Sviluppo embrionale, DNA fetale e chimerismo: un opportunità per la scienza

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Roma, 11 maggio 2016

- ***Sviluppo embrionale***
- ***Il mosaicismo***
- ***Il chimerismo***
- ***La tolleranza***

"I believe we exist in a multiverse of universes"
Michiu Kaku

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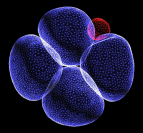
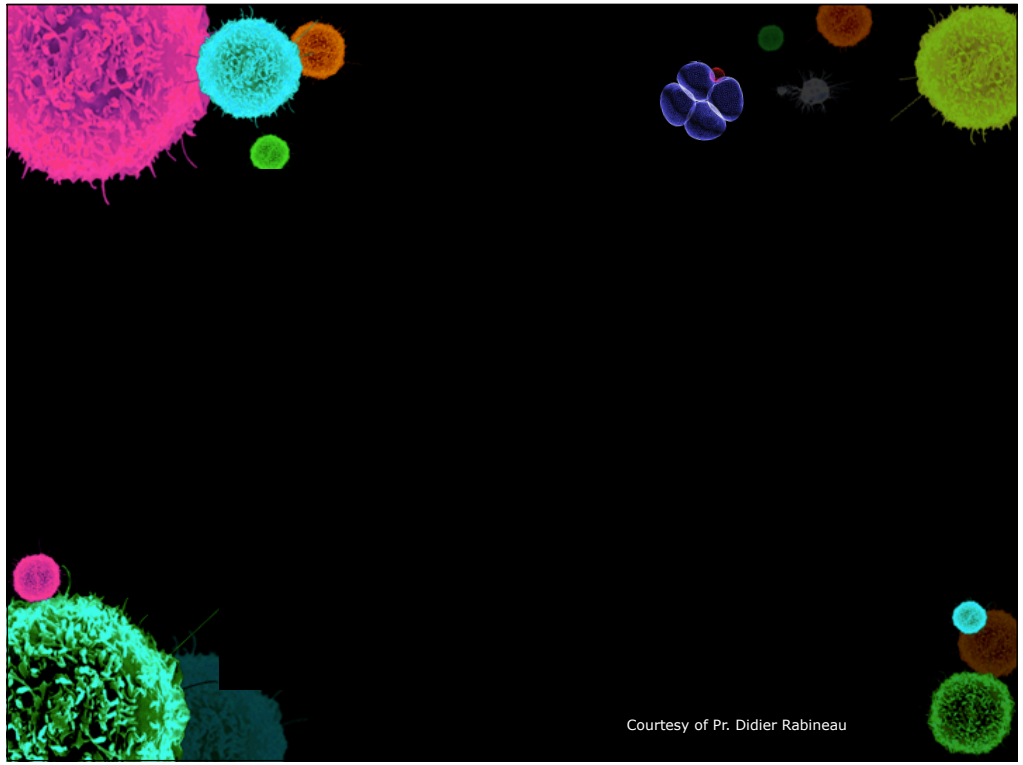



Courtesy of Pr. Didier Rabineau

Mammalian preimplantation development

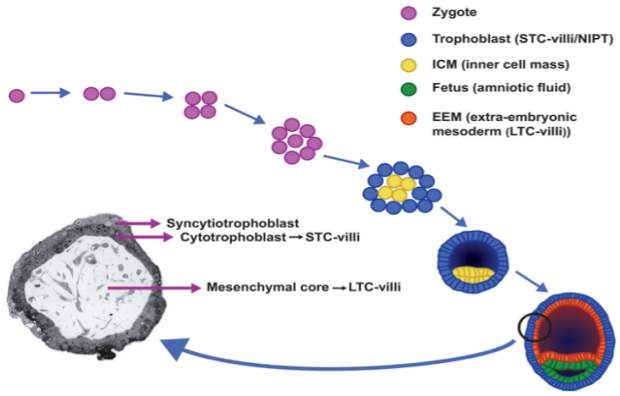
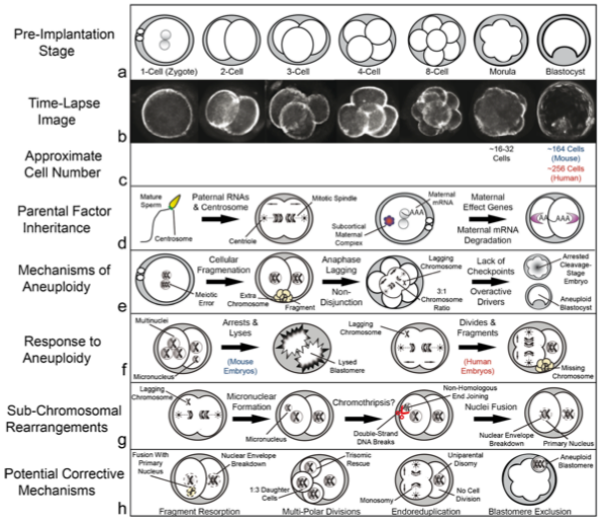


