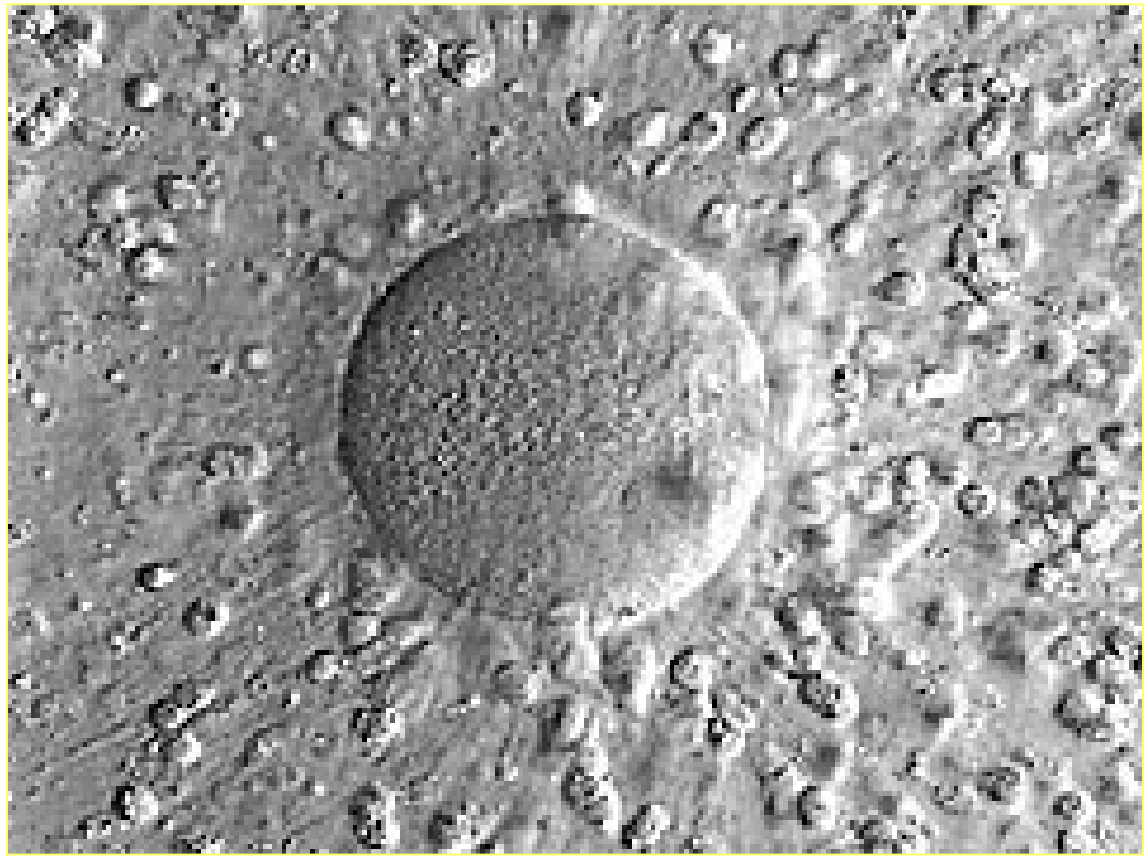
XVI Magister Reproducción Humana



Ovocito e Implantación

Dra. R.Núñez Calonge

"Ovo ex omnia"

