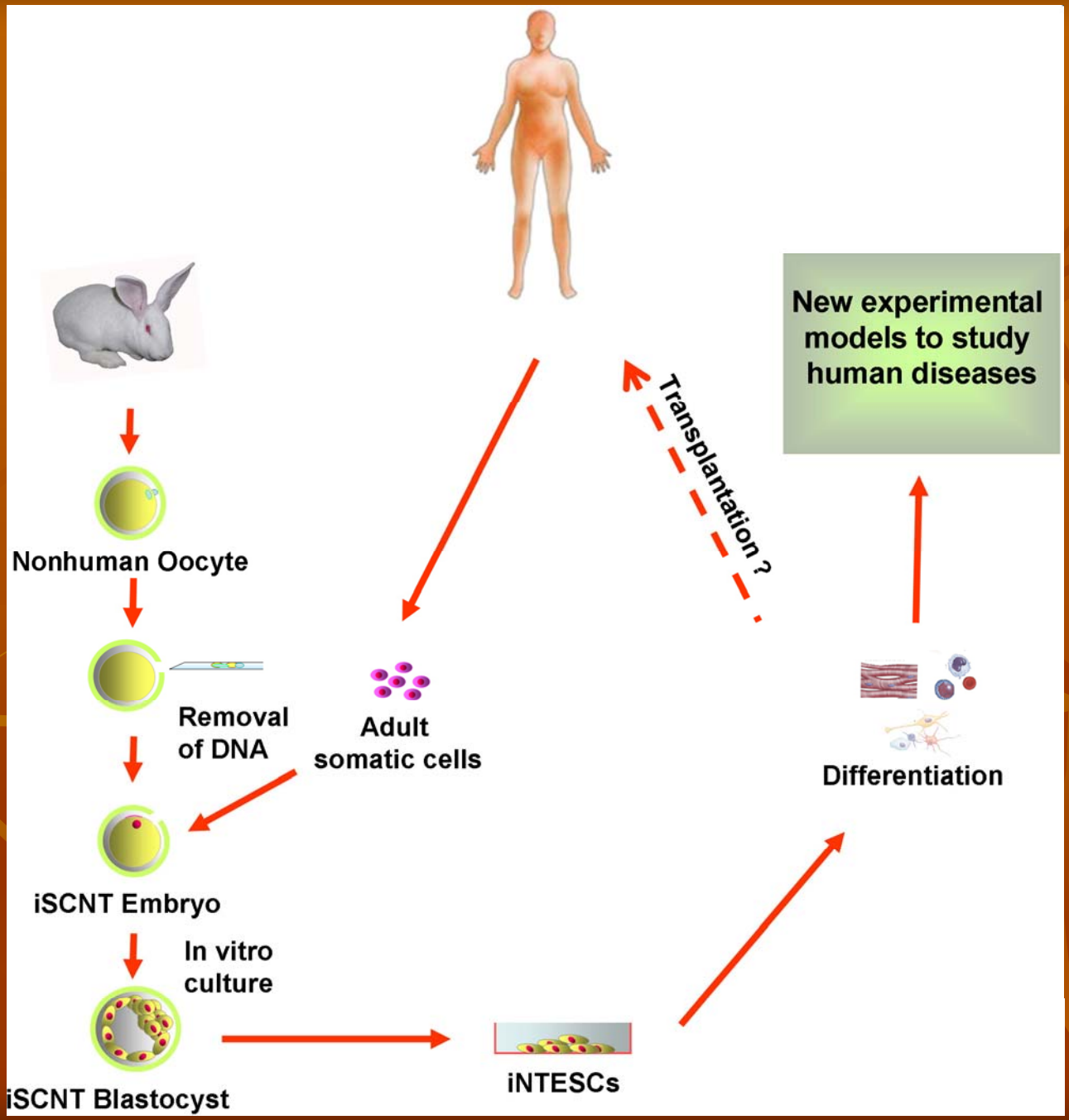
Prima di tutto la vita.

Riflessioni tra medicina, etica e pastorale sanitaria.

Andrea Manazza

Torino, 17 novembre 2011


ABORTO
Chimere interspecie
Riproduzione assisitita
Cellule embrionali a scopo terapeutico (Clinton)
Selezione
Clonazione umana
Congelamento
X-centesi
Diagnosi pre-impianto
Terapia genica germinale
Intercezione e contragestazione


New experimental models to study human diseases
Transplantation ?
Nonhuman Oocyte
Removal of DNA
Adult somatic cells
Differentiation
iSCNT Embryo
In vitro culture
iSCNT Blastocyst
iNTESCs

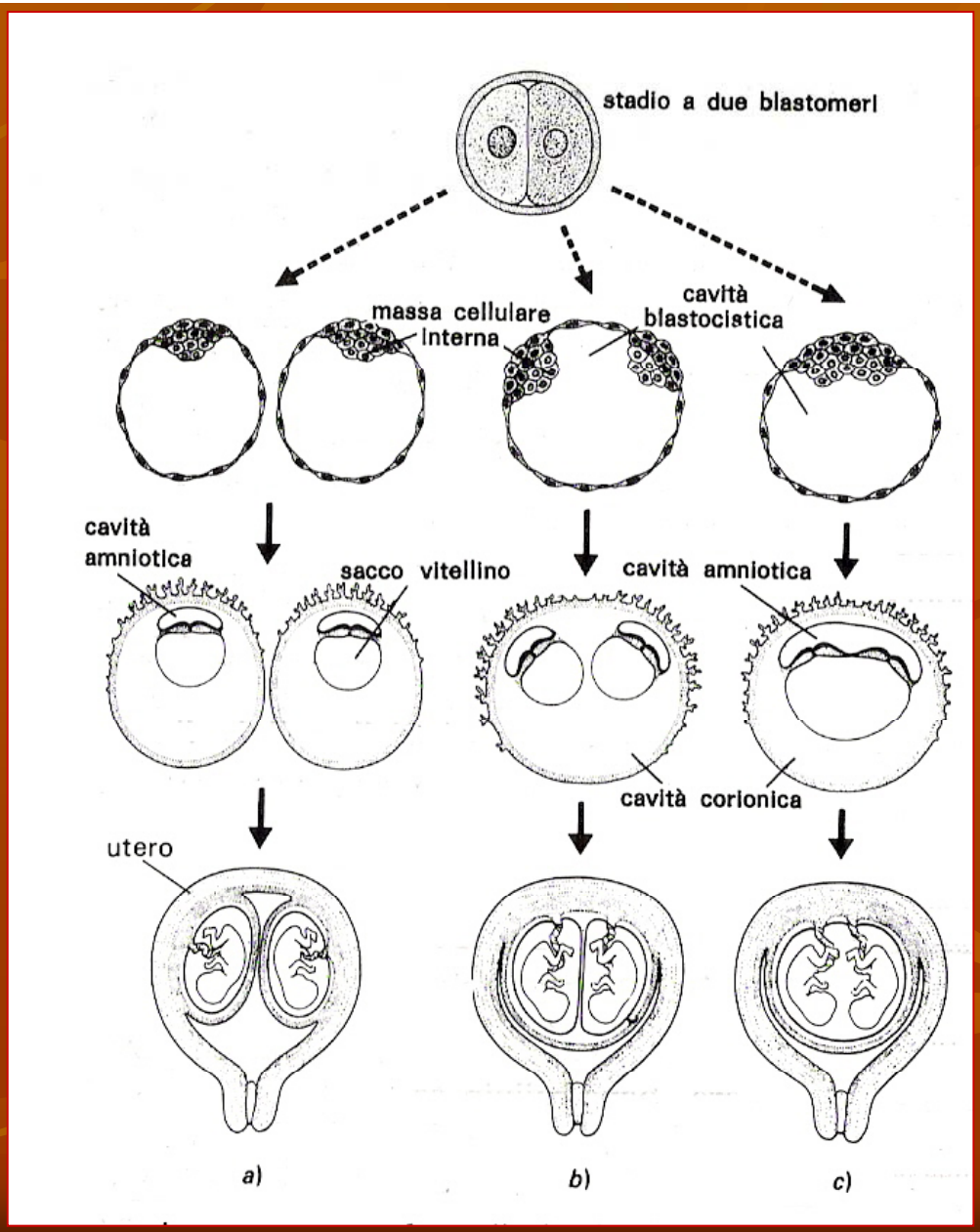
Qual è il momento in cui ha origine la vita umana?

Del resto, tale è la posta in gioco che, sotto il profilo dell'obbligo morale, basterebbe la sola probabilità di trovarsi di fronte a una persona per giustificare la più netta proibizione di ogni intervento volto a sopprimere l'embrione umano.

Note di fisiologia dello sviluppo

Cosa è l'embrione umano?

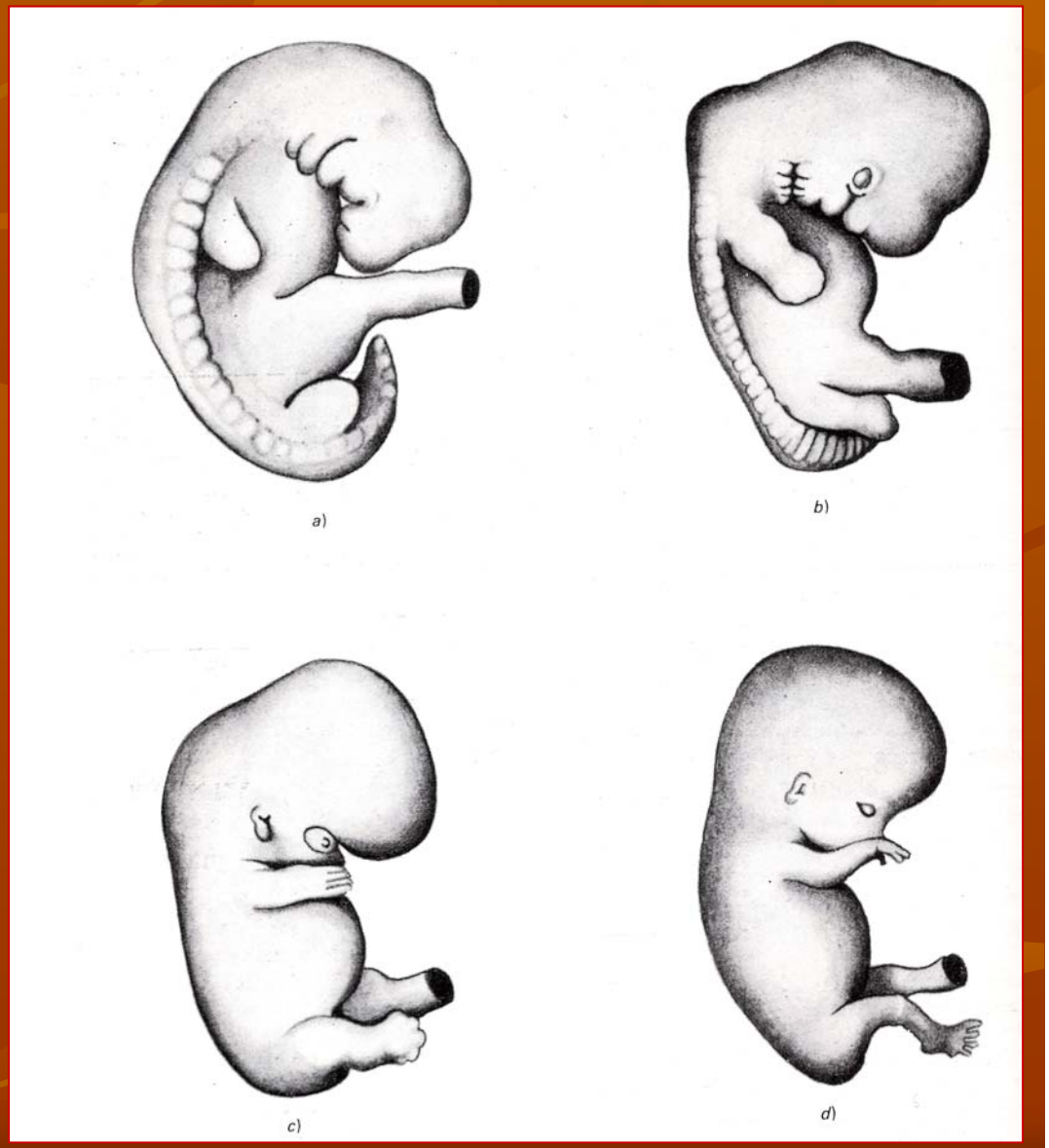
Per embrione umano si intende l'organismo umano nei primi stadi del suo sviluppo, dalla fertilizzazione al terzo mese di vita intrauterina



