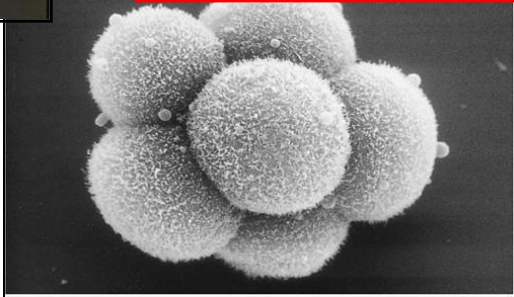
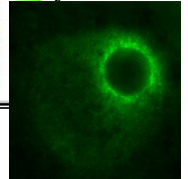
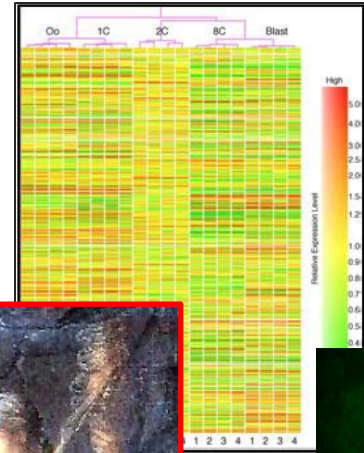
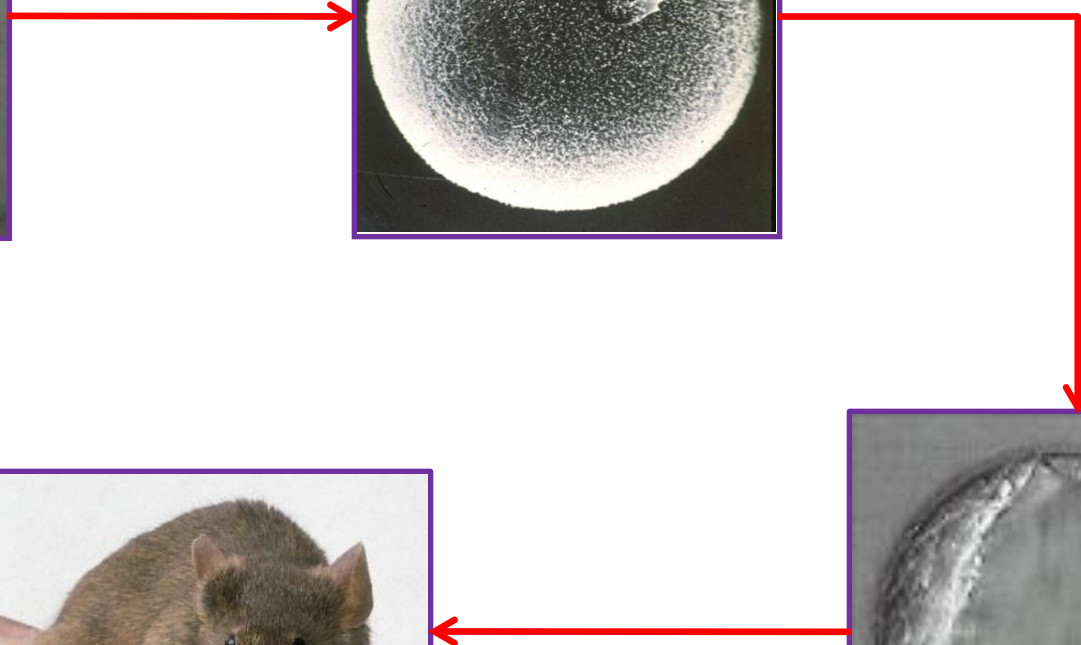
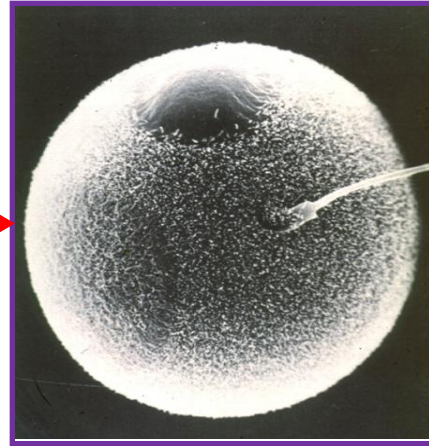


L'eredità
citoplasmatica
dell'oocita
determina il destino
dello sviluppo
embrionale

