5. Doppelstunde ESF II 2018

Teil 2 Herstellung von Lebewesen aus einzelnen diploiden Zellen (5. bis 7. Doppelstunde)

1. Der weibliche Reproduktionszyklus ex vivo
2. Der männliche Reproduktionszyklus ex vivo
3. Herstellung von Zygoten
4. Herstellung von Blastozysten aus Stammzellen
5. Herstellung von Plazenten aus Stammzellen
6. Autonome Morphogenese
7. Ethische und juridische Überlegungen zur Herstellung von Leben

Die Herstellung von Lebewesen aus einer lebenden diploiden Zelle.

Es geht hier nicht um die Herstellung von Leben an sich!

Vorgeschichte /Einleitung /Wiederholung:

Was sind Keimzellen (Primordial Germ cells) und wie entstehen sie?

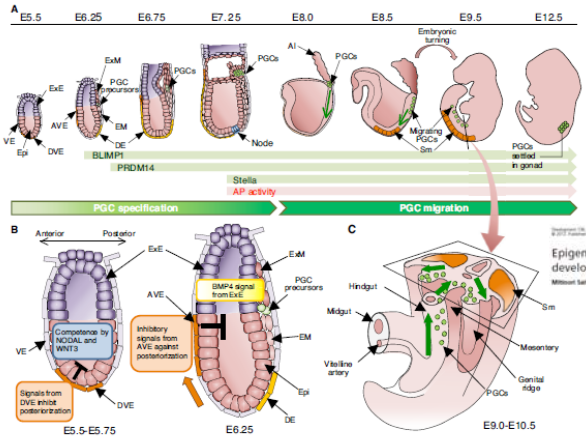
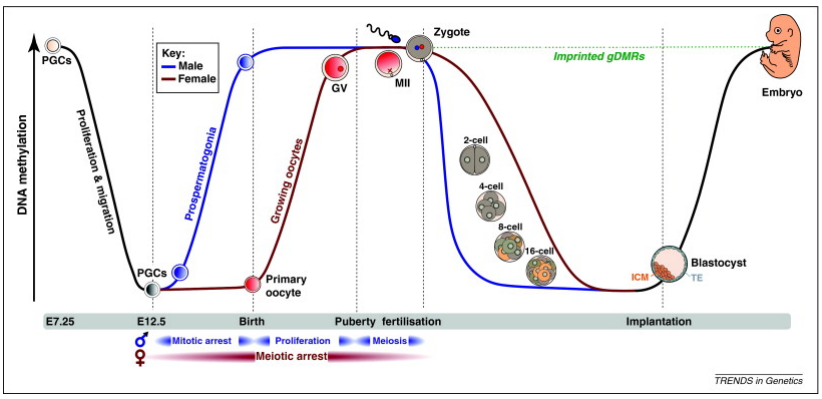


Fig. 2. Specification and migration of mouse primordial germ cells. (A) A schematic of germ cell specification and migration in developing mouse embryos (prospective anterior is towards the left). Primordial germ cell (PGC) precursors (E6.25) and PGCs are shown as green circles in embryos from E6.25 to E12.5, and the direction of PGC migration is denoted by a green arrow. The timing of expression of key genes (*Blimp1*, *Prdm14* and stella) and alkaline-phosphastase activity is shown below. (B) Signalling activities for PGC specification at E5.5-E5.75 and at E6.25. (C) A detailed view of PGC migration from the hindgut through the mesentery to genital ridges at E9.0-E10.5. The direction of PGC migration is denoted by a green arrow and anterior is towards the top. Al, allantois; AVE, anterior visceral endoderm; DE, distal endoderm; DVE, distal visceral endoderm; EM, embryonic mesoderm; Epi, epiblast; ExE, extra-embryonic ectoderm; ExM, extra-embryonic mesoderm; PGCs, primordial germ cells; Sm, somite; VE, visceral endoderm.