Note di fisiologia dello sviluppo

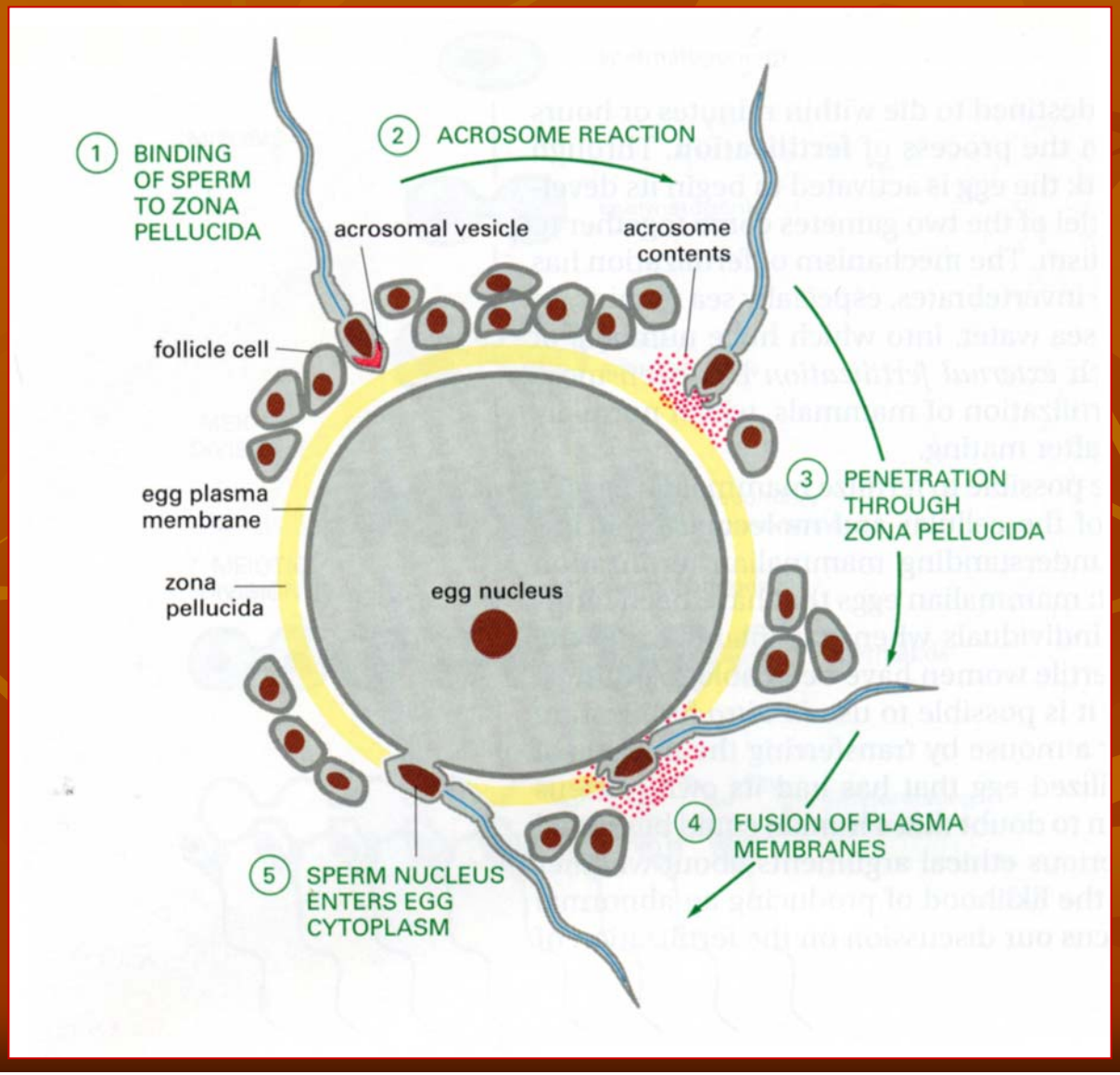
Cosa è il feto umano?

Per feto umano si intende l'organismo umano nella seconda parte del suo sviluppo, dal terzo mese di vita intrauterina sino alla nascita



Note di fisiologia dello sviluppo

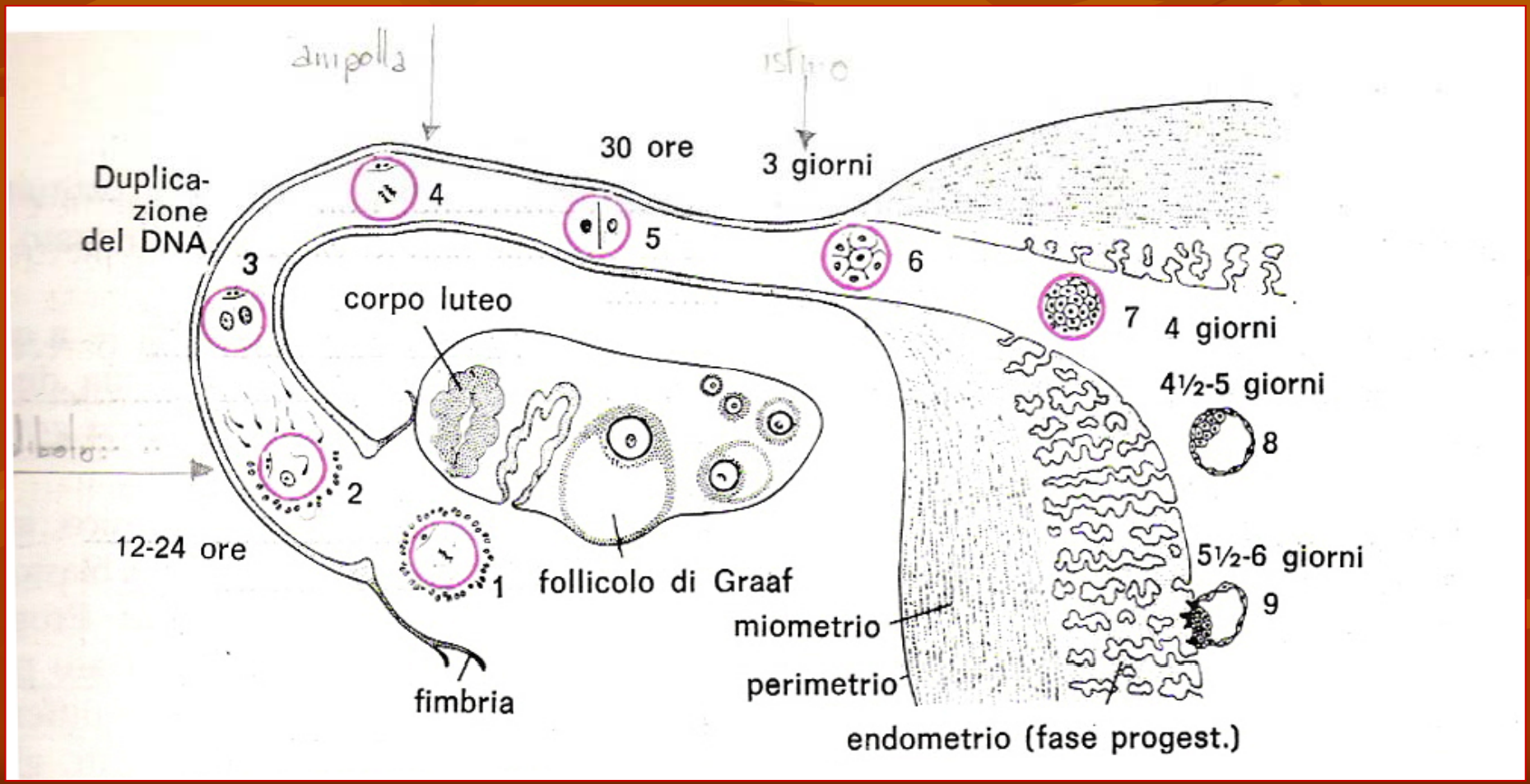
Cosa è la fertilizzazione?



Note di fisiologia dello sviluppo

Dove avviene la fertilizzazione?

La fertilizzazione avviene negli organi genitali femminili, in particolare nella porzione più esterna delle tube uterine.



Note di fisiologia dello sviluppo

Quando avviene la fertilizzazione?

Essa avviene in una finestra temporale ristretta, poiché l'oocita ha una finestra di disponibilità di circa 24 ore, rispetto alla sopravvivenza dello spermatozoo, che è di circa 6 giorni.

Note di fisiologia dello sviluppo

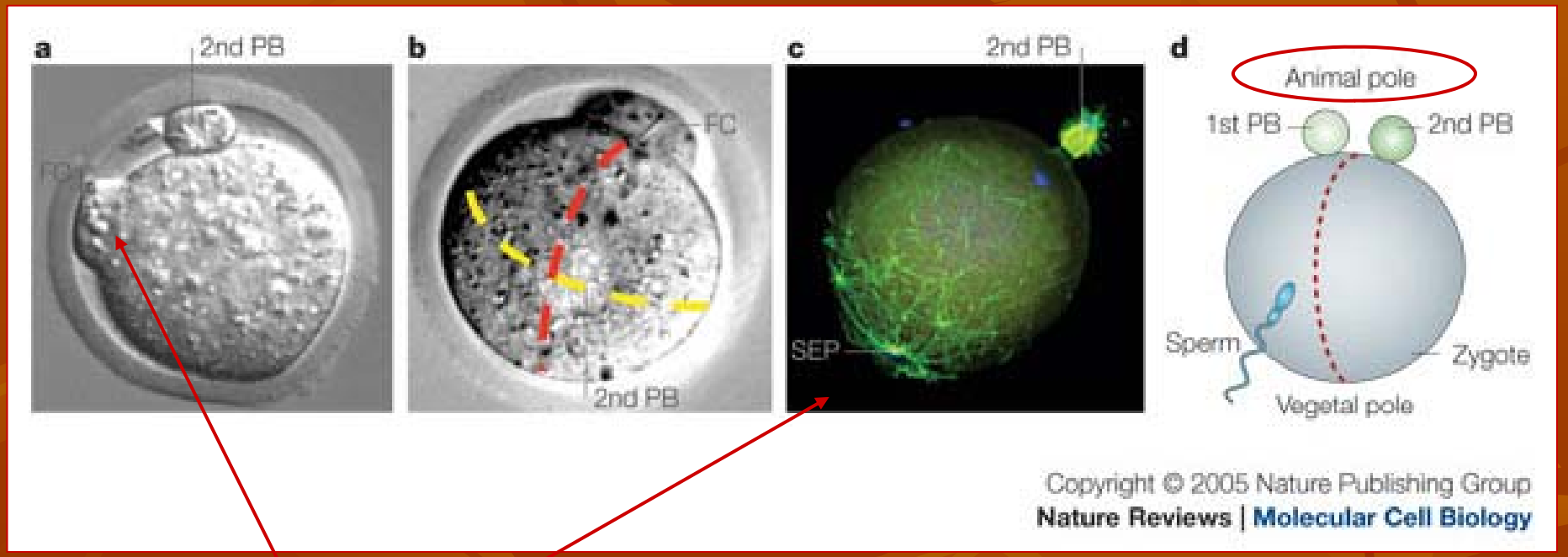
Cosa succede dopo la fertilizzazione?