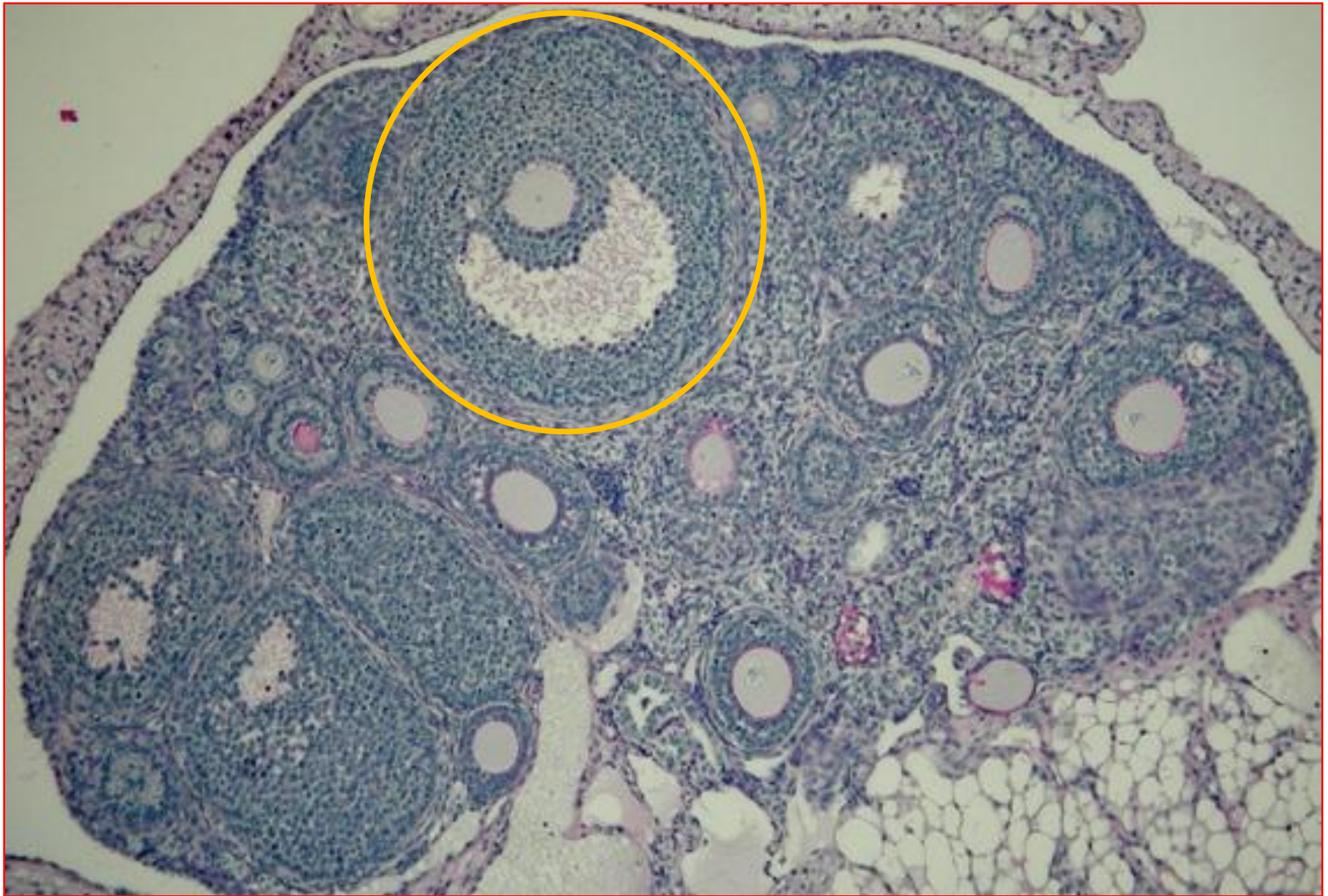


Developmental competence

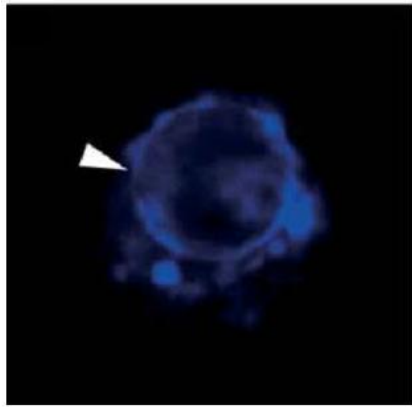


The oocyte saga

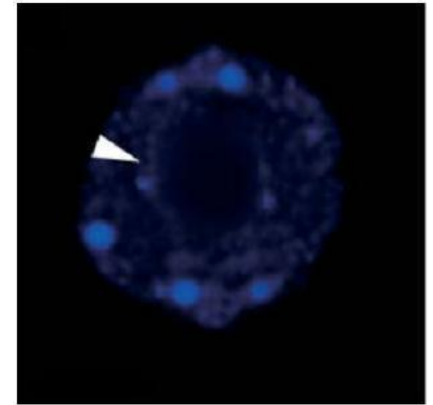
Does predestination exist?



