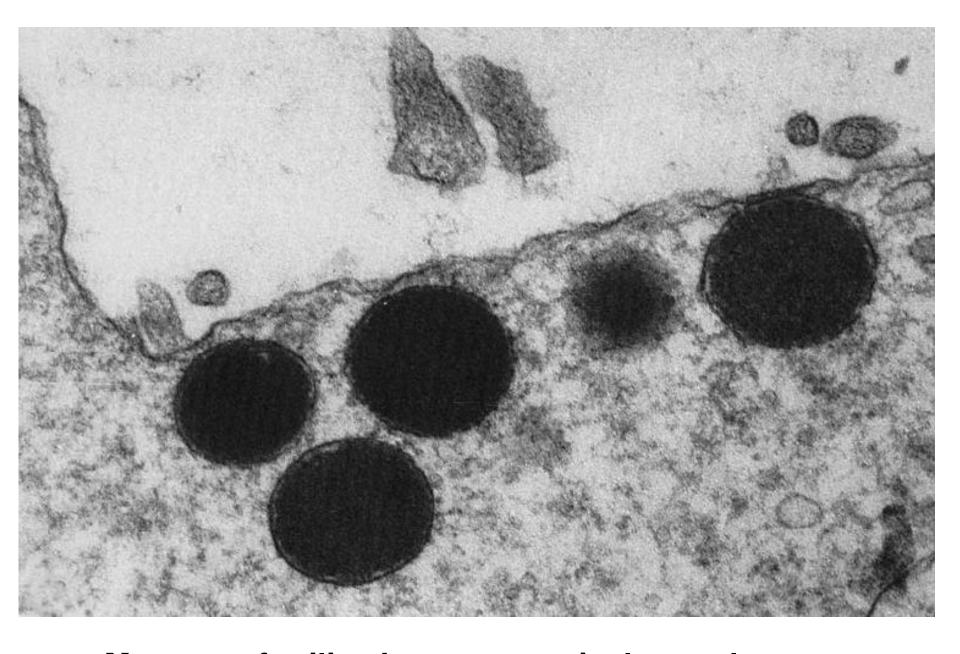
The fast block to polyspermy is mainly used by eggs from external fertilizers. In the fast block, fertilization activates a depolarization of the egg.



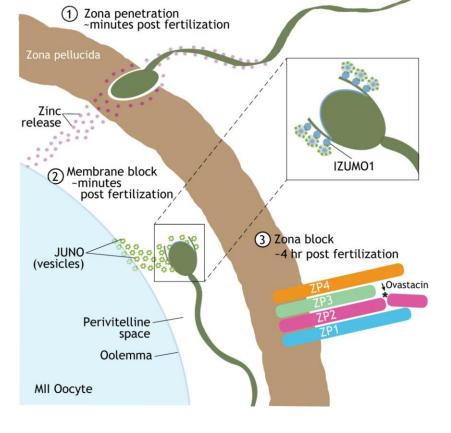
Polyspermy is a lethal condition where more than one sperm nucleus interacts with the female nucleus.



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Mature unfertilized oocyte, cortical granules beneath the oolemma. TEM, 70000X

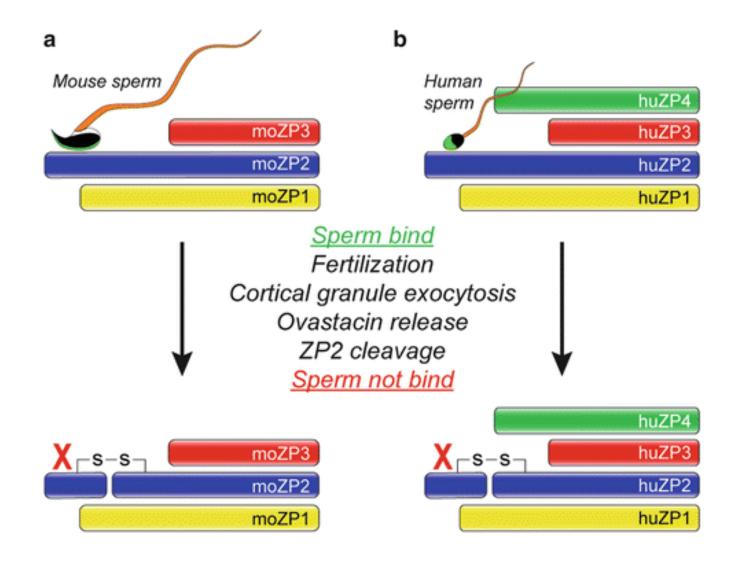


(1) Zinc release: zinc released within a few minutes of fertilization affects the forward motility of sperm that are binding or have initiated penetration of the zona, thus possibly providing a block to penetration to hyperactive sperm *in vivo*.

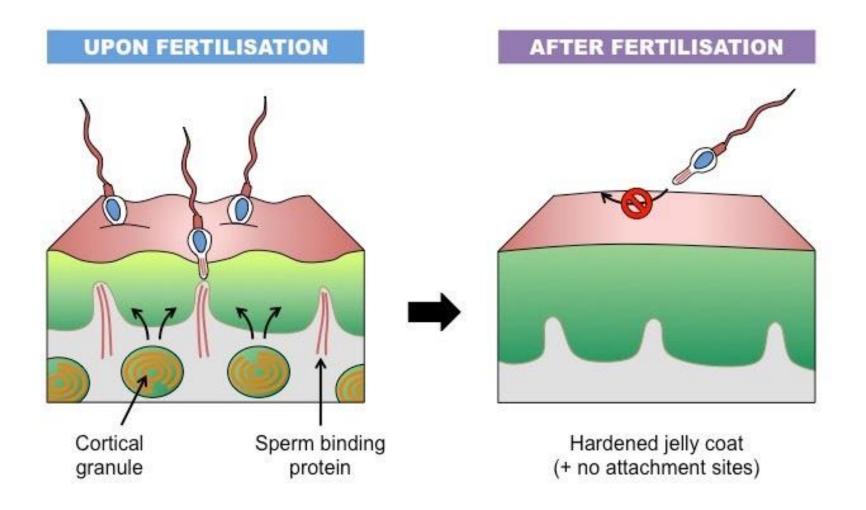
Effective post-fertilization block to polyspermy guarantees monospermic fertilization.