- Insensibilità ad ulteriori fertilizzazioni
- Alterazione elettrochimica della membrana dell'*oocita*
- Fusione dei patrimoni genetici
- Sintesi delle proteine (TMZ)
- Spostamento in utero

Note di fisiologia dello sviluppo

Quando inizia una nuova realtà biologica?

Nel momento in cui la reazione diventa autonoma ed irreversibile.



In life sciences, information is quite different from what we perceive (e.g. prion proteins).

Information is: DNA sequence

DNA structure

DNA attached molecules

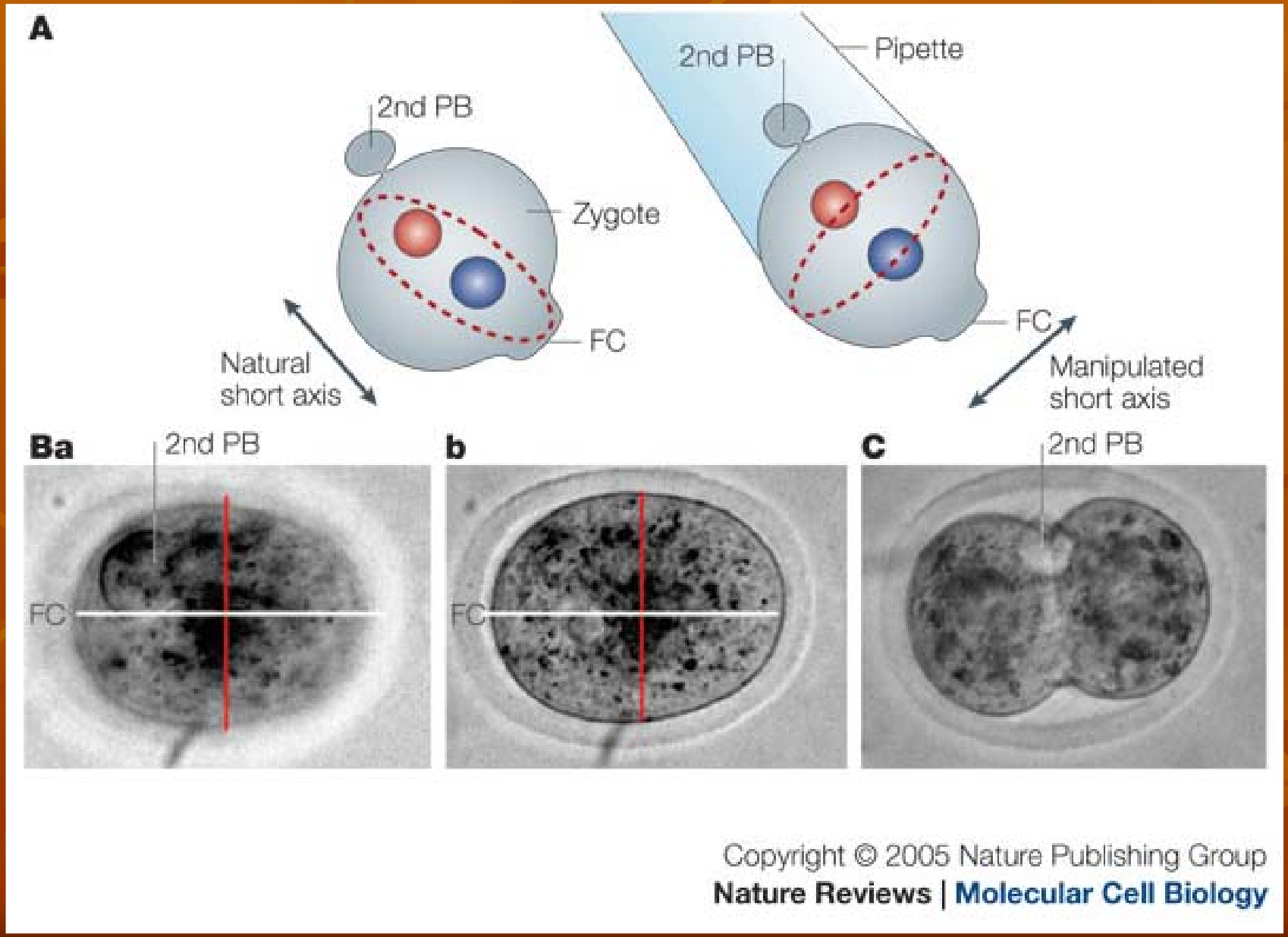
RNA world

intracellular segregation of TF & GF

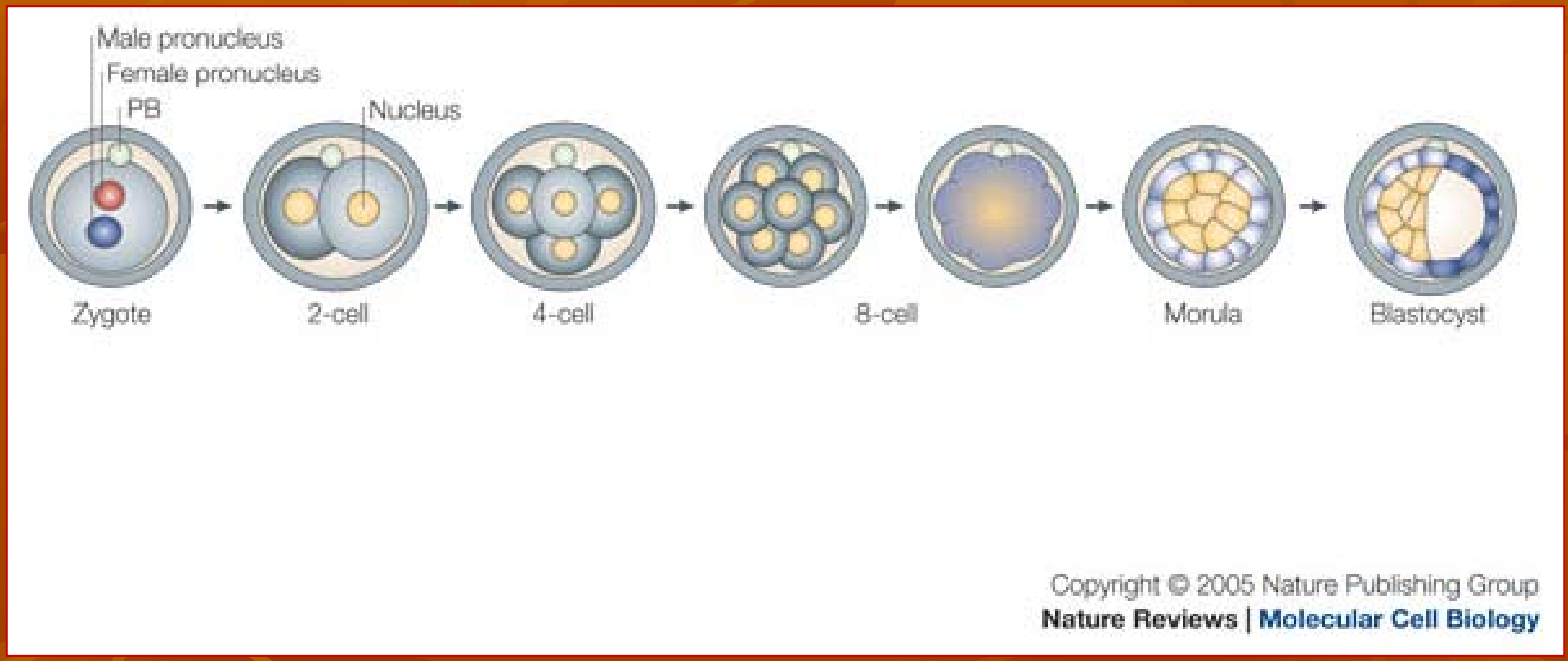
intercellular communication

too many others

La morfologia è informazione di per sé?

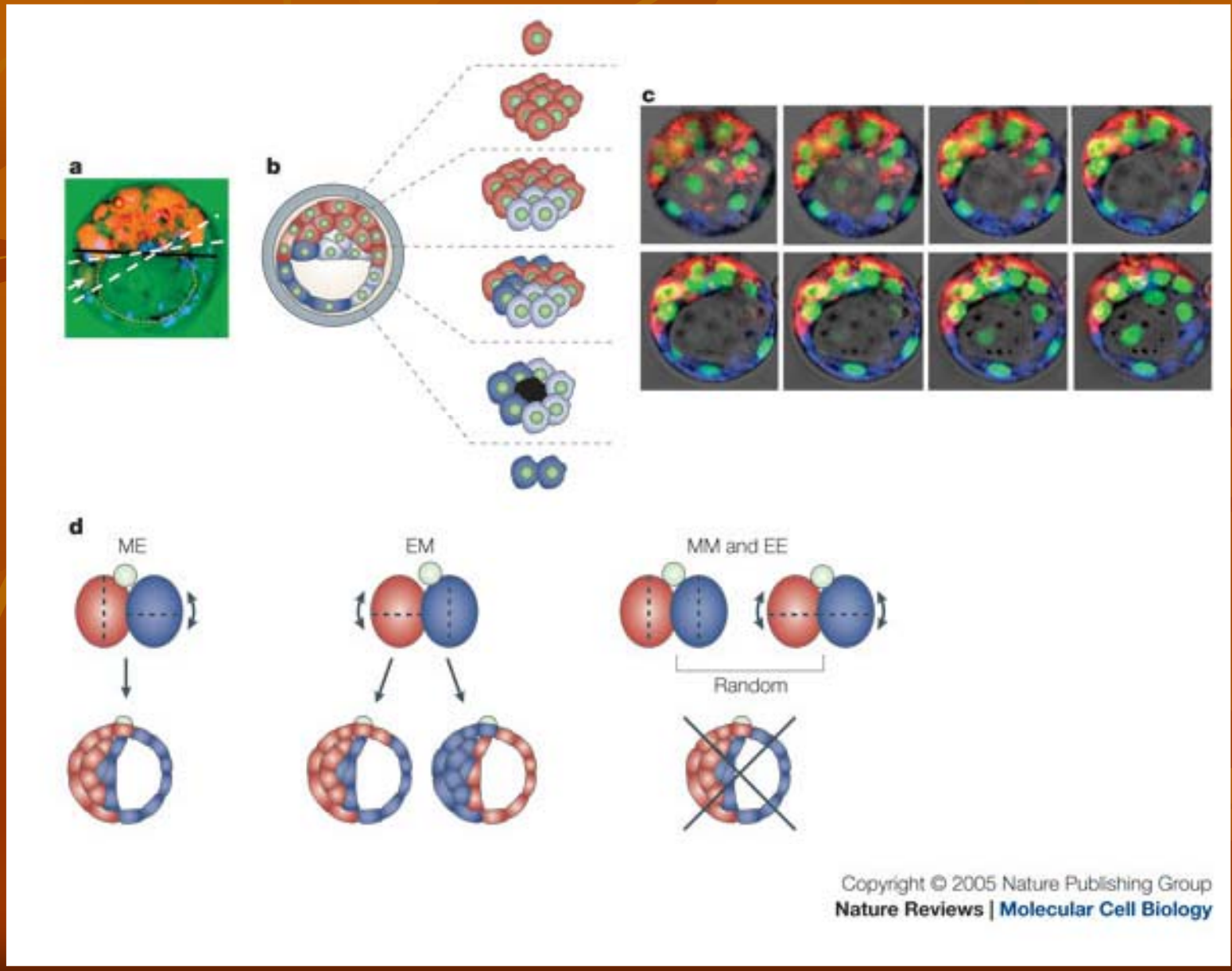


Note di fisiologia dello sviluppo



Oct-4 e TE;