Oocyte competency is the key to embryo potential

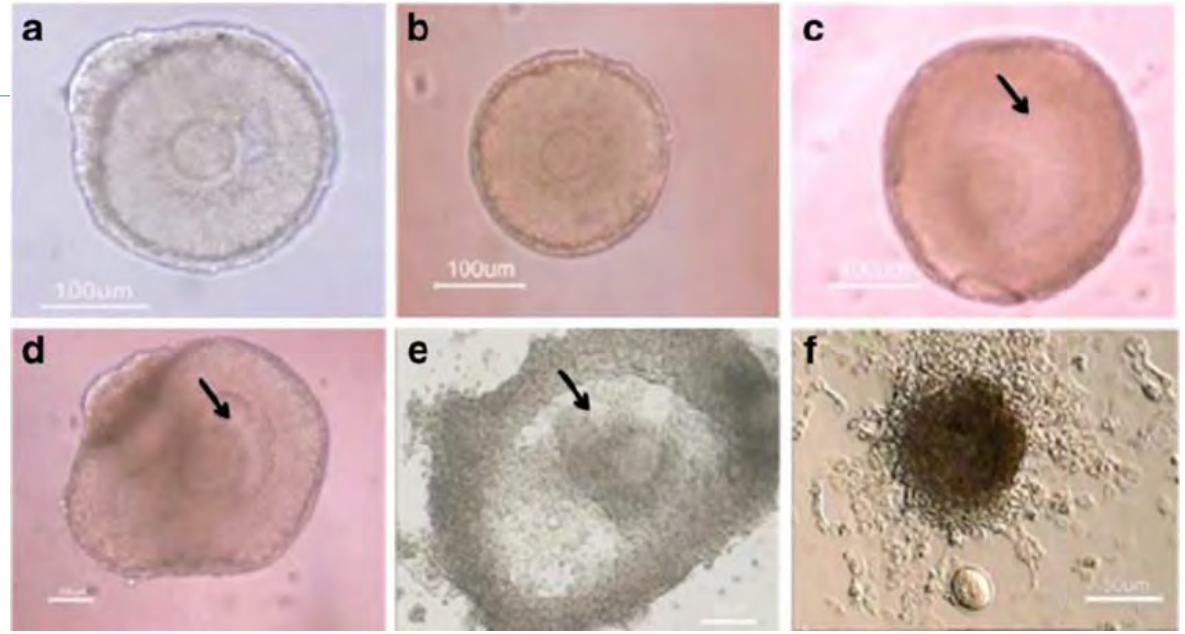
David Keefe, M.D., Molly Kumar, M.D., and Keri Kalmbach, M.S.

Department of Obstetrics and Gynecology, New York University Langone Medical Center, New York, New York

Fertility and Sterility® Vol. 103, No. 2, February 2015

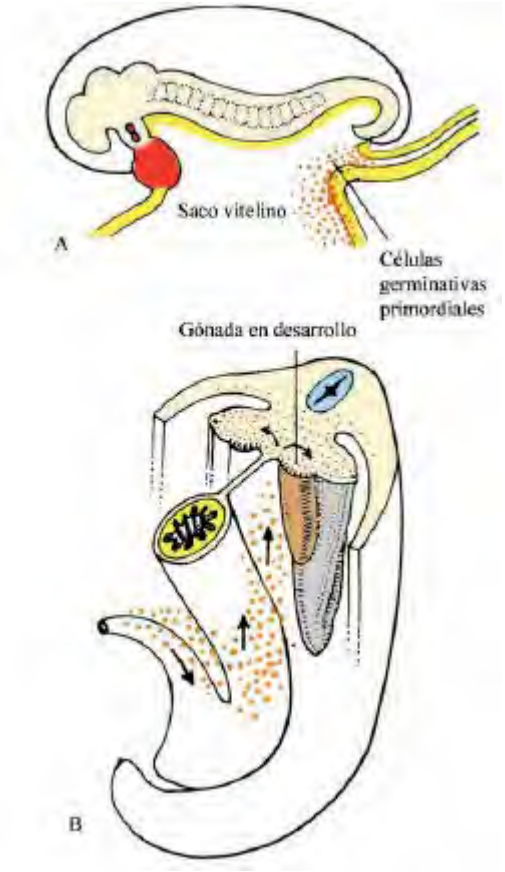
Embryogenesis begins during oogenesis
–E. B. Wilson, 1918

Indice



1. Formación del ovocito
2. Crecimiento folicular
3. Meiosis
4. Estructura del ovocito
5. Maduración ovocitaria
6. Aspectos prácticos