After fertilization and cortical granule exocytosis, two immediate blocks and one delayed block occur to prevent polyspermic fertilization, which is embryonic-lethal.

- (2) Membrane block: ~40 min after fertilization, JUNO is shed from the oolemma within vesicles (green) into the perivitelline space to act as a decoy that blocks any supernumerary sperm from adhering and fusing with the oolemma.
- (3) Zona block: within 4 h post-fertilization, ovastacin cleaves ZP2 at the N terminal region (asterisk) and the cleavage of ZP2 provides a definitive block by preventing further sperm binding to the zona pellucida.



Ovastacin cleaves ZP2 within the zona pellucida and provides a definitive block to sperm binding in the early embryo



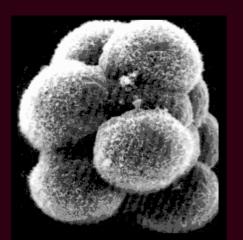
Polyspermy describes the **fertilization of an egg by more than one sperm**. Diploid organisms normally contain two copies of each chromosome, one from each parent.

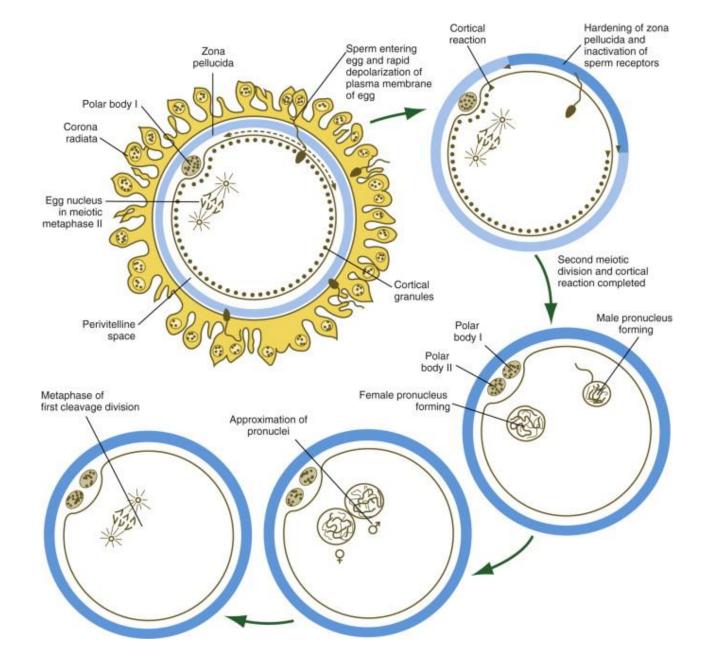
RESULTS OF FERTILIZATION

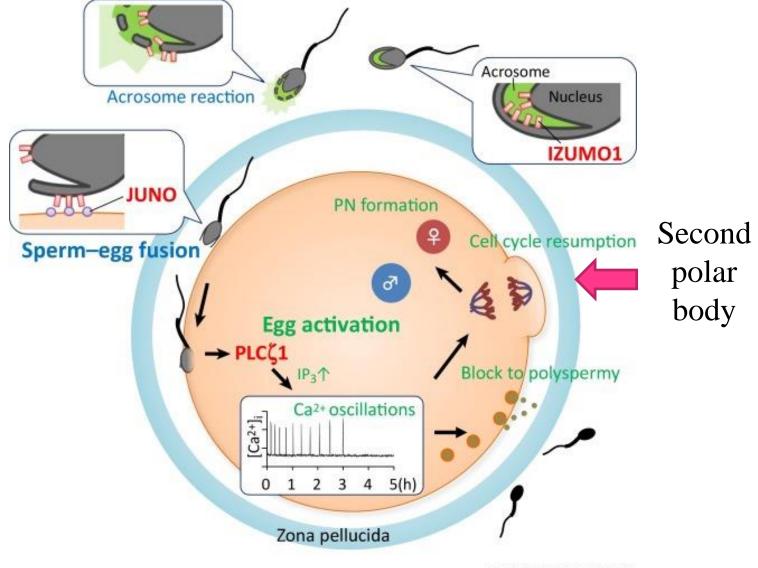
- RESUMPTION OF THE SECOND MEIOTIC DIVISION
- RESTORATION OF DIPLOID NUMBER OF CHROMOSOMES

(from haploid male and female pronuclei)