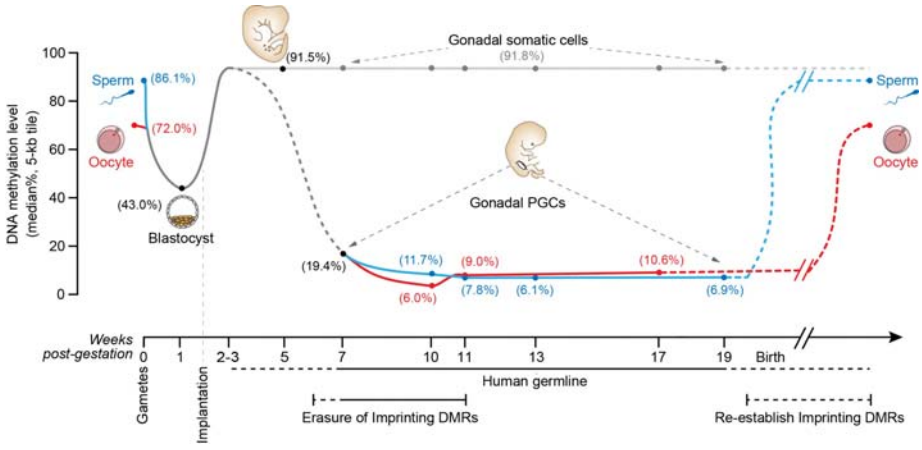
Epigenetic reprogramming in mouse pre-implantation development and primordial germ cells

DNA methylation changes during development of Primordial germ cells (PGCs).



https://www.sciencedirect.com/science/article/pii/S0168952511001582

Figure 1. DNA methylation changes during developmental epigenetic reprogramming. Primordial germ cells (PGCs) emerge in embryos at E7.5 and, concomitant with their proliferation and migration towards the genital ridge, DNA methylation is globally erased (black line). Following sex-determination, new DNA-methylation landscapes are established in germ-cell precursors in an asymmetrical fashion in male and female embryos. In the male embryo (blue line), *de novo* methylation takes place before meiosis in mitotically arrested cells (G1-phase; prospermatogonia) and is completed before birth. In the female embryo (red line), primary oocytes enter meiosis and arrest in prophase-I (diplotene stage); DNA methylation is established after birth during the follicular/oocyte growth phase. At puberty, under specific endocrine triggers, fully-grown germinal vesicle (GV) oocytes resume the first meiotic division. After extrusion of the first polar body, oocytes arrest in metaphase of the second meiotic division (MII oocytes) and meiosis is completed only upon fertilisation. Following fertilisation, a new wave of DNA demethylation takes place that is distinct on the parental genomes. In the zygote, DNA methylation of the paternal genome is rapidly erased by an active mechanism (blue line). Demethylation of the maternal genome is slower (red line) and is dependent on DNA replication (passive demethylation). These post-fertilisation demethylation events do not include imprinted gDMRs (green dotted line), resulting in parental-allele-specific methylation of these elements in early embryos and consequent parental-allele-specific expression of associated imprinted genes. Concomitant with blastocyst implantation and cell-lineage determination, new methylation landscapes become established, associated with cellular differentiation.



http://biopic.pku.edu.cn/english/content.aspx?id=260

The epigenetic genome-wide reprogramming cycle involves two phases of DNA erasure in the mouse (from [[91],[161],[162]]). (1) A first wave of DNA demethylation takes place in the male (blue curve) or female (red curve) primordial germ cells (PGC) of the F1 individuals; this occurs throughout the genome, including the imprinted genes (embryonic day (E10.5-13.5). (2) Then, the genome of the gametes undergoes de novo methylation, with maternal methylation marks established at a later stage (ovulation) than paternal marks (E14). (3) A second wave of DNA demethylation takes place after fertilization in the F2 zygote (E0.5), with a more rapid demethylation in the paternal than the maternal genome. However, the paternal and maternal imprinted genes maintain their methylation pattern throughout this preimplantation reprogramming (dotted curves), allowing the inheritance of parent-specific monoallelic expression in somatic tissues of the F2 individual. (4) Finally, genome-wide remethylation occurs in both parental genomes at about the time of implantation (E3.5). Altogether the very early embryonic development corresponds to an epigenomic reprogramming step, during which the new epigenetic marks are more prone to being impacted by the environment. This explains why the environment experienced during early development has a greater impact on the adult phenotype than that experienced later in life [163]. Moreover, the timing of the two global DNA demethylation and remethylation waves differs between male and female genomes, possibly explaining why they may be differently impacted by a stress applied during these stages [91,164].