1. Formación del ovocito: ovogéneis



Formación en el endodermo del saco vitelino

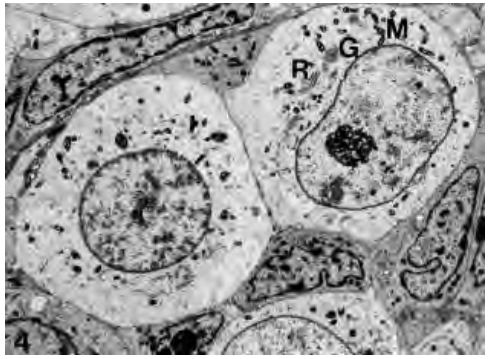
(3ª semana)

Cresta genital

5ª semana

Ovario primitivo → Ovogonias

Origen del ovocito: ovogéneis



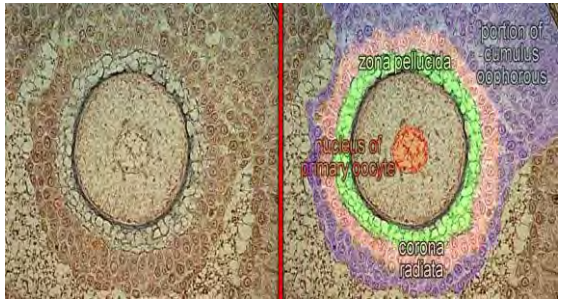
ovogonias

(10.000 en 6º-7º semana)

Mitosis

Meiosis

(8º semana)



Ovocitos primarios

Nacimiento

(1-2 millones)

Pubertad

(500.0000)

Ovocitos secundarios

Oogenesis: Prospects and Challenges for the Future

P. RODRIGUES, D. LIMBACK, L.K. MCGINNIS, C.E. PLANCHA,AND D.F. ALBERTINI

J. Cell. Physiol. 216: 355–365, 2008.

El objetivo de la oogénesis es siempre el mismo: producir un ovocito competente para originar descendencia viable. Sin embargo, en humanos, no es un proceso eficiente.