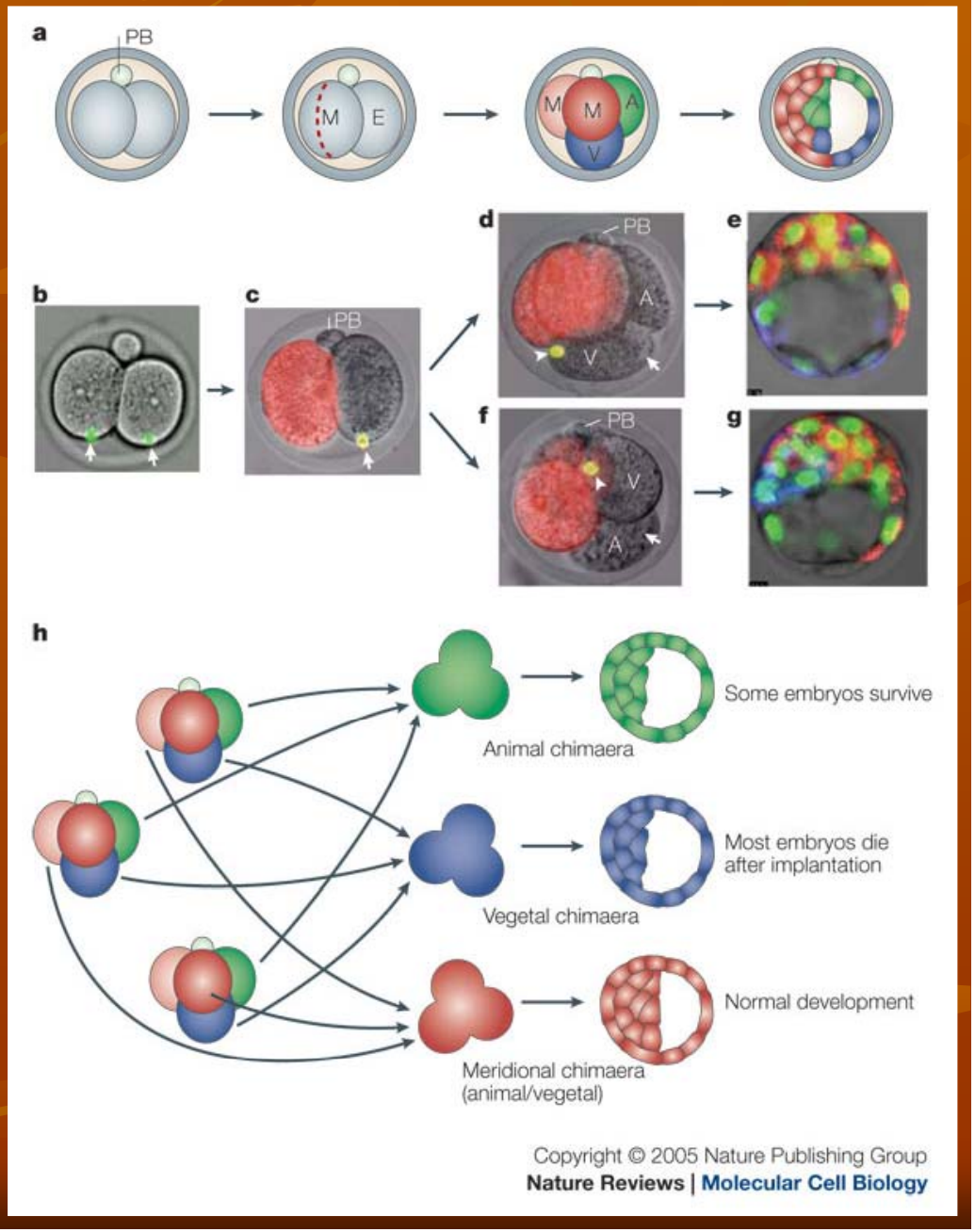
La seconda segmentazione regola l’embrione



Are 4 cells stage blastomeres equivalent?
Not at all.

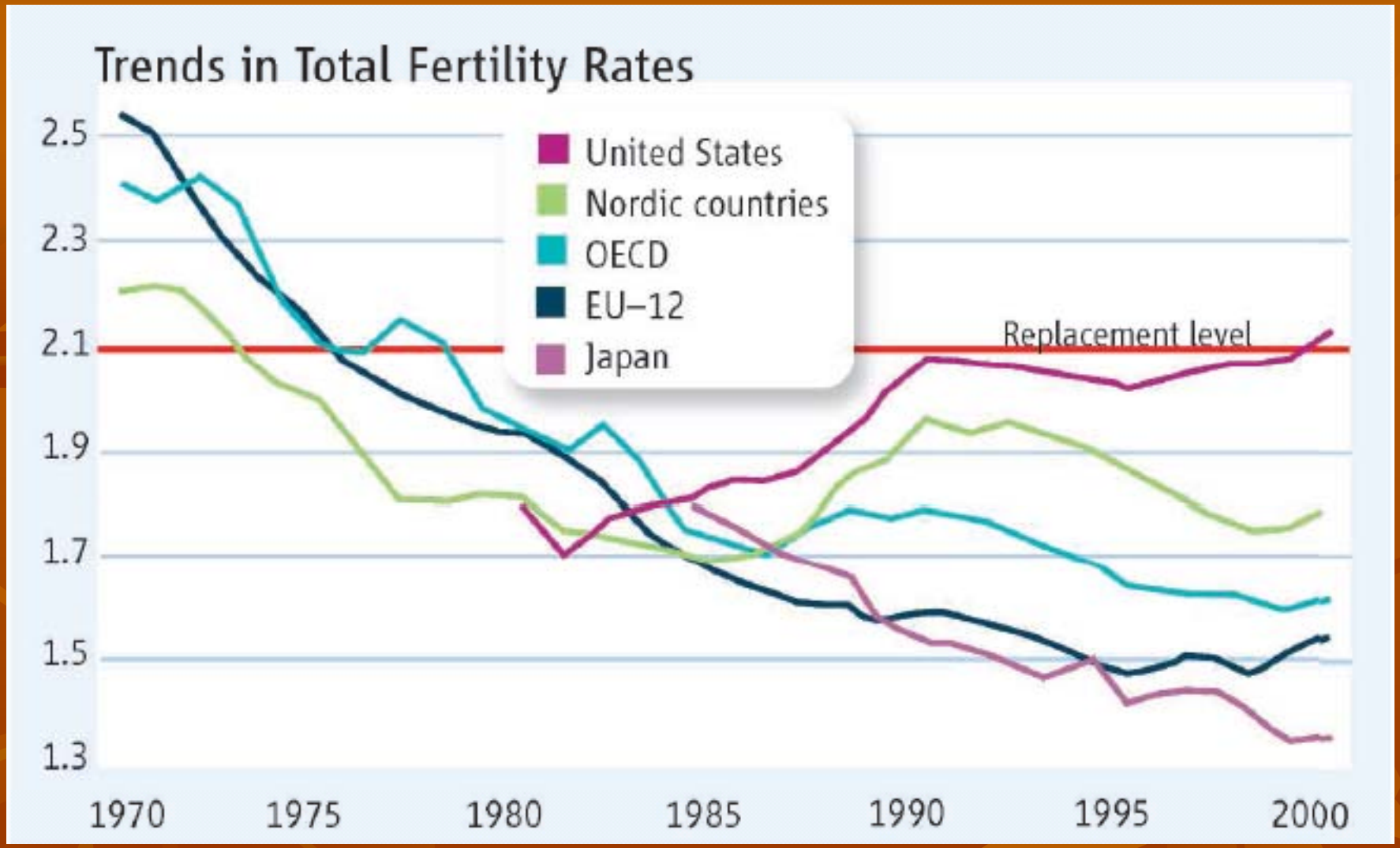
The differences rely on information inheritance and timing of division.

Position seems to be irrelevant.