Fig 1. Early embryonic development from zygote to blastocyst. The cytotrophoblast which is studied in short-term cultured villi (STC-villi) and with NIPT is derived from the trophoblast of the blastocyst, whereas the mesenchymal core, investigated in long-term cultured villi (LTC-villi) originates from the extra-embryonic mesoderm (EEM). Both EEM and fetus are derived from the inner cell mass (ICM) of the blastocyst.

doi:10.1371/journal.pone.0146794.g001

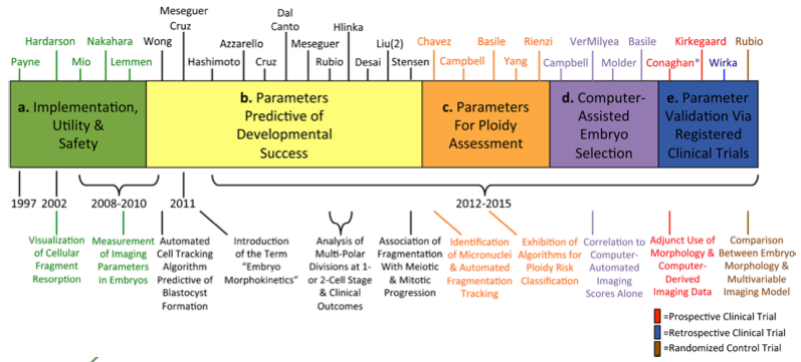
Van Opstal et al., 2016 PLOSone

Mammalian preimplantation development



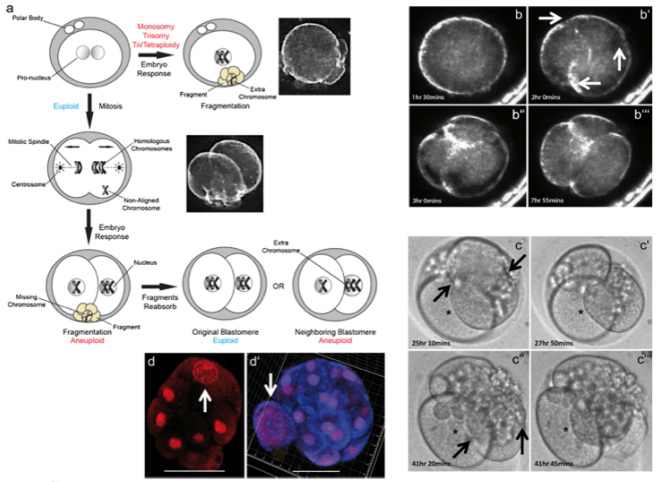
Daughtry and Chavez, 2015. Cell Tissue Research

Milestones on embryo viability



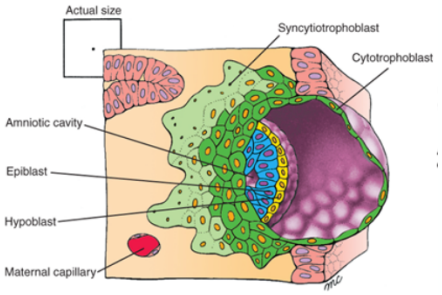
Daughtry and Chavez, 2015. Cell Tissue Research

Aneuploidy resolution



Daughtry and Chavez, 2015. Cell Tissue Research

Confined placental mosaicism: a strategy for embryo correction during implantation



8 days

Schoenwolf et al: Larsen's Human Embryology, 4th Edition.
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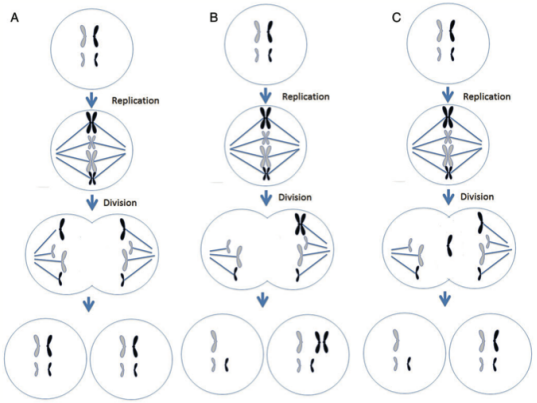
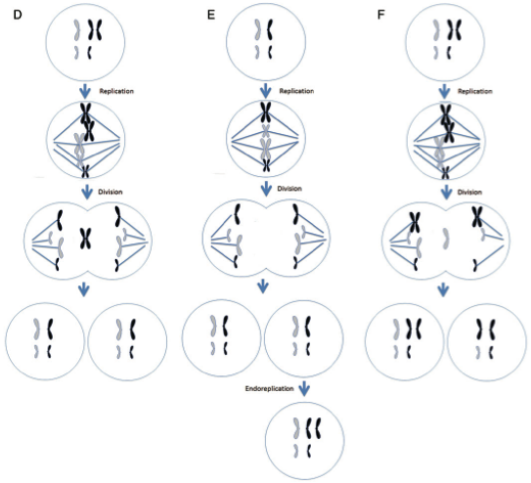
Mechanism of malsegregation