- -DETERMINATION OF THE CHROMOSOMAL SEX
- -INITIATION OF CLEAVAGE



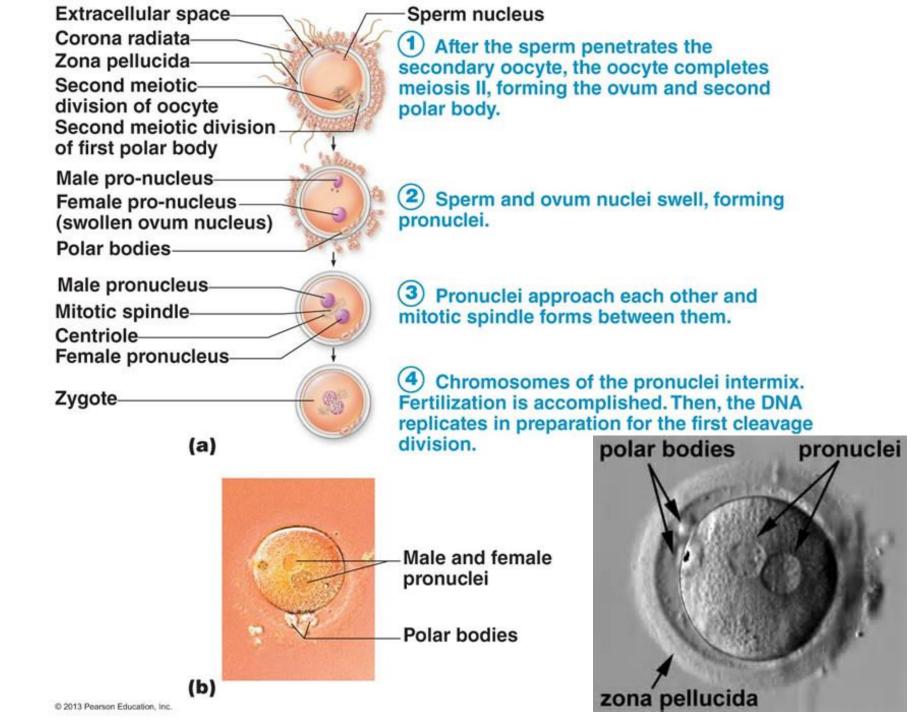


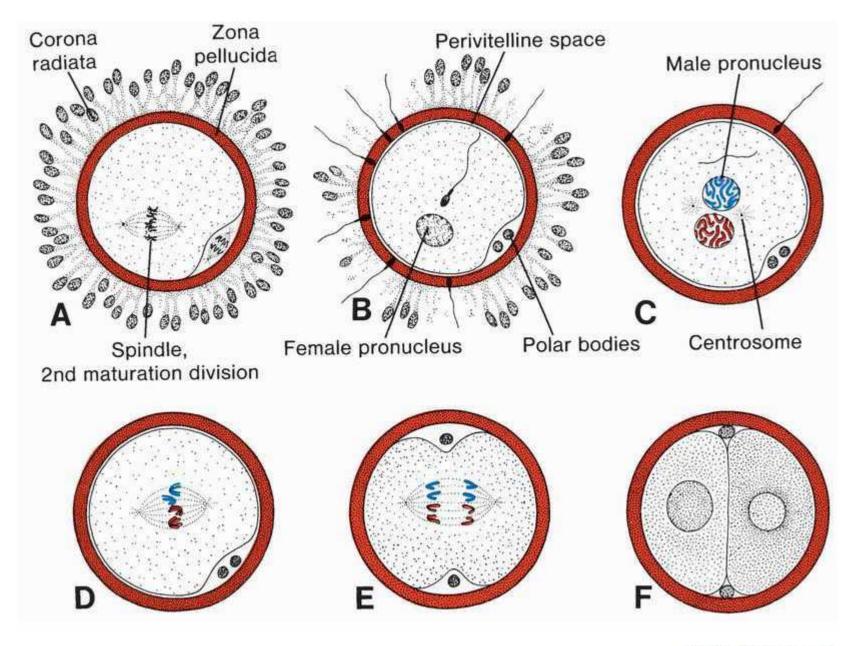


Trends in Biochemical Sciences

The trigger of Ca2+ oscillations is phospholipase ζ (PLC ζ)—a sperm-specific PLC isoform—which produces inositol-1,4,5-triphosphate (IP3) via hydrolysis of phosphatidylinositol-4,5-biphosphate (PIP2). IP3 binds to IP3Rs on the endoplasmic reticulum (ER) to elicit Ca2+ release from internal stores.







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Cleavage and blastocyst formation

Cleavage – mitotic divisions which produce a large numer of smaller cells called blastomeres

8 cell stage - Compaction is the process by which a loosely bound cluster of blastomeres spread their adhesion interfaces to form a tightly packed mass of cells called morula.

12-16 cell stage - Morula formation — inner and outer cell mass formation, enter the uterine cavity

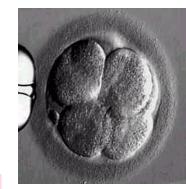
16 - 32 cell stage – cavitation – blastocele formation, Na+, K+ pump, exocytosis

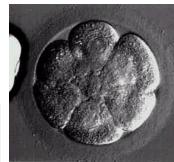
Blastocyst – inner cell mass (embryoblast) – gives rise to the embryo proper

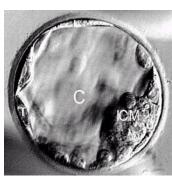
- Outer cel mass (trophoblast) – gives rise to the placenta

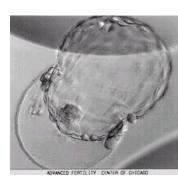
Days 4,5 – 5 zona pellucida shedding

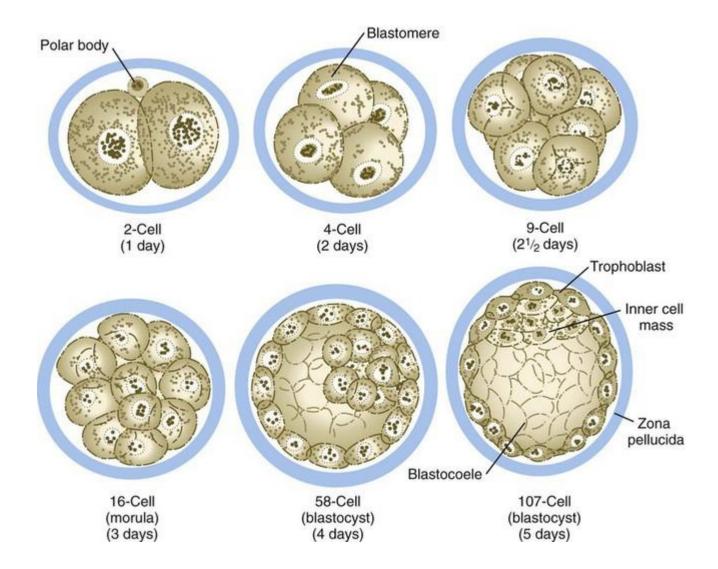
Days 6 – 7 implantation







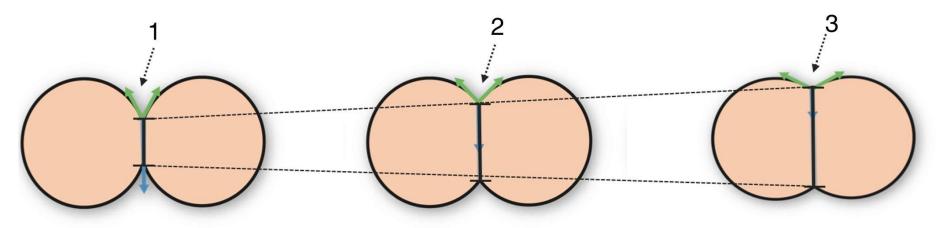




At the 8 cell stage the human **embryo** undergoes a process called **compaction**.