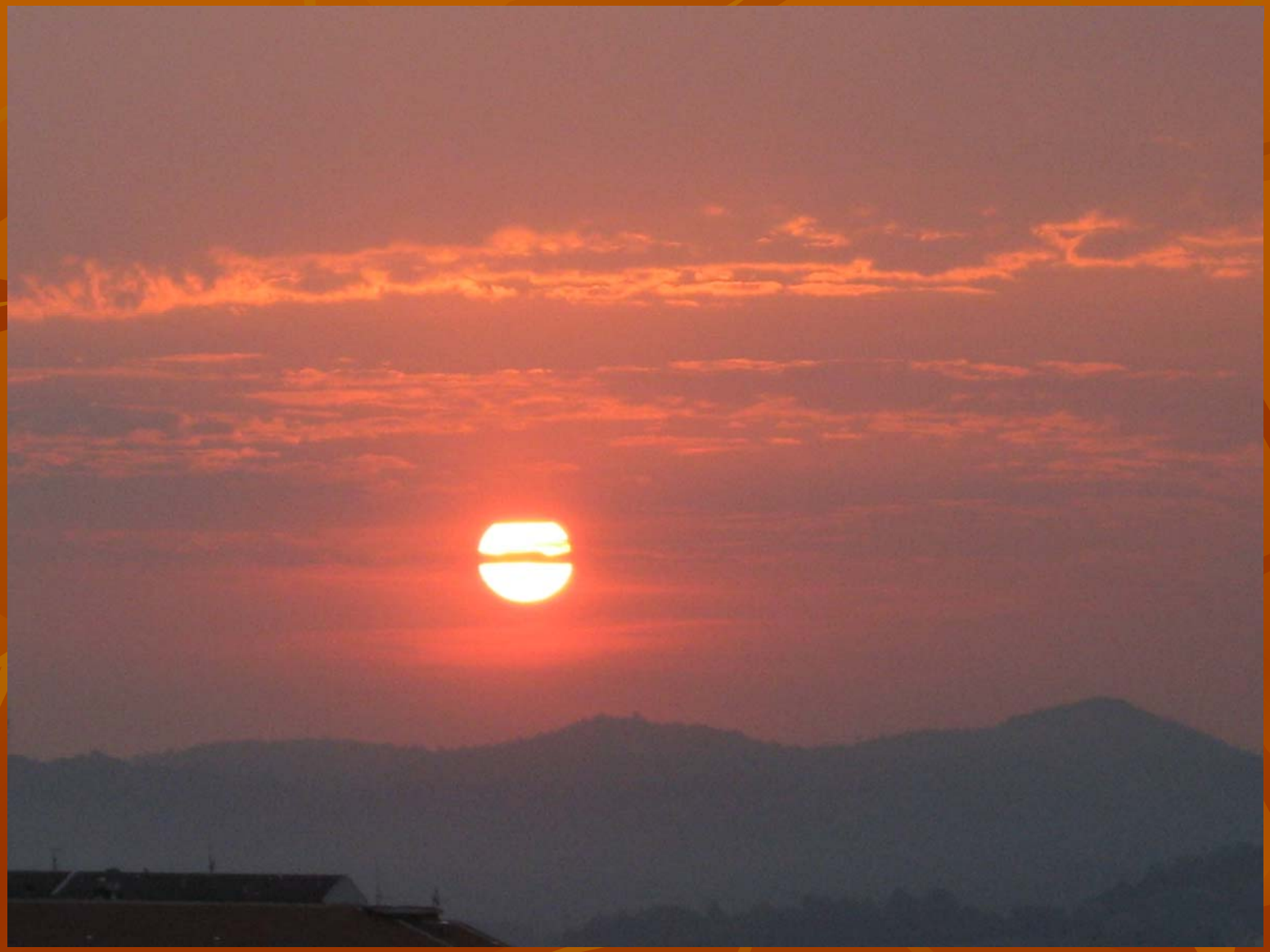


Alcuni argomenti per discutere

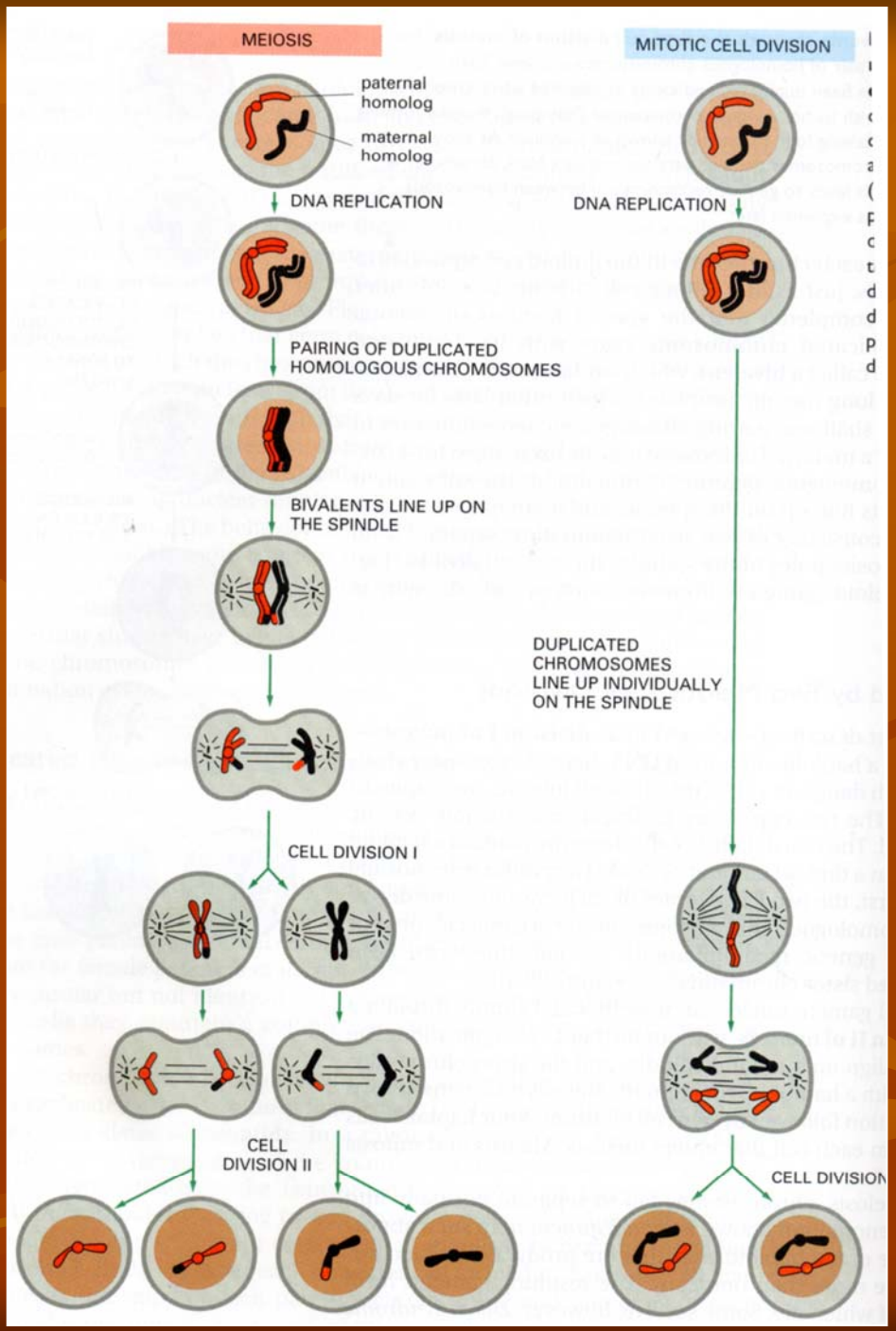
- Embryo is no more than a small amount of cells. (C.F.)
- Lettera a Ban-Ki-Moon del 14 ottobre ultimo scorso


Trends in Total Fertility Rates
2.5
2.3
2.1
1.9
1.7
1.5
1.3
United States
Nordic countries
OECD
EU–12
Japan
Replacement level
1970
1975
1980
1985
1990
1995
2000

Nel 2050 < 2.05

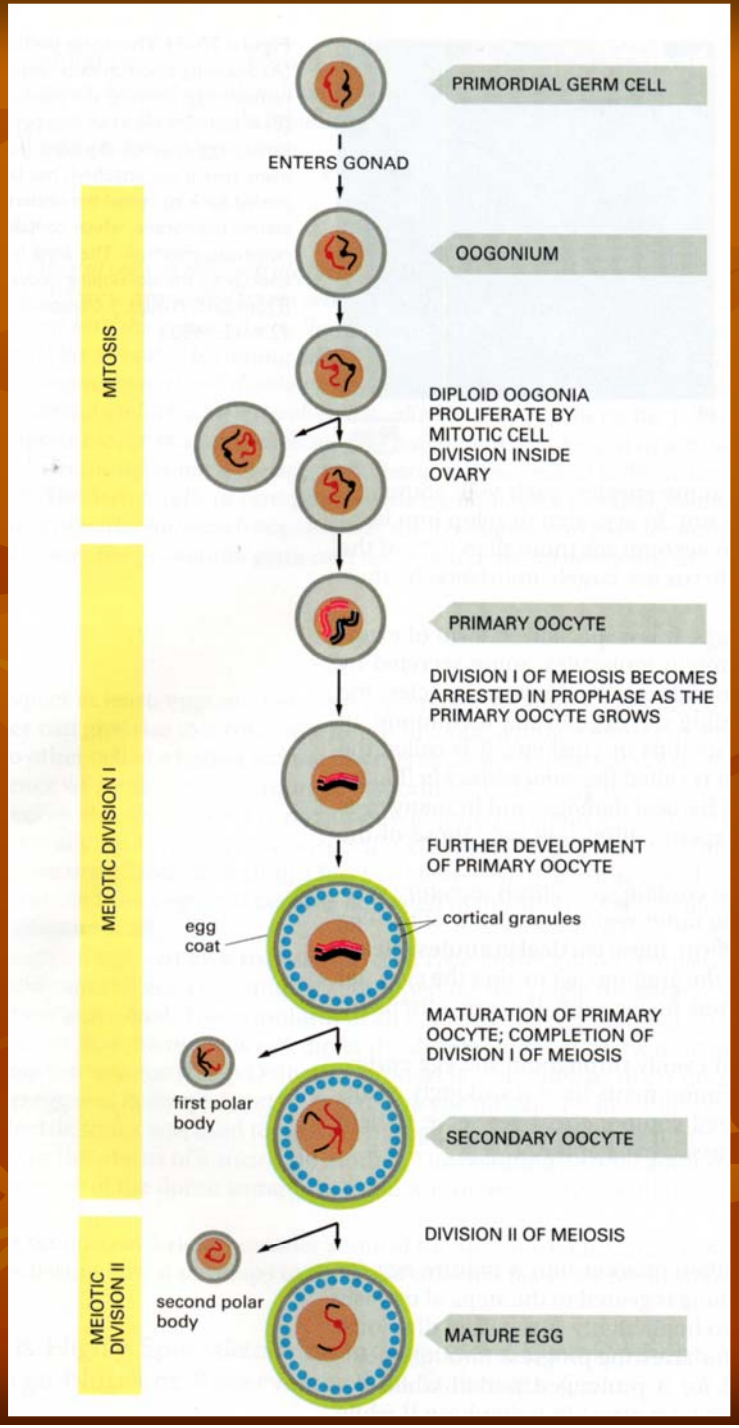


A small help to remind you the basics of cell biology -1



From B.Alberts et al, Molecular biology of the cell, 4th edition

A small help to remind you the basics of cell biology-2



From B.Alberts et al, Molecular biology of the cell, 4th edition

Mouse embryo development is regulative:

•Flexible

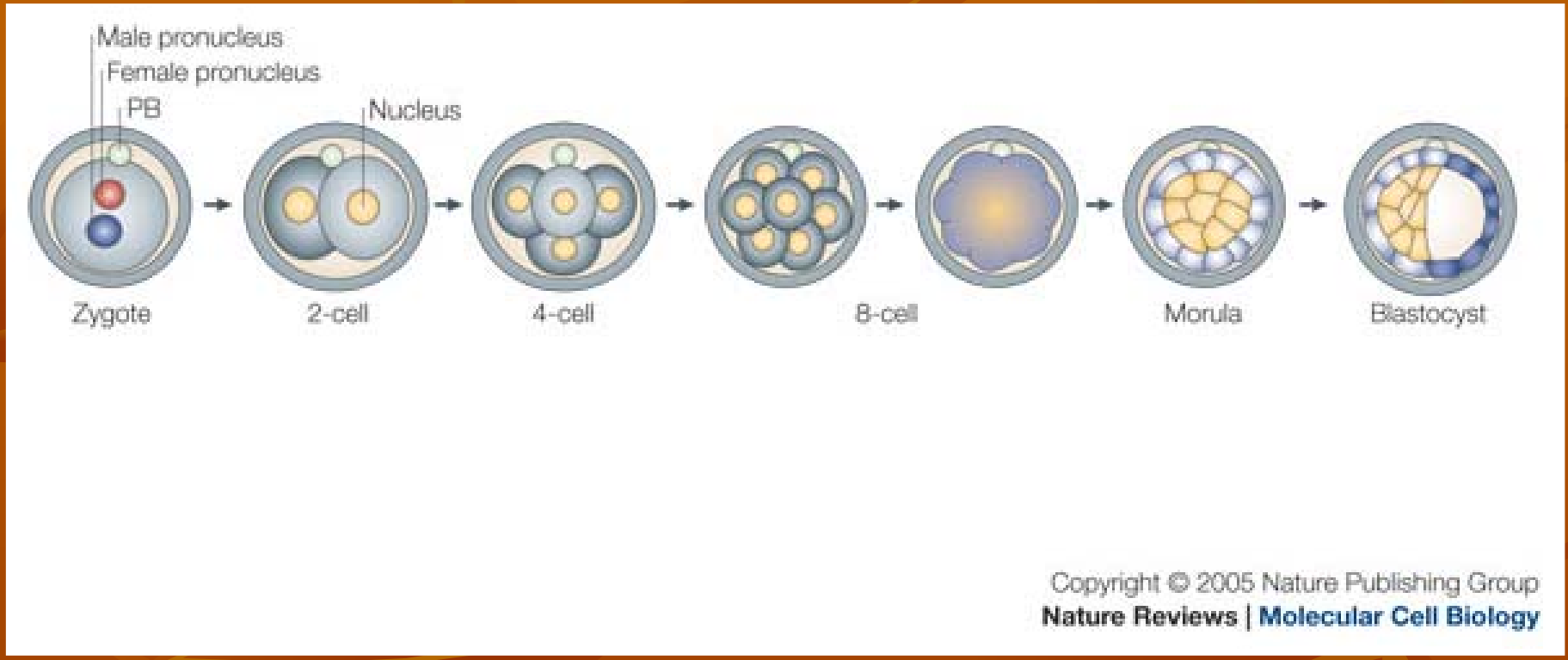
•Responsive to intervention

Suggestion, not commands

1. Disorder → order **2. Basic order → increasing levels of order**

LOSS OF FLEXIBILITY

Pre-emplantation events are not random

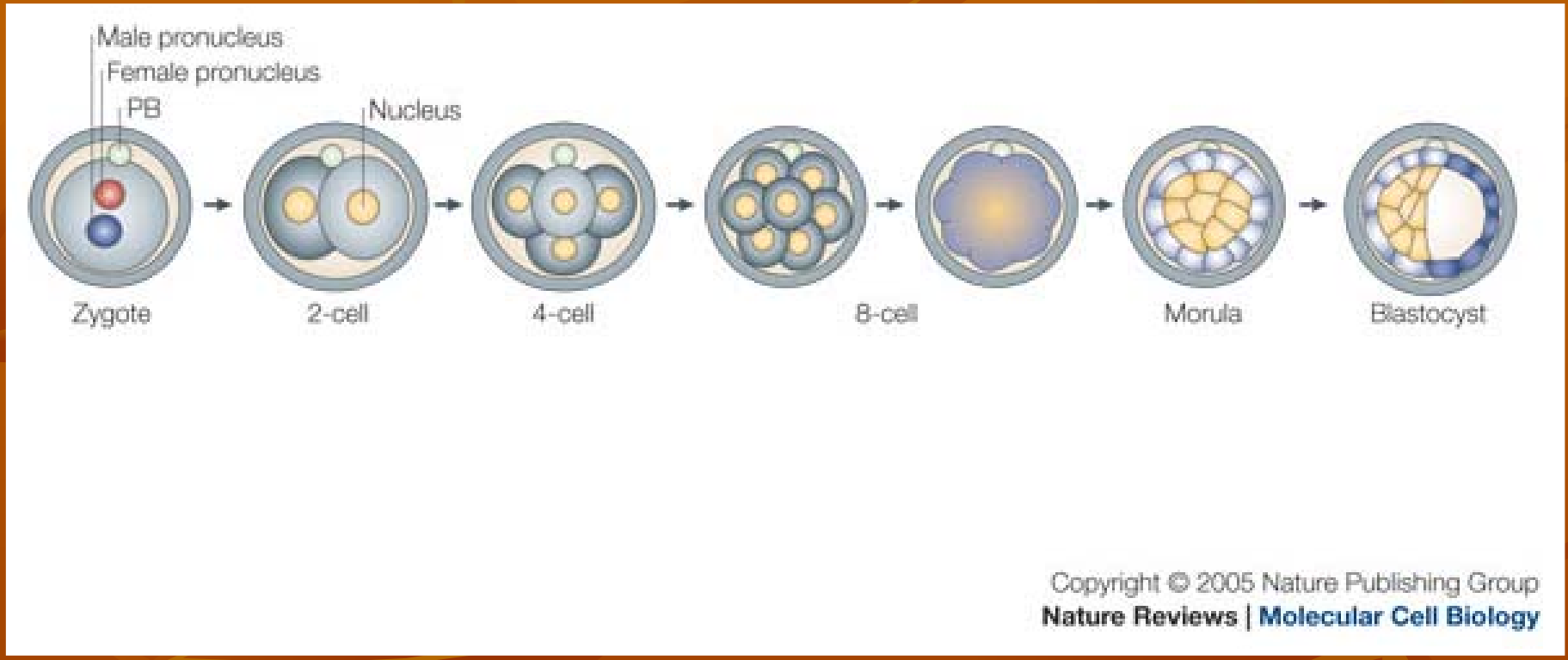


- Maternal-zygotic transition of gene expression control
- Polarization (conservative or differentiative divisions)
- Blastocyst formation

ICM can be put outside

TE may segregate nonetheless (<32cells)

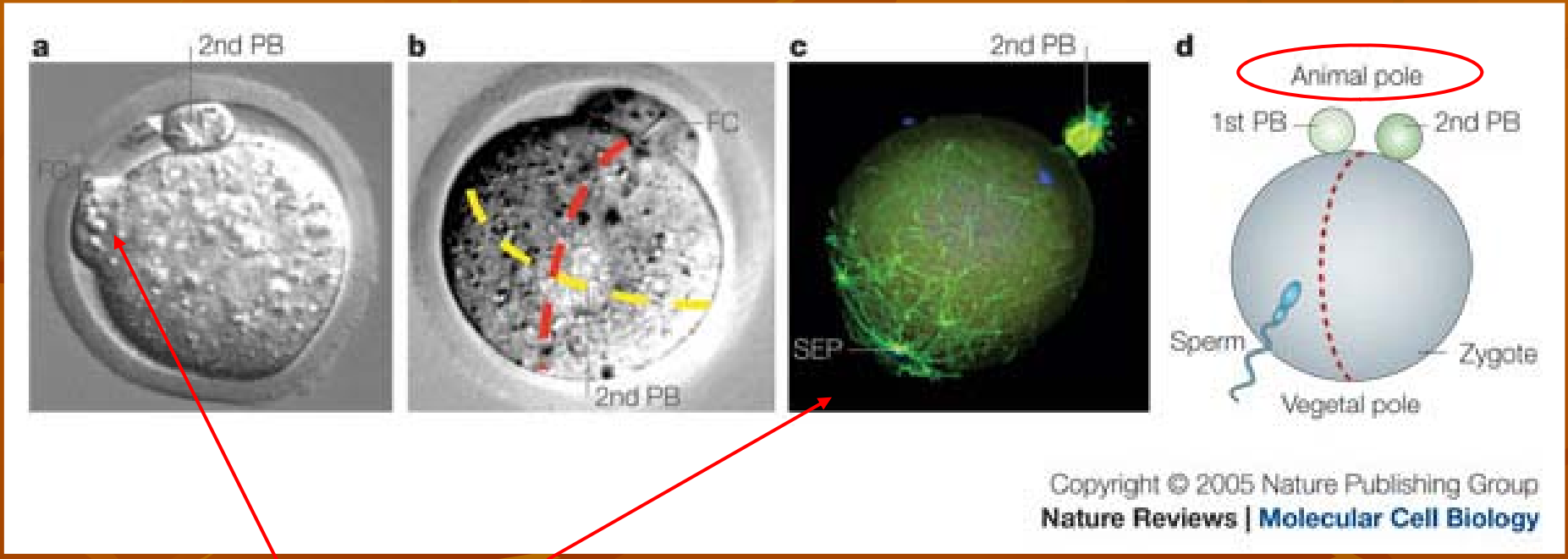
Pre-emplantation events are not random-2



Are 2-cell stage blastomeres equivalent? Apparently, yes.

Are 4 cells stage blastomeres equivalent? You may obtain chimaeras, but not quadruplets; tracing their fate could be interesting.

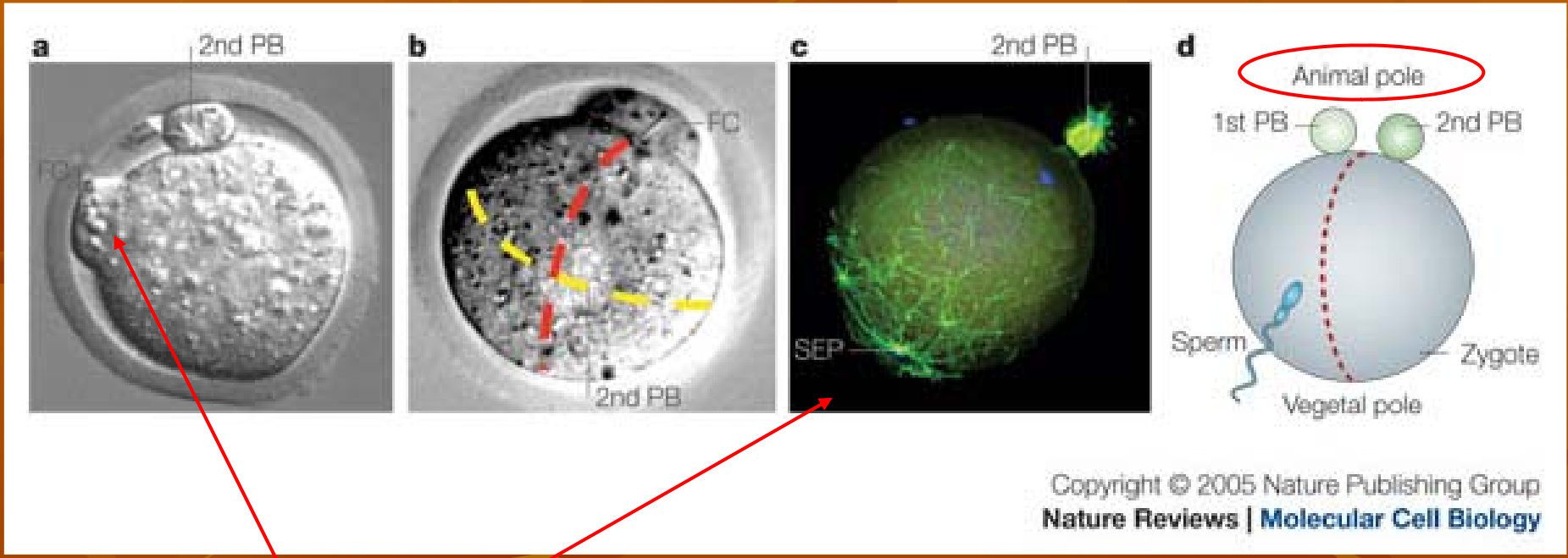
What does it happen at fertilization?



The first cleavage will occurr within 30° from PB.

Duplicating PB means arresting the development.