2.- Crecimiento folicular

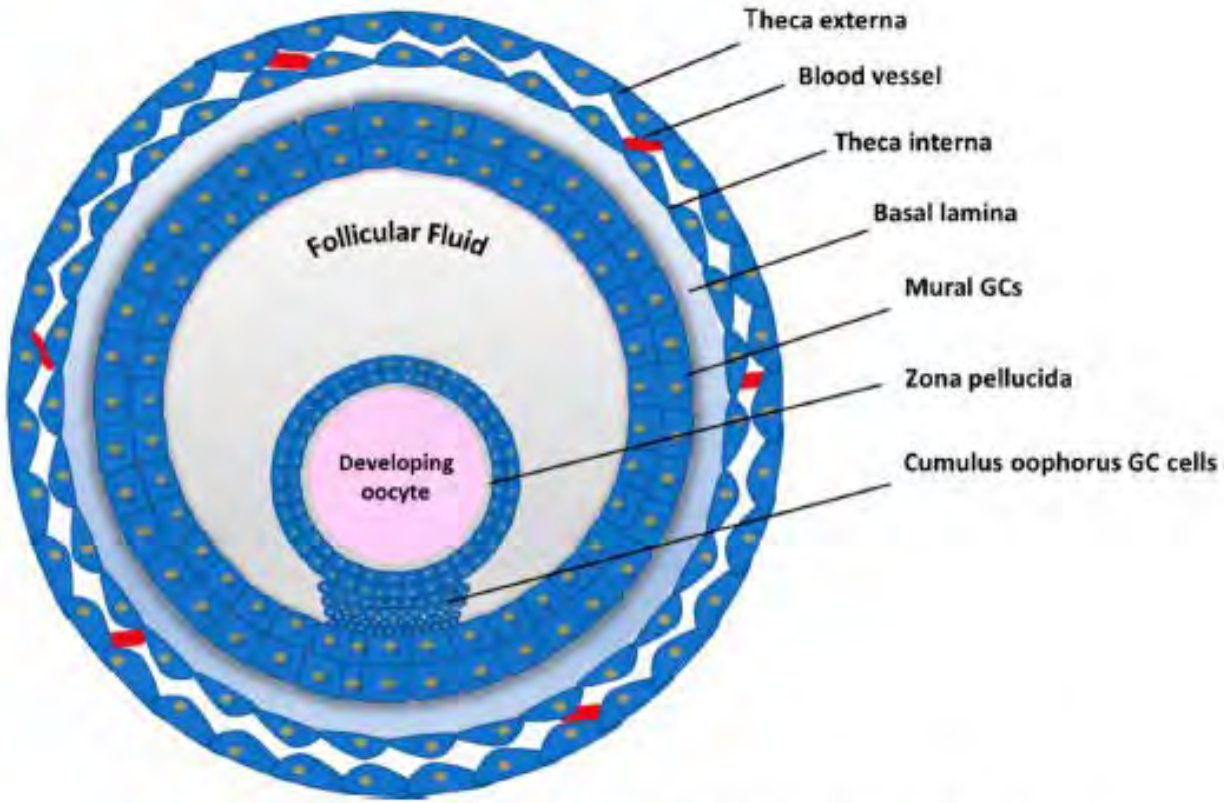
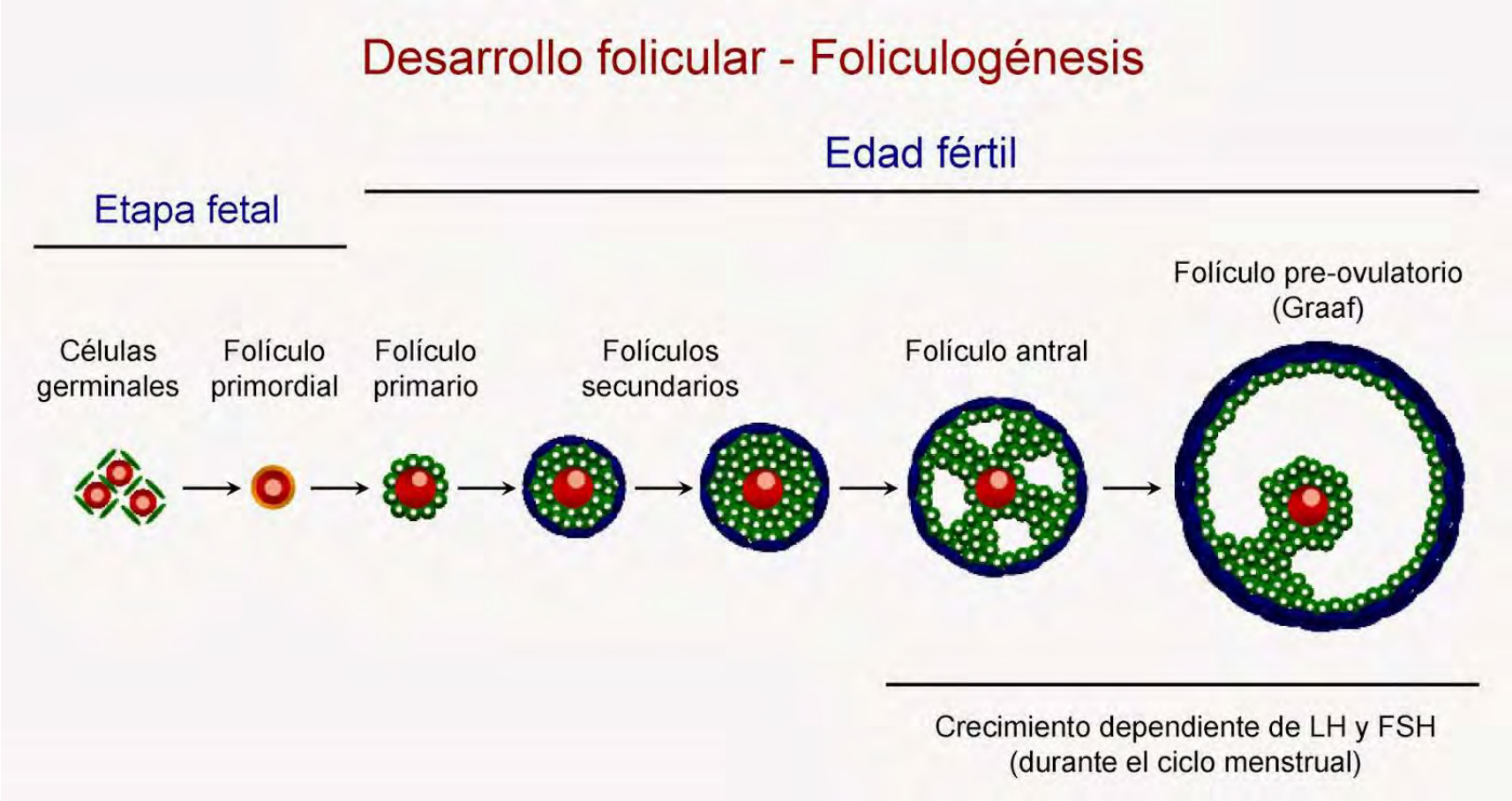