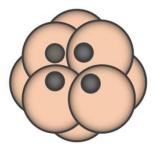


....segregates inner cells, which communicate by gap junction, from outer cells



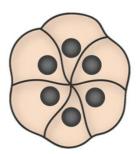
a Non-compacted

Early 8-cell stage



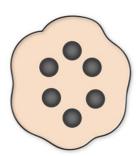
b Compacting

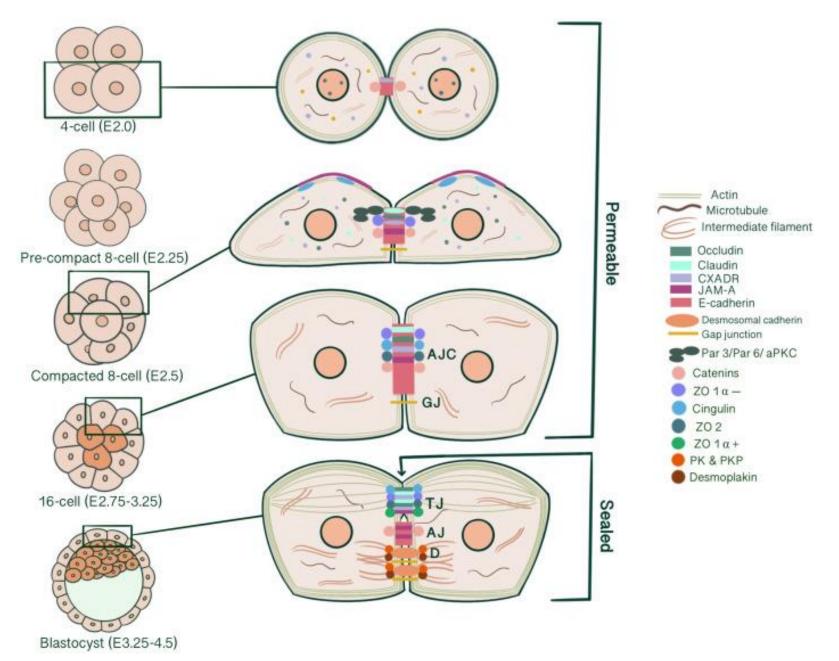
Mid 8-cell stage



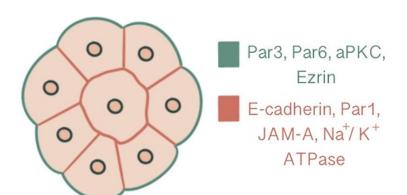
b Fully compacted

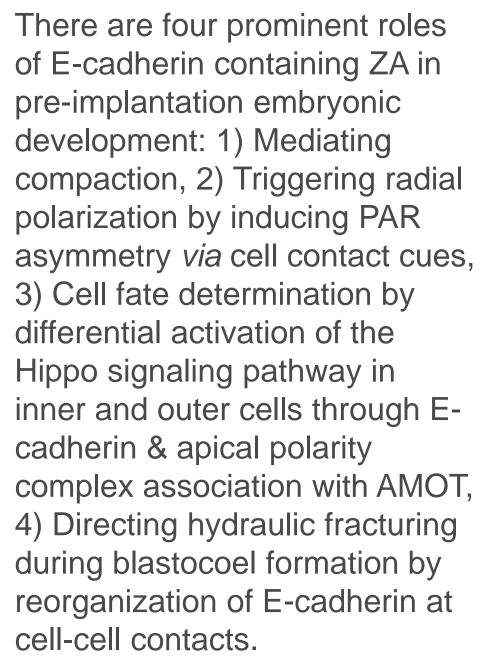
Morula Stage





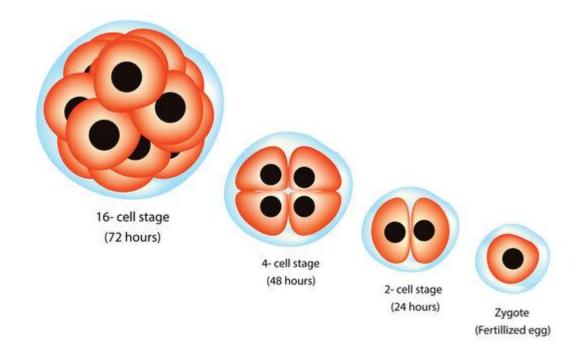
E-cadherim







3 days after fertilization, cells divide again to form a 16-cell morula

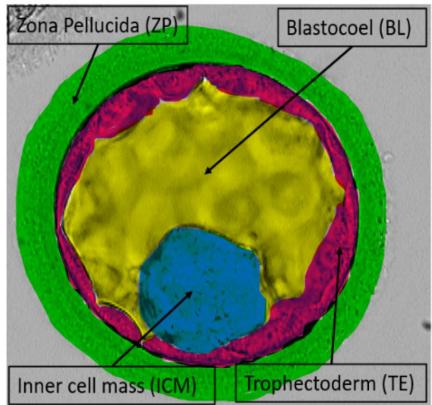


Inner cells of the morula constitute the inner cell mass, and surrounding cells compose the outer cell mass