The oocyte saga



Surrounded nucleolus – SN



Not surrounded nucleolus – NSN



Chromatin condensation

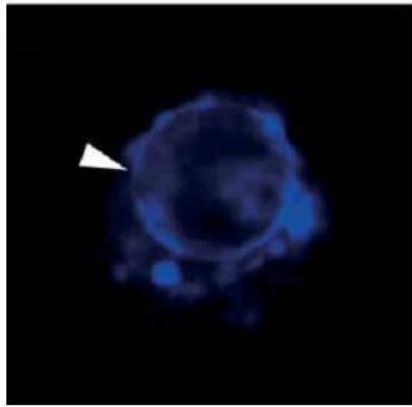


Transcriptional activity

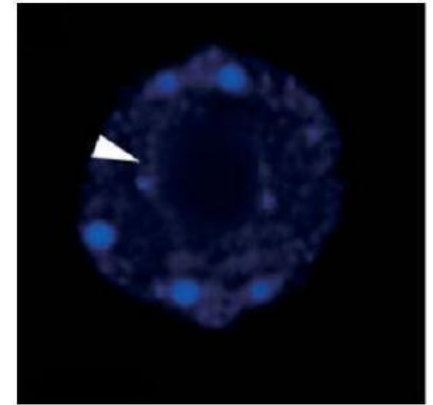


Meiotic competence





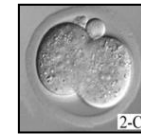
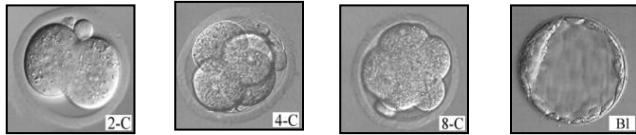
Surrounded nucleolus – SN