Epigenetic reprogramming in mouse pre-implantation development and primordial germ cells
Mitinori Saitou, Saya Kagiwada, Kazuki Kurimoto
Development 2012 139: 15-31; do: 10.1242/dev.050849

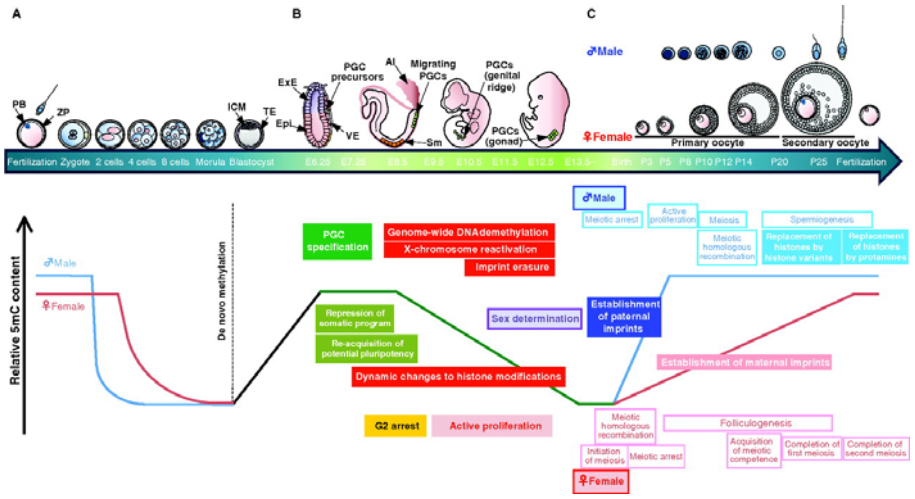


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Fig. 1. A schematic of mouse pre-implantation and germ cell development. (Top) A schematic of pre-implantation and germ-cell development in mice. (**A**) Pre-implantation development stages; (**B**) post-implantation embryonic development, following blastocyst implantation at around E4.5; and (**C**) postnatal germ cell development and maturation. Primordial germ cell (PGC) precursors (E6.25) and PGCs are shown as green circles in embryos from E6.25 to E12.5. (Bottom) Key genetic and epigenetic events are shown that are associated with pre-implantation and germ cell development, together with relative levels of 5-methylcytosine (5mC) at different developmental stages. Al, allantois; Epi, epiblast; ExE, extra-embryonic ectoderm; ICM, inner cell mass; PB, polar body; PGCs, primordial germ cells; Sm, somite; TE, trophectoderm; VE, visceral endoderm; ZP, zona pelucida.

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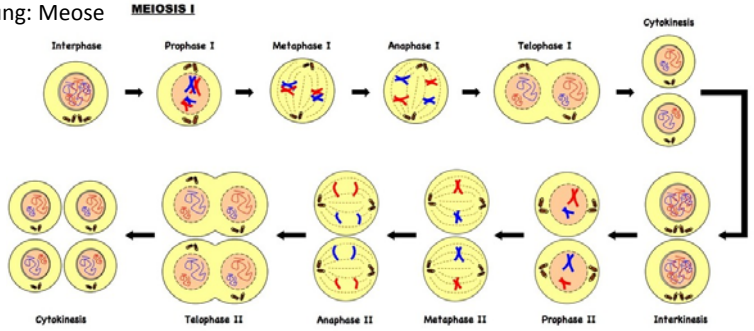
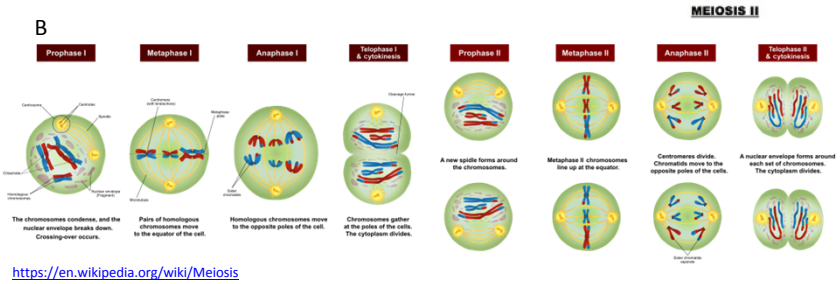
Zur Erinnerung: Meose