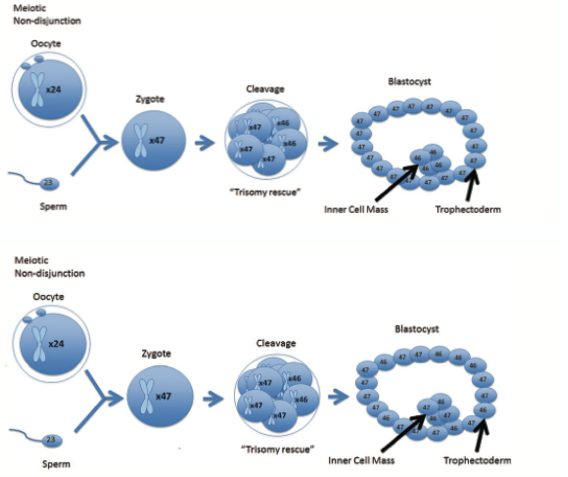
Taylor et al.,2014. Human Reproduction

Mechanism of malsegregation



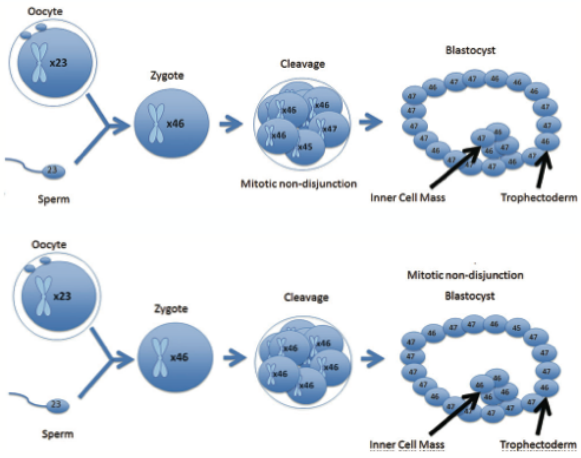
Taylor et al.,2014. Human Reproduction

A meiotic error



Taylor et al.,2014. Human Reproduction

A mitotic error



Taylor et al.,2014. Human Reproduction

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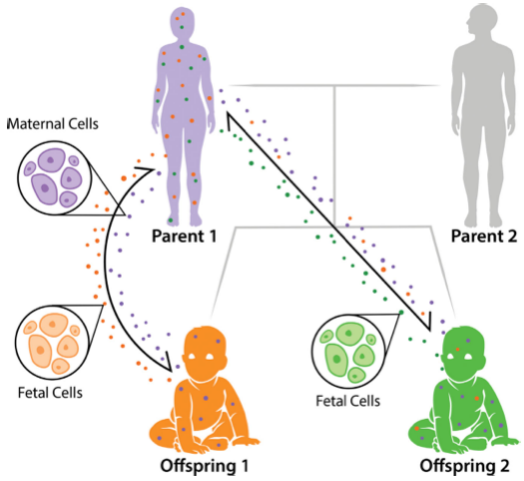
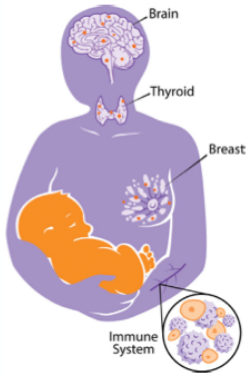
Microchimerism



Boddy et al., 2015.Bioessays

Mother offspring



Boddy et al., 2015.Bioessays

Another kind of chimerism

ILLUSTRATION BY MICHAEL SPECHT

Prepare for unexpected prenatal test results

Women are learning about their own health problems through fetal screening. Revise consent forms and raise awareness, urges **Diana W. Bianchi**.