Not surrounded nucleolus – NSN



In vitro maturation and *in vitro* fertilization



From one to many

Zygotic gene activation

Zygotic gene activation

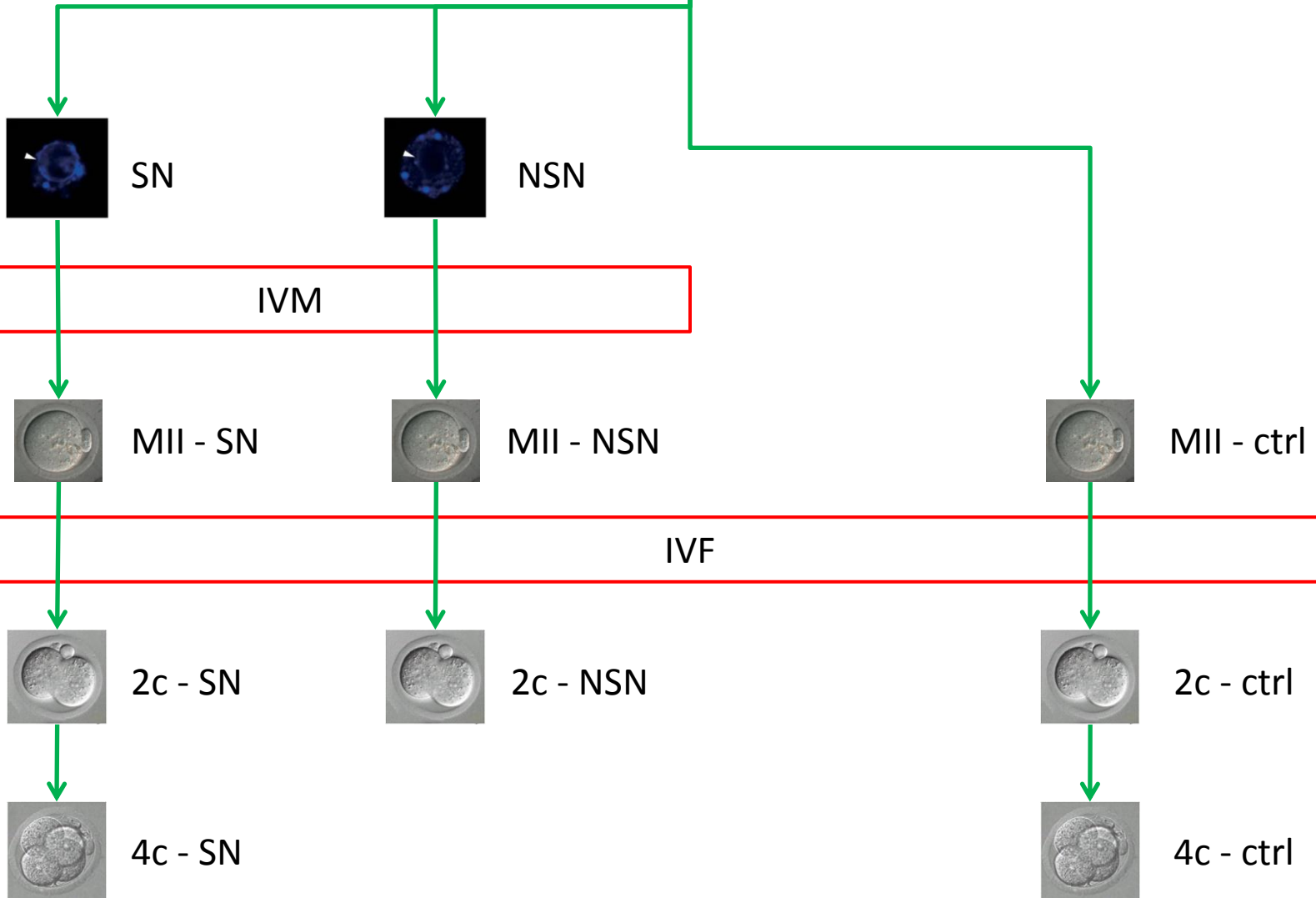
Maternal mRNAs undergo degradation shortly after fertilization.

Transition from the maternal to the zygotic control of embryo development.

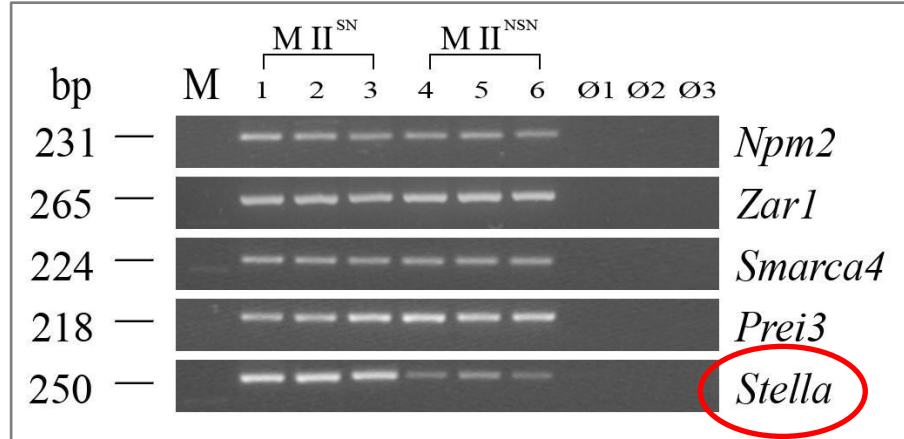
Sheep and rabbit (morula stage), human and cow (4-/8-cell stage), mouse (2-cell stage).

Results

Genes and protein expression



Maternal-effect genes



Stella is downregulated (1.4 fold change) in MII^{NSN}.