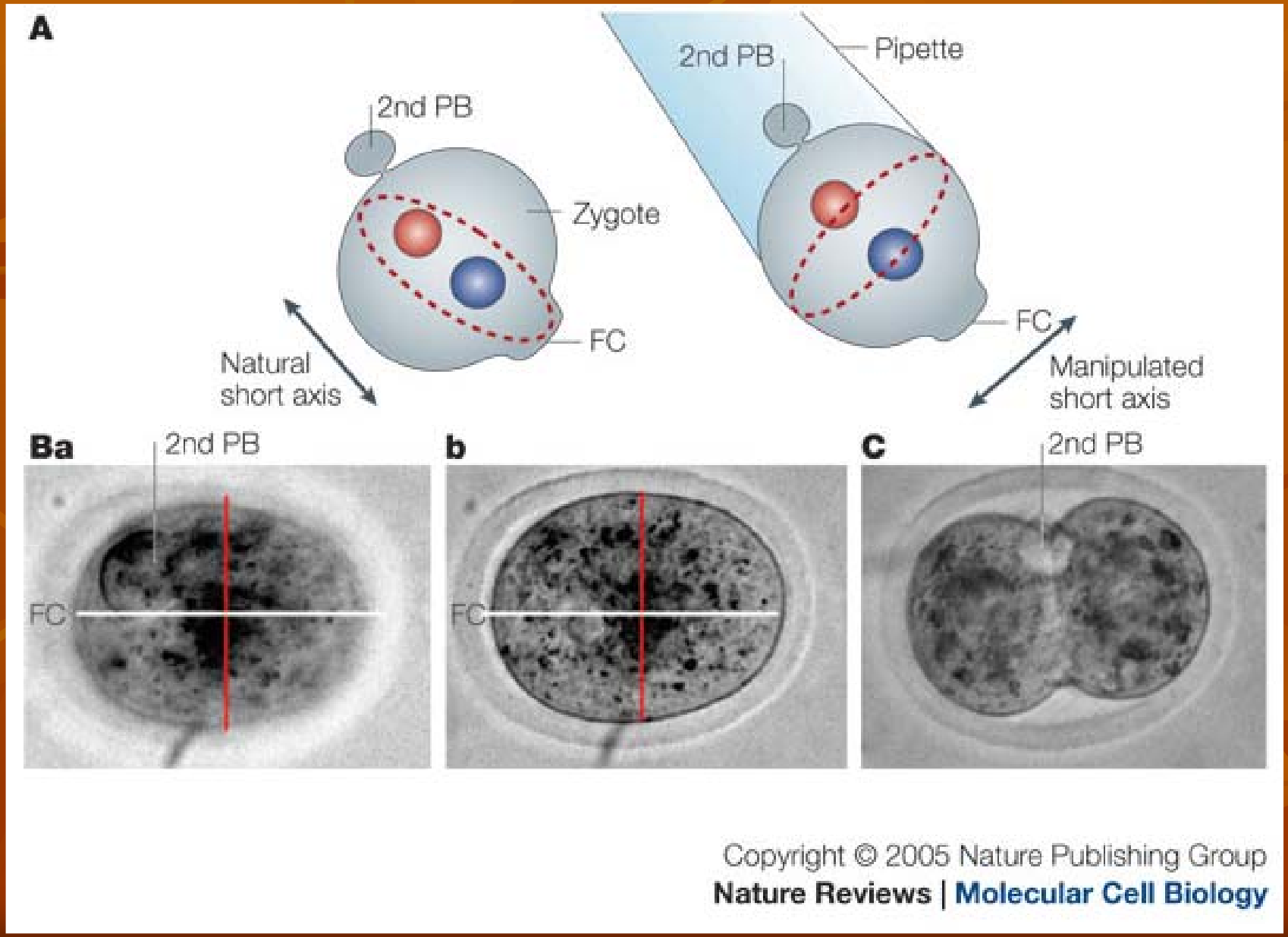
Is shape an information itself? YES



SEP generates the fertilization cone, it changes the zygote's shape, thus controlling the onset of the first cleavage;

PB-SEP axis, the *short axis* from now on, is the cleavage site.

Is shape an information itself? YES



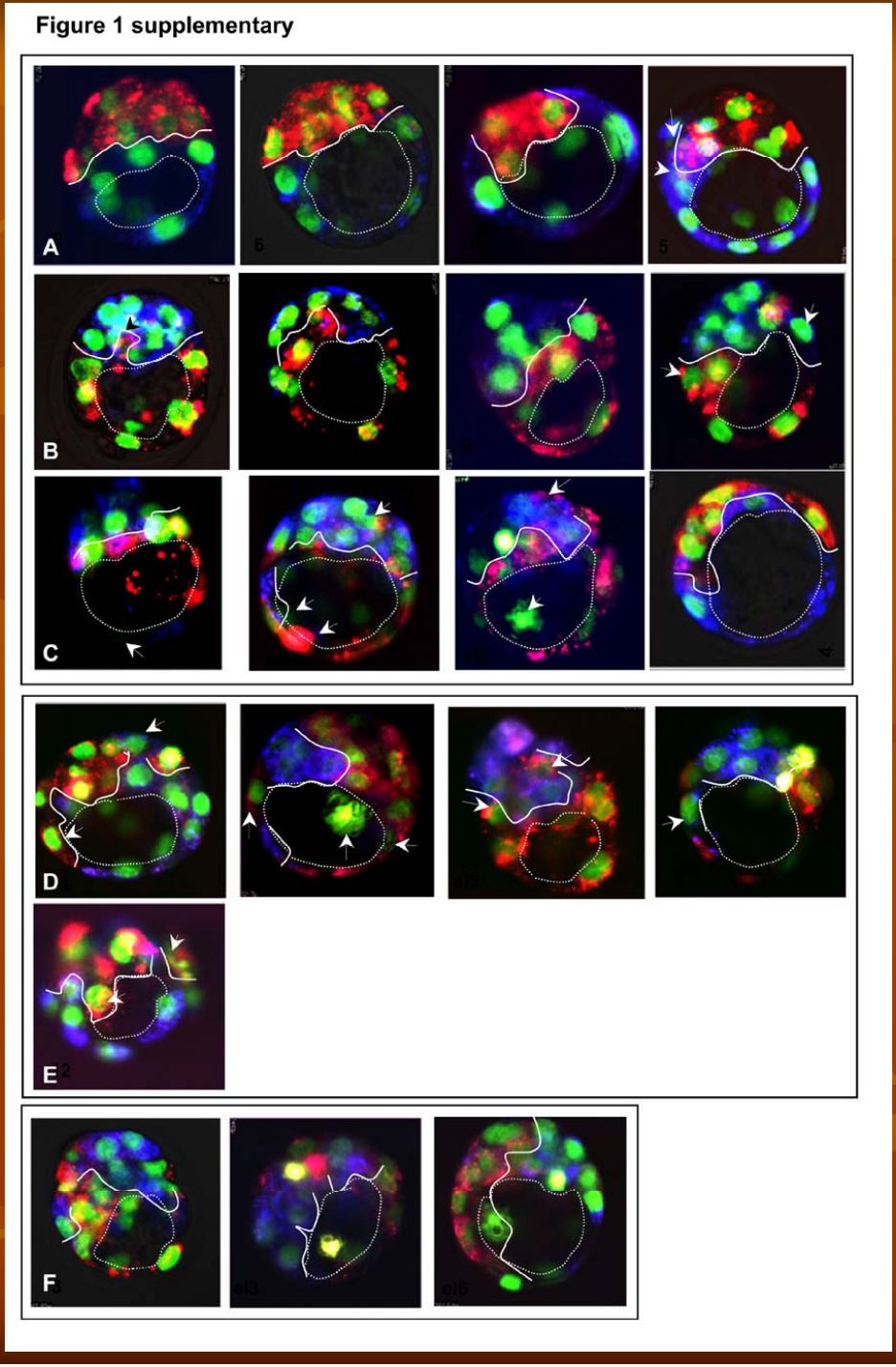
Are the two blastomeres different? YES

Can you find it out easily? NO

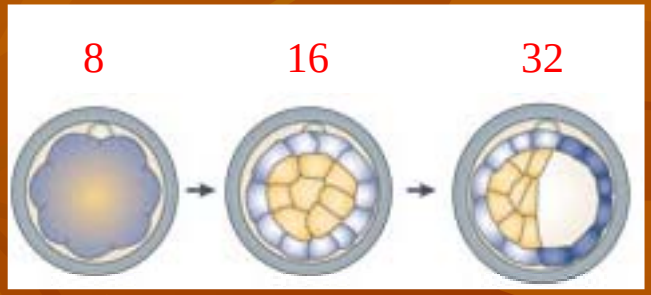
1. The blastomere division are metachronous
2. Tetrahedral form is distorting the boundaries
3. Separating cells with a theorical plane might be misleading

Who’s who??

☹

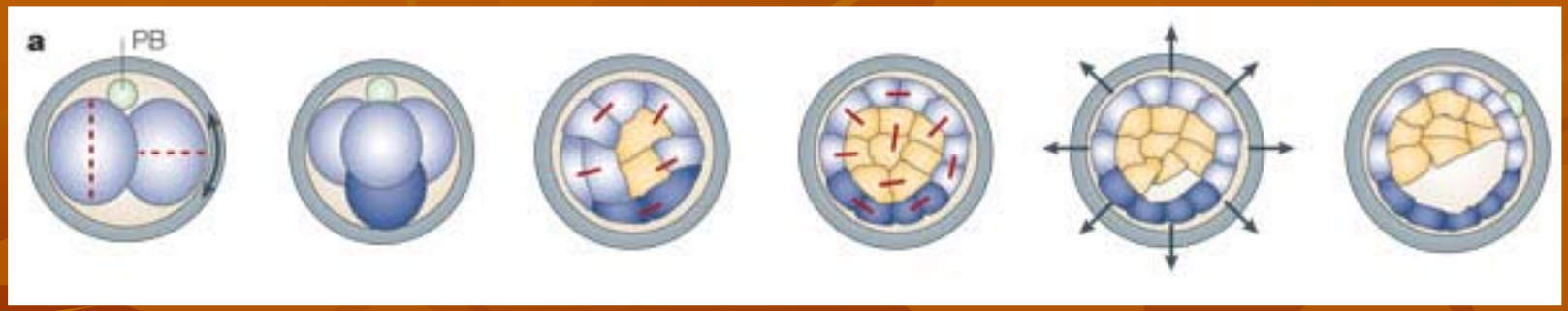


How does the blastocyst arise?



At 32-cells stage Na^+/K^+ channel transport is activated, fluid is accumulated, thus generating a cavity.