Bianchi, 2015. Nature

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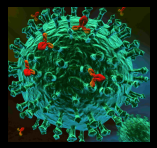
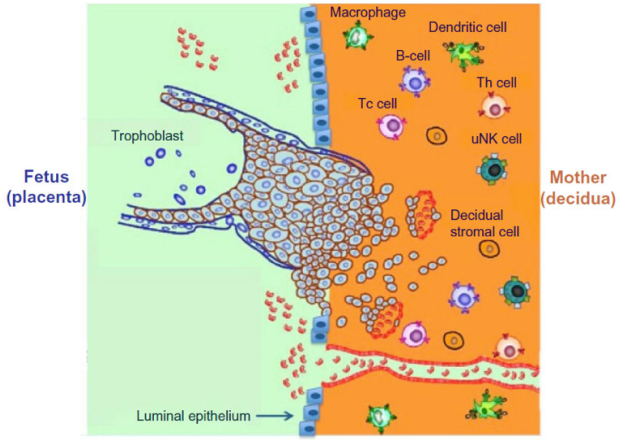
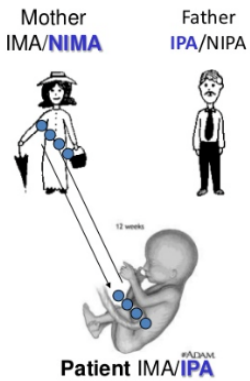


Immunological recognition



Bracamonte-Baran and Burlingham, 2016 BioMed J

A battle field or a mutual acceptance?



NIMA = non inherited maternal antigens

NIPA = non inherited paternal antigens

IMA = inherited maternal antigens

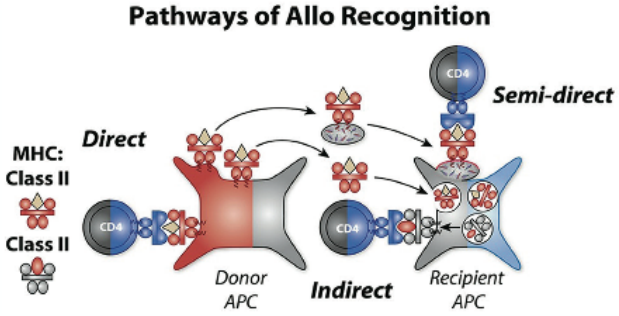
IPA = inherited paternal antigens

The mother develops B and T cell immunity against the IPA of the fetus, which is controlled by T reg.

Likewise, the fetus develop immunity and T reg against the NIMA.

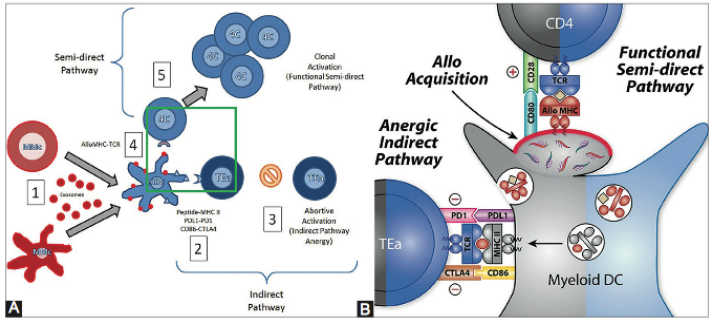
Immunity can be lifelong in both mother and child.

Pathways of Allo Recognition



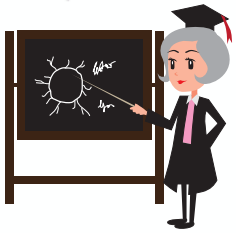
Bracamonte-Baran and Burlingham, 2016 BioMed J

Model for NIMA tolerance



Bracamonte-Baran and Burlingham, 2016 BioMed J

Conclusions



Embryo development is at a major risk of failure before implantation. Although the regulation is able to amend some errors (meiosis, early mitosis), this is the moment when mosaicism occurs more easily.

NIPT screening will never be diagnostic due to the unpredictable discrepancy between free DNA and epiblast after the formation of the blastocyst (confined placental mosaicism) and to the chimerism with the mother.
Mosaicism occurs with a rate of **7,6 %** of screened **NIPT** (risk to overestimate the rate?) while **confined placental mosaicism in 1-2%**.
Meiotic and mitotic errors due to non disjunction, anaphase, endoreplication parental disomy are the causes of aneuploidies.

Recent publications are describing **fetal micro-chimerism** with more accuracy and the effects of fetal lineages show to be both positive and negative.
NIPT allow to screen mosaicism of mother's origin that ends to be linked to non-diagnosed cancer cells (inner chimerism).

IPA and **NIMA** establish the threshold of tolerance between the mother and the fetus.
Allo-tolerance happens to give a higher rate of success in transplantation.
NIPT allow to investigate further on immunological crosstalk during pregnancy.

Question Time

Grazie

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