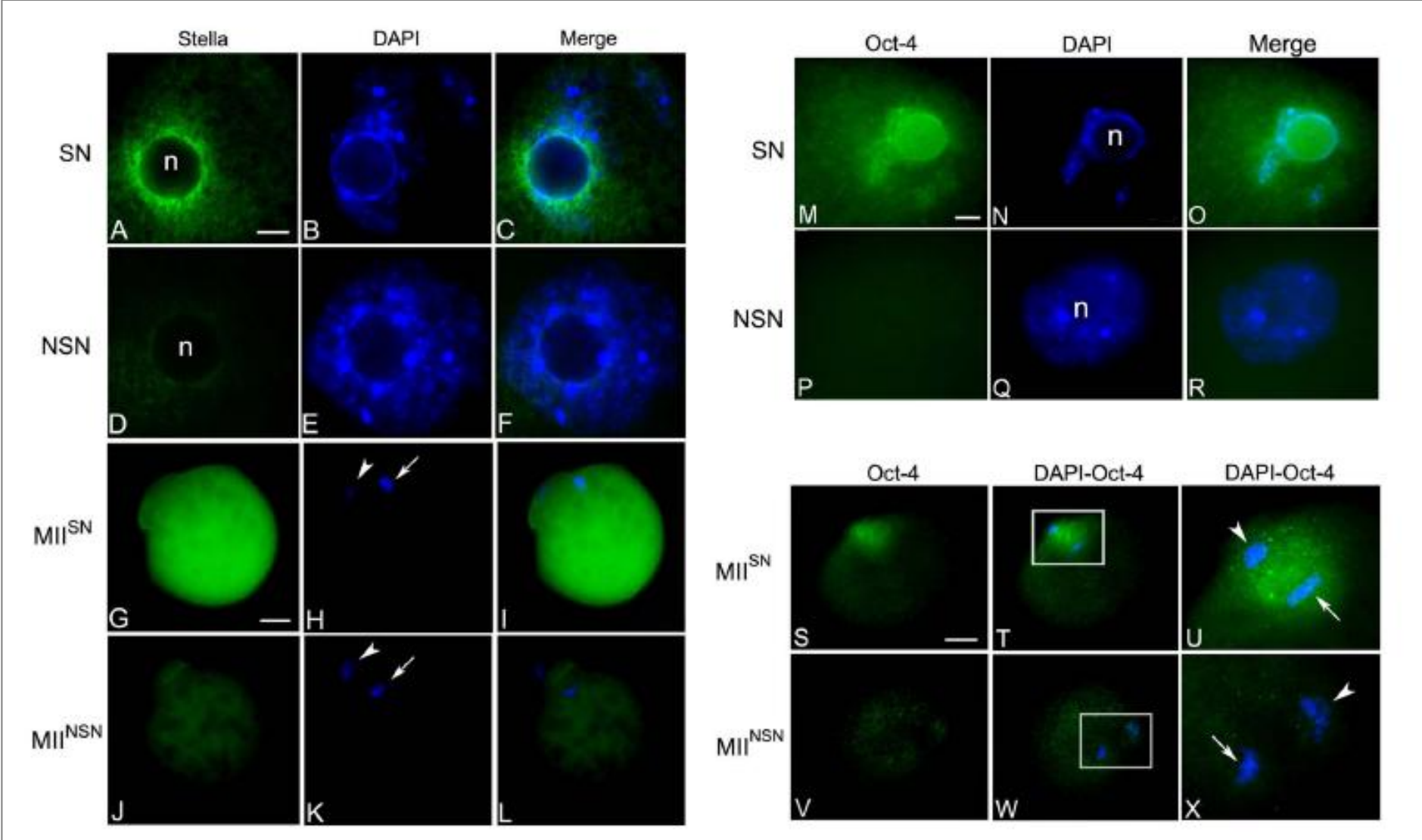
Stella protects against inappropriate DNA demethylation during epigenetic reprogramming after fertilisation.

Oocytes from *Stella* ^{-/-} females can be fertilized but most of the resulting embryos block their development at the 2-cell stage.

Stella is known to be regulated by Oct-4 in ES cells.

Oct-4 is downregulated (1.8 fold change) in MII^{NSN}.

Oct-4 is more expressed in GV^{SN} than in GV^{NSN} (Monti et al., 2006).



Oct-4 (Pou5f1)

the herald of pluripotency

- ❖ is a member of the POU family of transcription factors.
- ❖ is involved in the maintenance of a high differentiation potential in PGCs, type A spermatogonia, oogonia, blastomeres of early preimplantation embryo, cell of inner cell mass, embryonic stem cells.
- ❖ is one of four factors that, once induced in fibroblasts, reprogramme these terminally differentiated somatic cells into pluripotent cells (iPS).

Identification of Oct-4 target genes

25 regulated genes
in MII^{SN} vs MII^{NSN}.