How does the blastocyst arise? -2

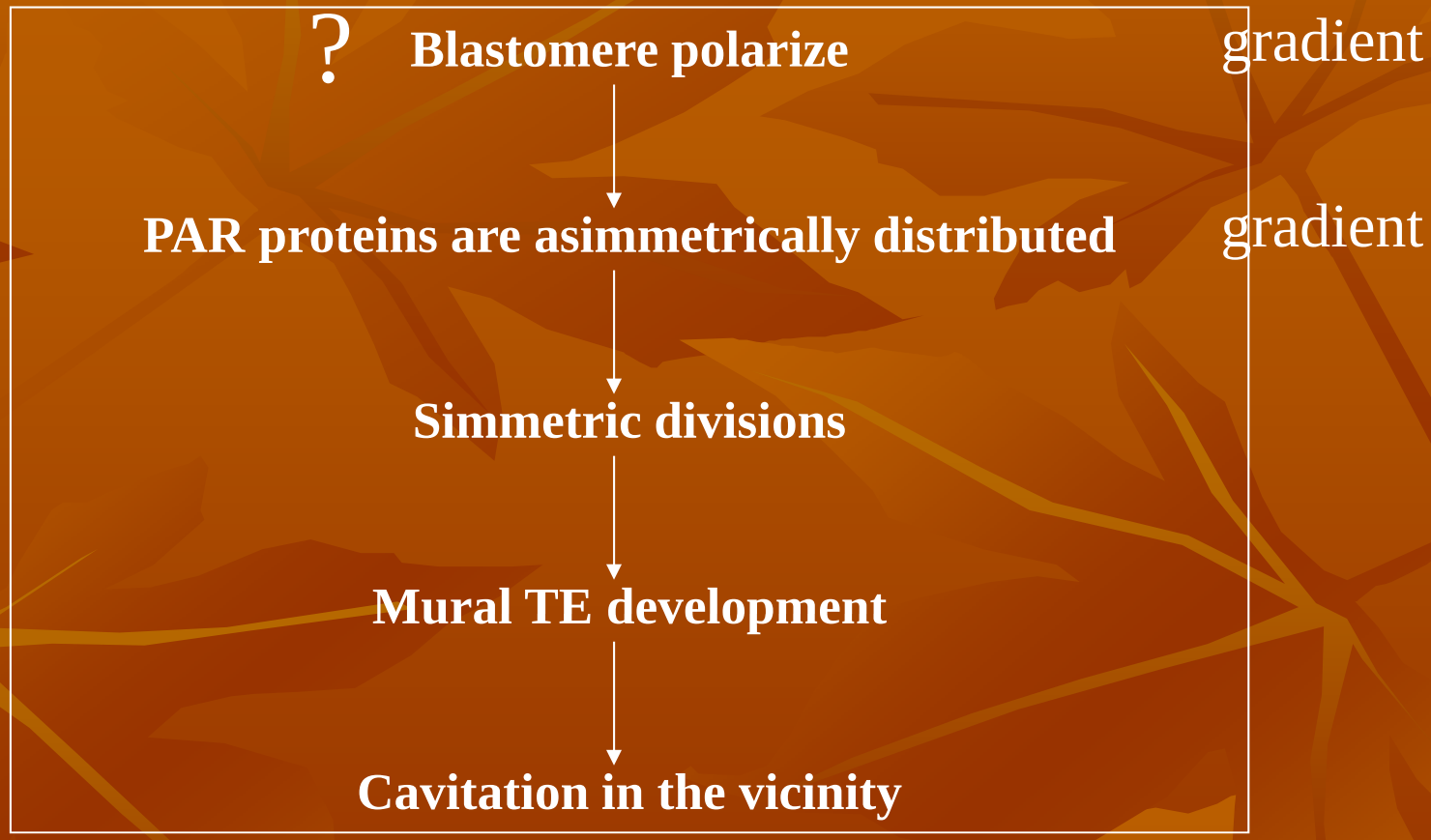


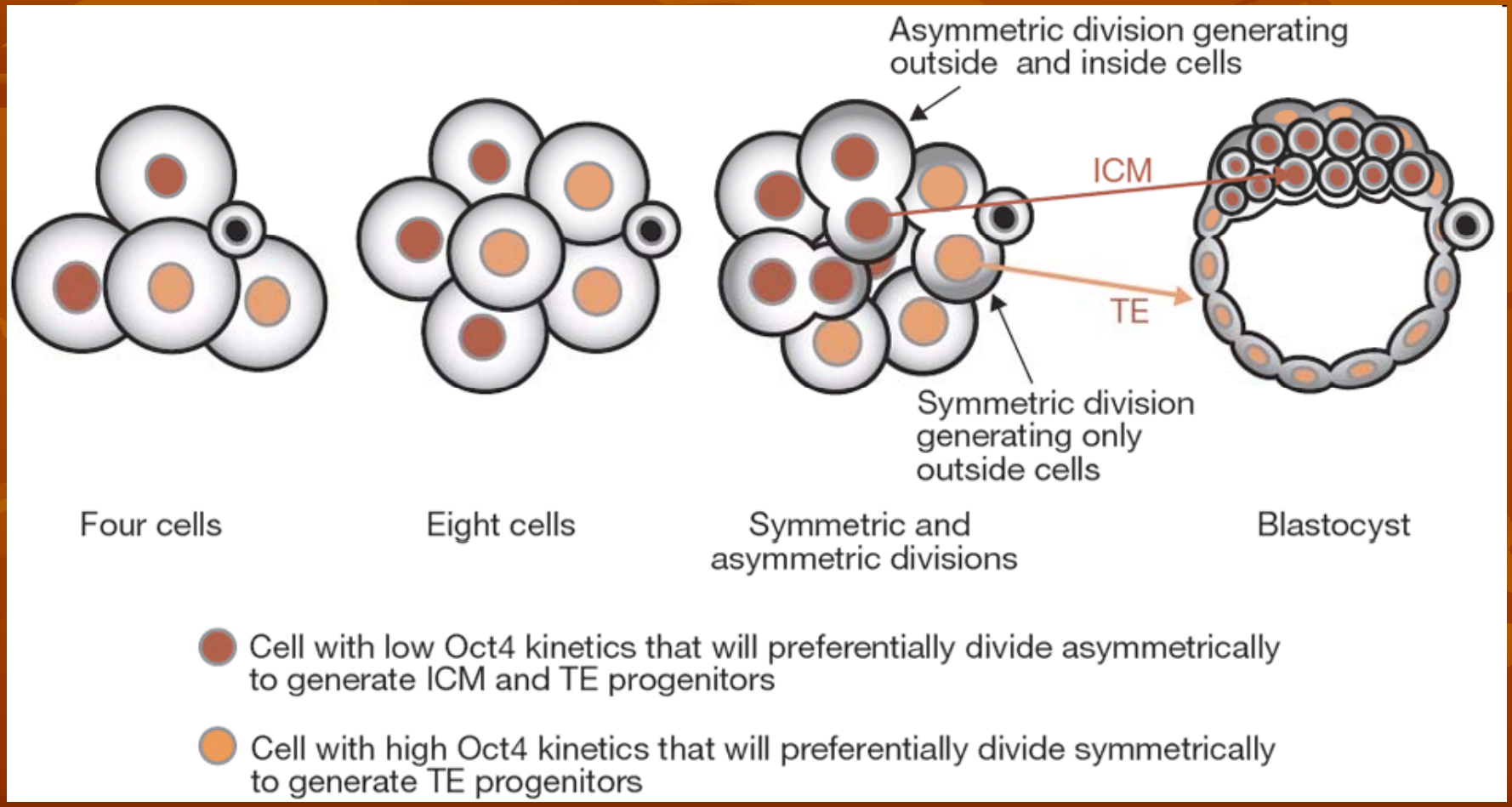
a- Cavitation might depend on intercellular links:

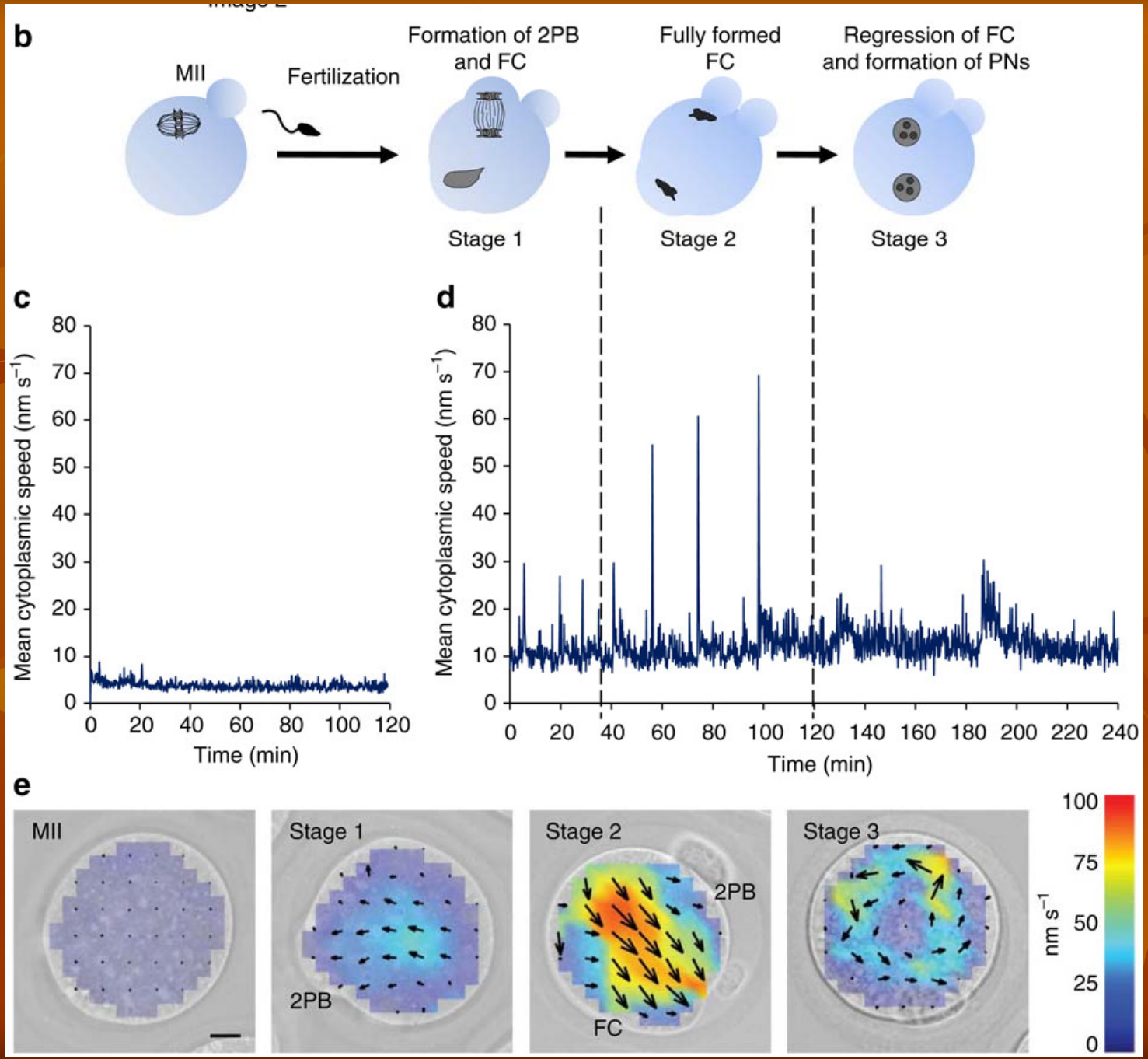
Some ICM cells come from outer cells

Other ICM cells come from inner cells, neighbouring TE is mural, weak points lead to cavitation

How does the blastocyst arise? -4




Asymmetric division generating outside and inside cells
ICM
TE
Symmetric division generating only outside cells
Four cells
Eight cells
Symmetric and asymmetric divisions
Blastocyst
Cell with low Oct4 kinetics that will preferentially divide asymmetrically to generate ICM and TE progenitors
Cell with high Oct4 kinetics that will preferentially divide symmetrically to generate TE progenitors


b
MII
Fertilization
Formation of 2PB and FC
Fully formed FC
Regression of FC and formation of PNs
Stage 1
Stage 2
Stage 3
c
Mean cytoplasmic speed (nm s−1)
Time (min)
d
Mean cytoplasmic speed (nm s−1)
Time (min)
e
MII
Stage 1
2PB
Stage 2
2PB
FC
Stage 3
nm s−1

Future investigations

Spatial dynamic of gene expression

Cell fate choice

Cell fate communication

Embryo is no more than a small amount of cells. (C.F.)