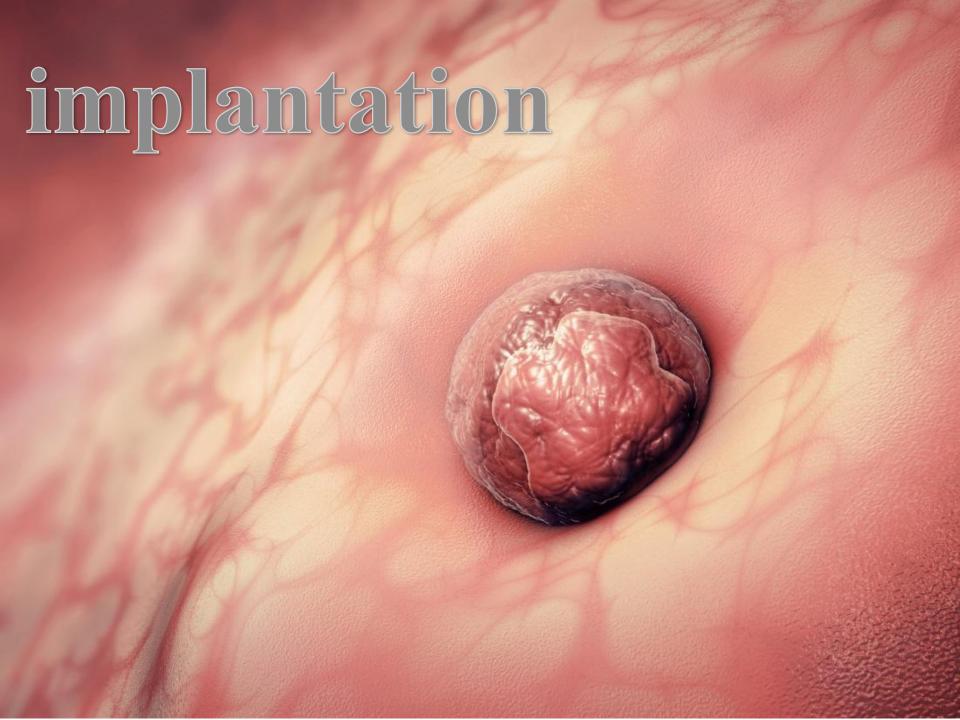
Fluid accumulation and formation of the blastocoel

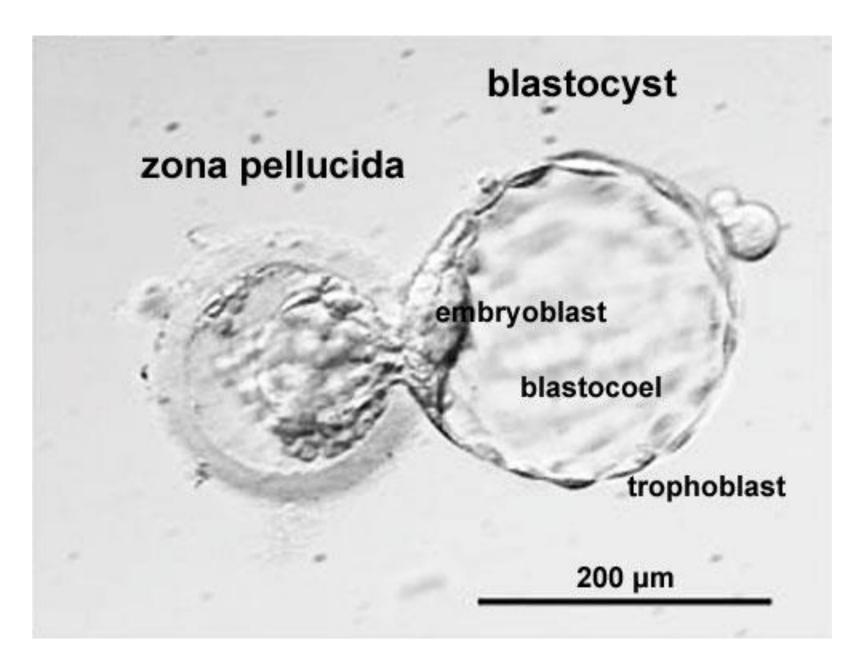
Blastocoel expansion and hatching





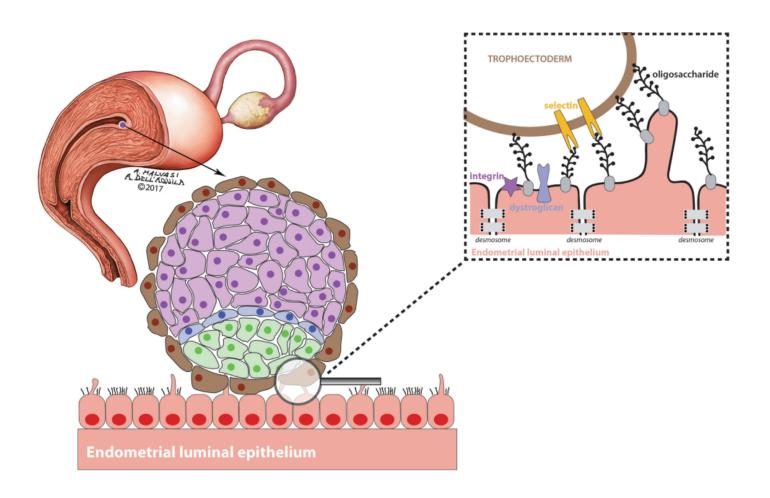






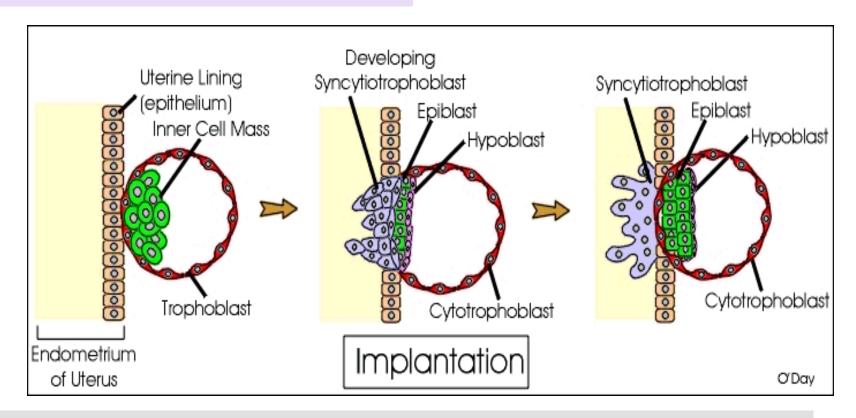
implantation

Adherence and attachment of the blastocyst to the endometrium (L-selectin on trophoblast cells and its carbohydrate receptors on the uterine epithelium)