Gene networks analysis

Network	Molecules in Network	Score	Focus Molecules	Top Functions
1	<i>Bat1, Cd58, Cpd, Ddx11, Ddx21, Dleu1, Dleu2, Dub2, Duox2, E2f1, Exosc9, Hivep3, Hn1, Il2, Jun, Mfap1, Mist, Myc, Nr2e1, Parp1, Prl2c2, Psat1, Psmc5, Psmc6, Psmc7, Ranbp1, Rbm14, Rps16, Rps18, Sec61g, Terf2ip, Tle4, Tmem126a, Trip4, Vhl</i>	28	12	Gene Expression, Cell Death, Hematological Disease
2	<i>Aatk, Bpi, Cdh1, Cldn11, Ctsc, Dhrs3, Dlx1, Eef1d, Foxd3, Gfra1, Hoxa7, Iqgap1 (Includes Eg:8826), Kif3c, Mcl1, Mt11, Nif311, Nkx2-3, Nrtn, Ogn, Optn, Pik3c3, Pla2g7, Pou5f1, Psmb2, Psmb9, Ptpru, Retinoic Acid, Rna Polymerase li, Serpinb8, Slc12a6, Tmem49, Tmsb10, Tnf, Zfp42, Zfp3611</i>	15	7	Cancer, Reproductive System Disease, Cell Death
3	<i>Cd79a, Mro</i>	3	1	Lipid Metabolism, Small Molecule Biochemistry, Viral Function
4	<i>Cggbp1, Fmr1</i>	3	1	Connective Tissue Development and Function, Developmental Disorder, Genetic Disorder
5	<i>Pgm, Pgm2, Pmm</i>	3	1	Carbohydrate Metabolism, Small Molecule Biochemistry
6	<i>Arsa, Arsb, Arsd, Arse, Arsf, Arsg, Arsi, Arsj, Gns, Ids, Sgsh, Sts, Sulfl, Sulf2, Sumfl</i>	2	1	Genetic Disorder, Metabolic Disease, Skeletal and Muscular System Development and Function

*: In bold are the Oct-4-regulated focus genes. Underlined is the Oct-4 (*Pou5f1*) gene.

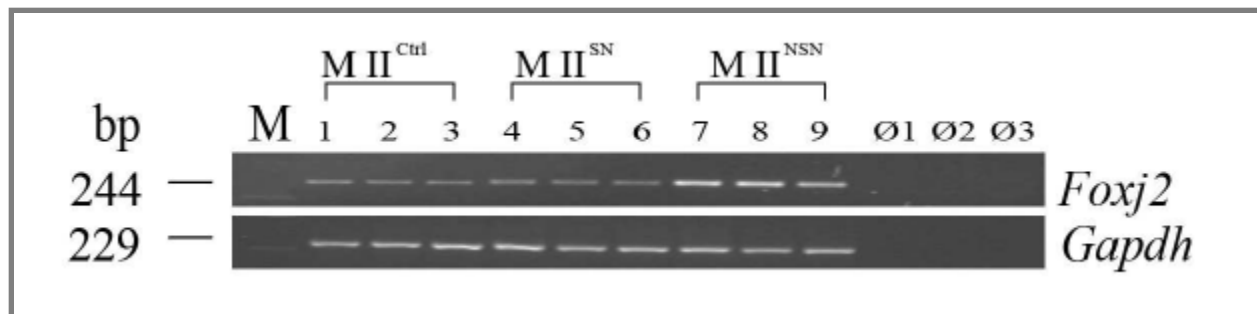
Foxj2

It is up-regulated in MII^{NSN}.

It colocalises within the locus containing *Stella*, the ***Nanog* locus** (Levasseur et al., 2008).

Oct-4 is necessary for maintaining a specific chromatin structure at the *Nanog* locus (Levasseur et al., 2008).

Induction of Foxj2 in mouse 1-cell embryos causes a developmental block at the 2-cell stage (Martin-de-Lara et al., 2008).



Conclusions

1. Oct-4 is a key regulator of the establishment of the developmental competence in mouse oocytes.
2. Oct-4 is down-regulated in MII^{NSN} oocytes.
3. Oct-4 absence in MII^{NSN} oocytes up-regulates the expression of some genes involved in pathways important for the oocyte survival.
4. The function of Oct-4 is directed at the *Nanog* locus, down-regulates *Stella*, a maternal factor required for the oocyte-to-embryo transition, and up-regulates *Foxj2*, an embryo-specific gene whose overexpression is involved in the 2-cell block.

Future perspectives

Analysis of developmental competence and genic expression in embryos obtained from NSN oocytes microinjected with small SN-derived cytoplasmatic portions.

Thank you!