A

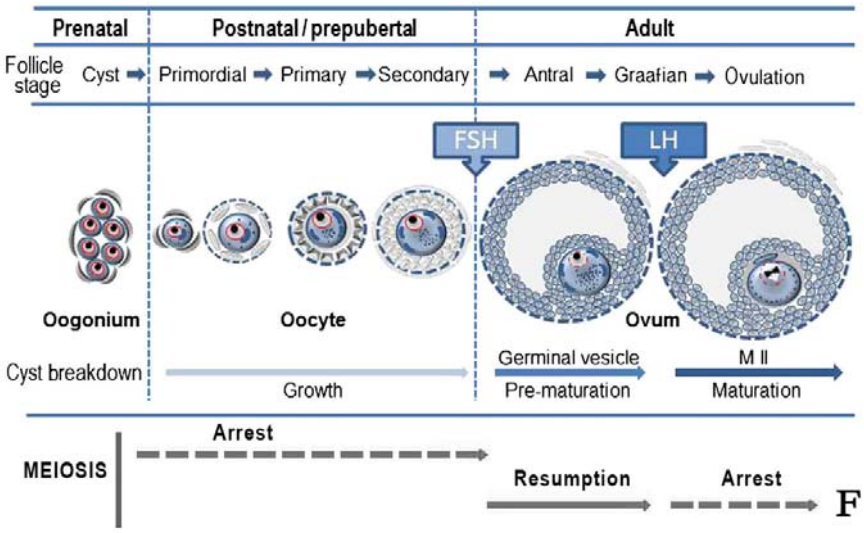


B



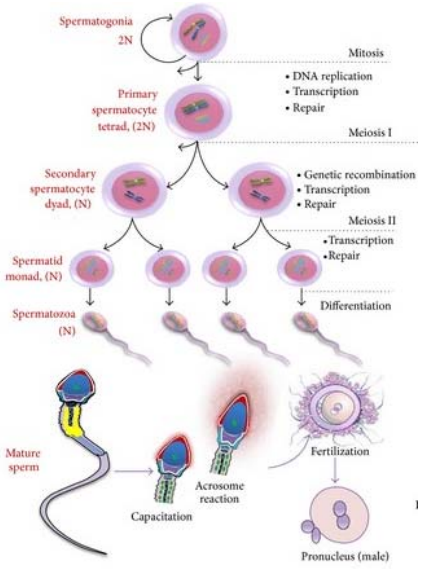
https://en.wikipedia.org/wiki/Meiosis

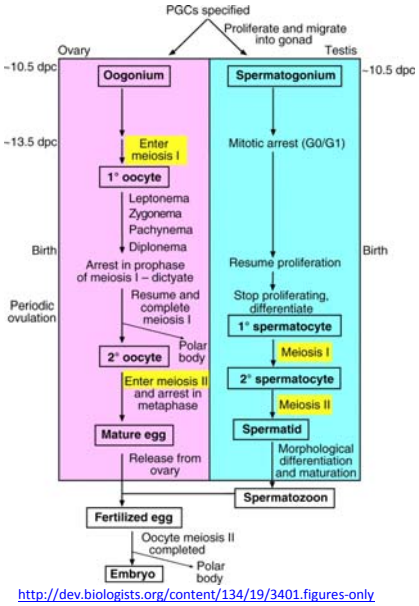
Zur Erinnerung: Entstehung der MII Oozyten und Spermien



https://embryologistmedia.weebly.com/patients/what-is-a-mature-egg-reasons-why-you-may-not-obtain-mature-eggs-in-your-art-cycle

Vergleich der Geschlechter:





http://dev.biologists.org/content/134/19/3401.figures-only

https://www.researchgate.net/figure/Schematic-diagram-showing-the-cellular-genetic-and-chromatin-changes-during_fig1_259450365

In vitro Reproduktion von Säugetieren inklusive Homo sapiens

Somatische Zelle → Keimbahnstammzellen (Primordial Germ Cells (PGCs) →

→ Oozyten und Spermien → in vitro Fertilisation (iVF) → künstlicher Uterus

und Plazenta → Embryonal und Fötalentwicklung → Neugeborenes Lebewesen.