implantation

Penetration of the epithelium Invasion into the endometrium

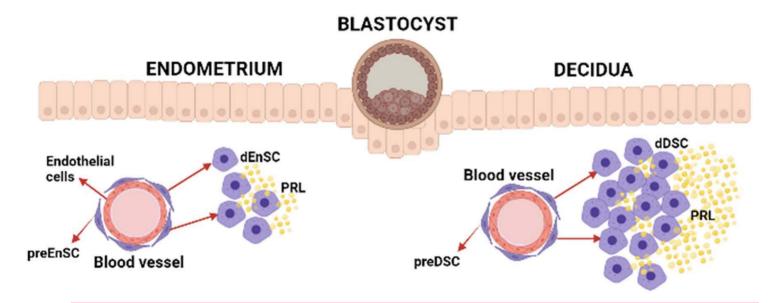


Synchronization of the embryo (expanded blastocyst) and the uterus (endometrial receptivness)

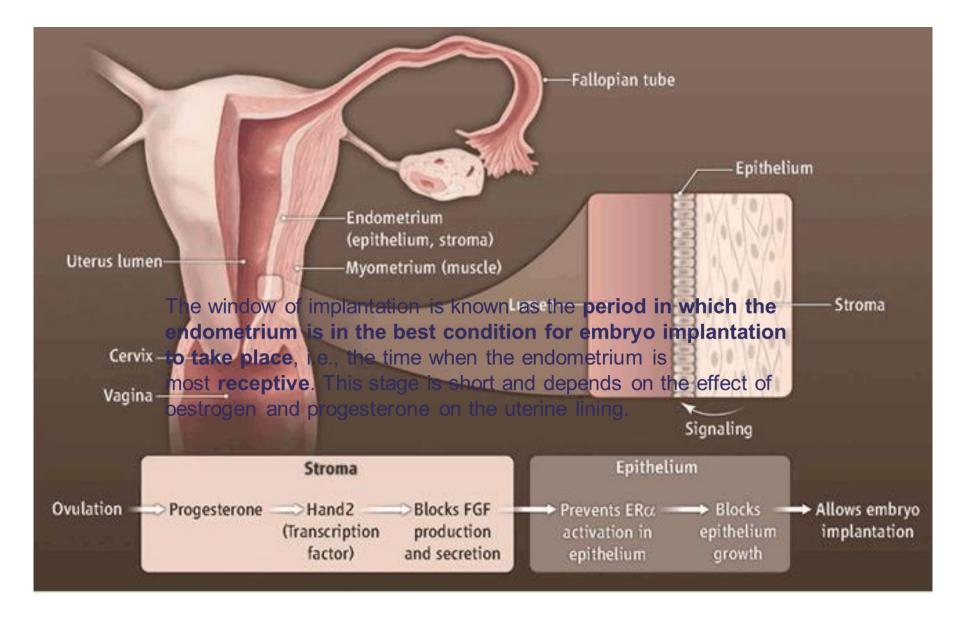


implantation

Decidualization, otherwise known as the decidual reaction, refers to a multifactorial process through which the endometrial stratum functionalis changes to allow a blastocyst to interact with the endometrium and implant.

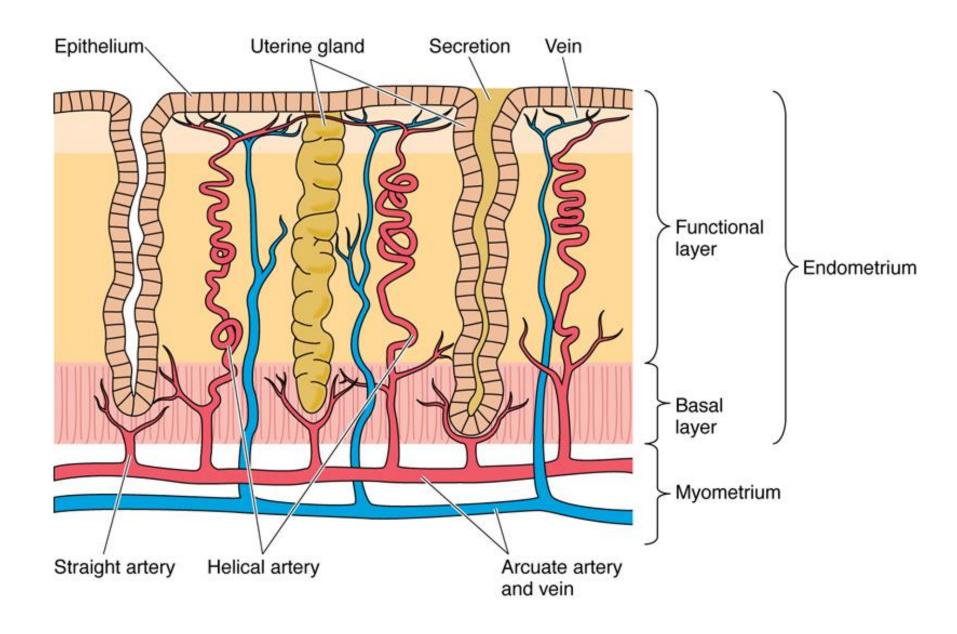


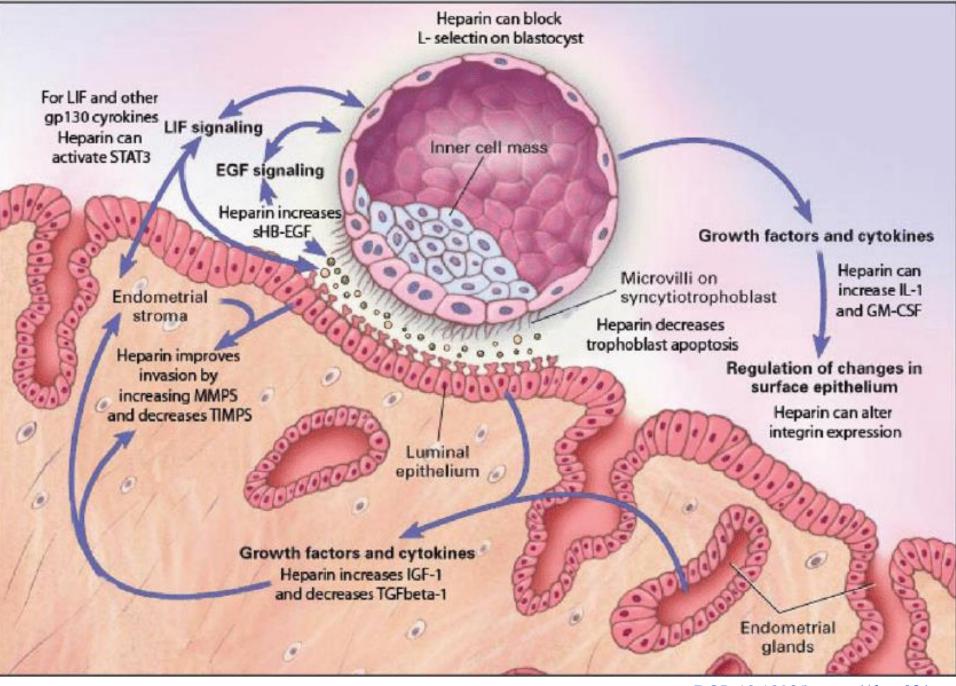
the differentiation of endometrial stromal cells to **decidual cells**, and leukocyte recruitment



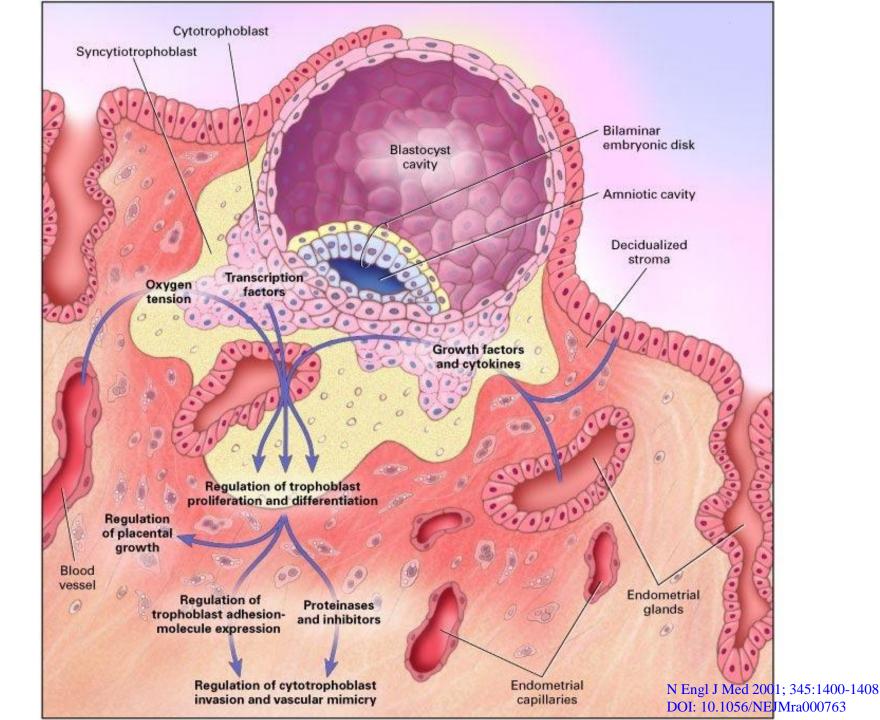
DECIDUA

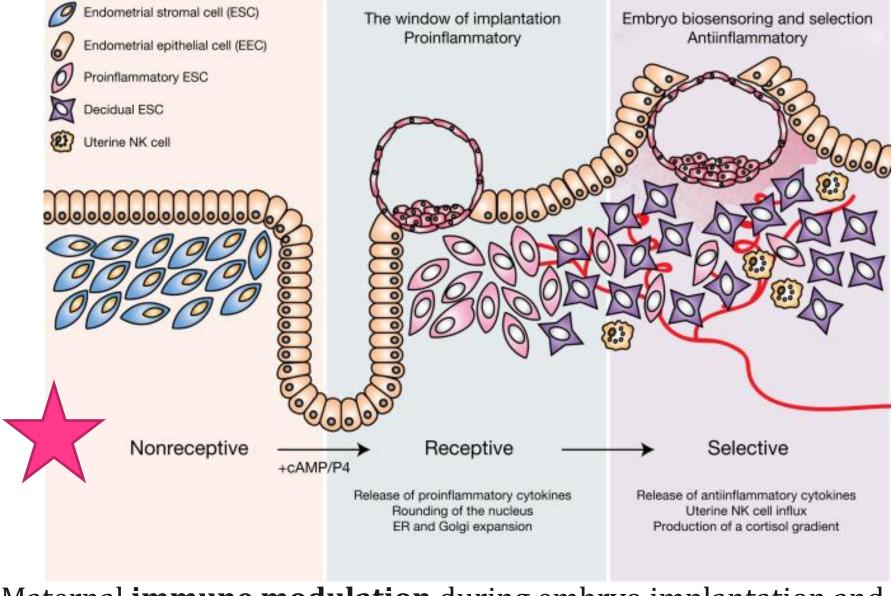
- STEPS OF FORMATION (DECIDUAL REACTION): ___, IMPORTANT IN DIAGNOSIS OF EARLY PREGNANCY
- 1. The endometrium becomes thicker & more vascular Increase vascular permeability (edema)
- 2. The endometrial glands become full of secretion
- 3. The connective tissue cells enlarge due to accumulation of lipid & glycogen. They are called "decidual cells"



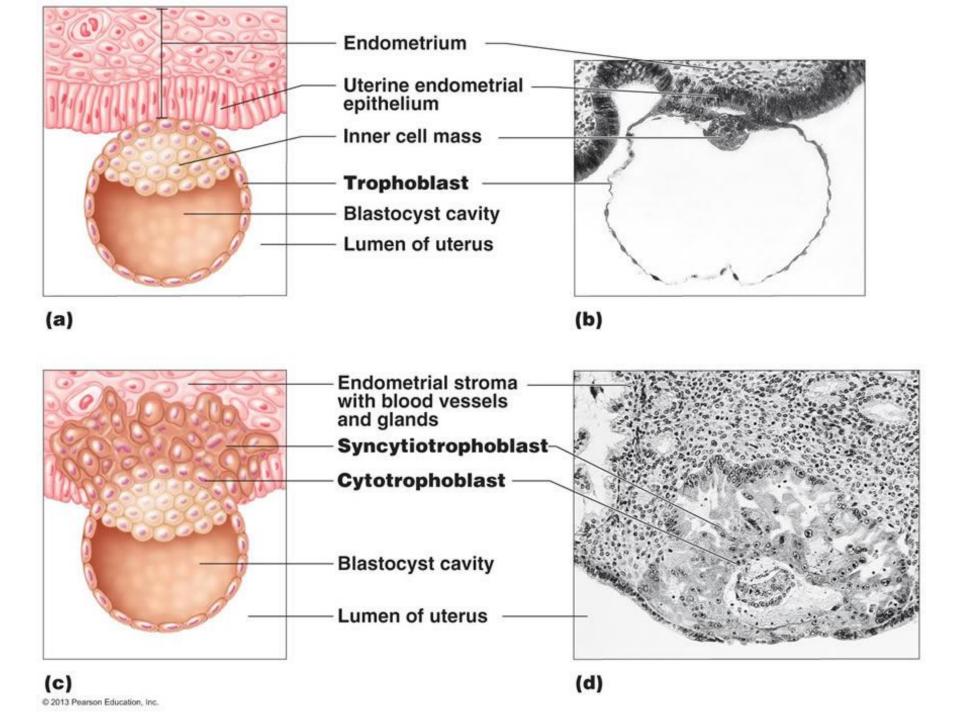


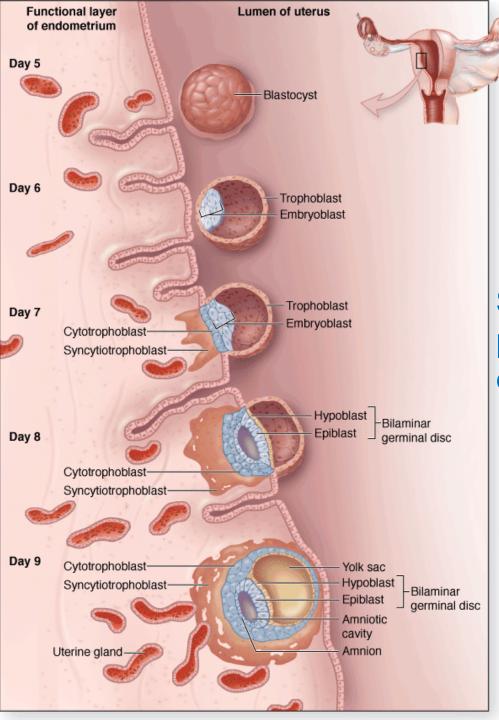
DOI: 10.1093/humupd/dmn031





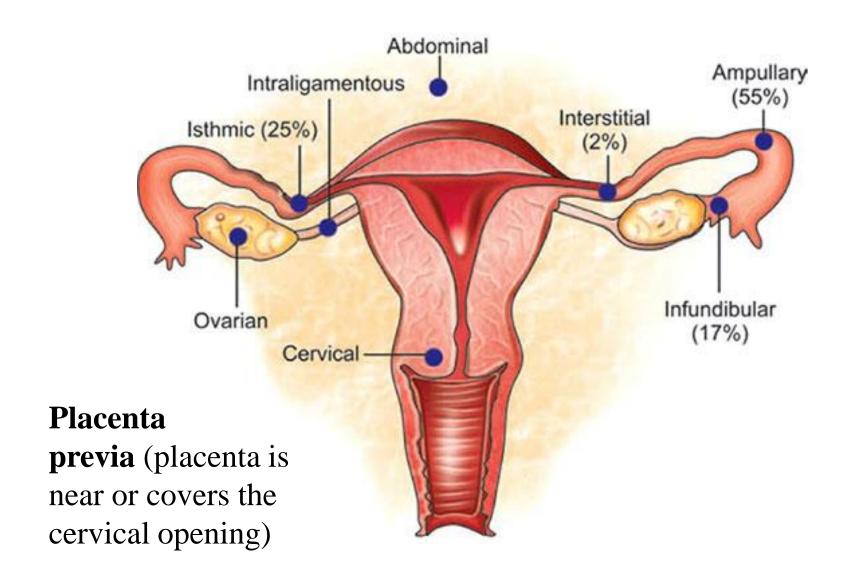
Maternal **immune modulation** during embryo implantation and subsequent pregnancy provides a tolerant microenvironment to keep the fetus from rejection





SITE: usually the upper posterior wall of the body of uterus

Abnormal implantation sites



Thank you for your attention