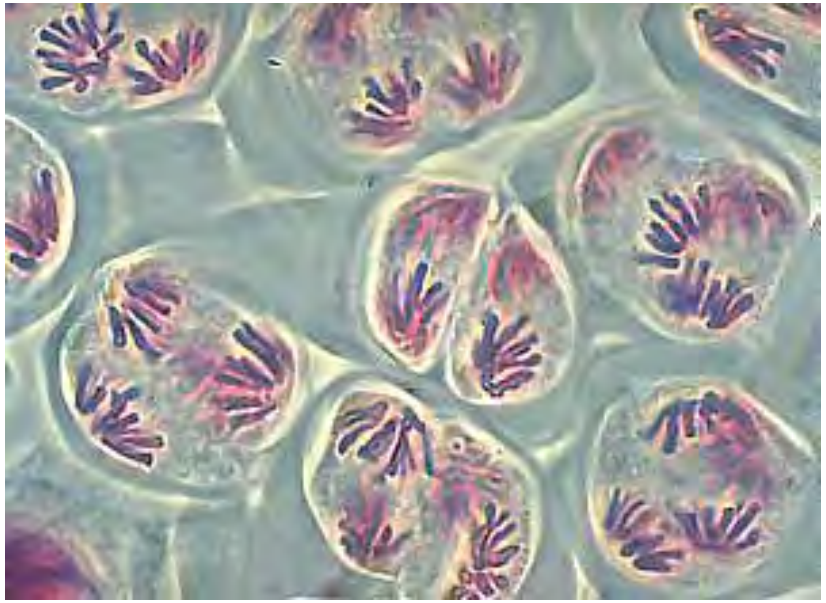
Figure 1. Schematic representation of the Ovarian Follicle structure.

Al nacer, el número de los folículos primordiales representan la reserva ovárica de la mujer. Después de la pubertad, cíclicamente, algunos de los folículos del grupo prenatal se desarrollan a través de diferentes etapas. Los folículos crecen, el ovocito se reanuda meiosis y después de una cuidadosa selección, solo se elige el folículo dominante para producir el ovocito maduro, listo para la fertilización. Los folículos ováricos representan las unidades reproductivas que consisten en el ovocito, células somáticas (cúmulos granulosas, células de la granulosa mural y teca) y líquido folicular (FF)



El crecimiento del ovocito ocurre a la vez y es mutuamente interdependiente del desarrollo y diferenciación del folículo

Hutt y Albertini, 2007.



3. Meiosis del ovocito

- Mantiene el nº haploide de crosomosmas
- Permite la diversidad genética
- Un único gameto viable con todo el citoplasma y 3 cuerpos polares
- Meiosis I y Meiosis II

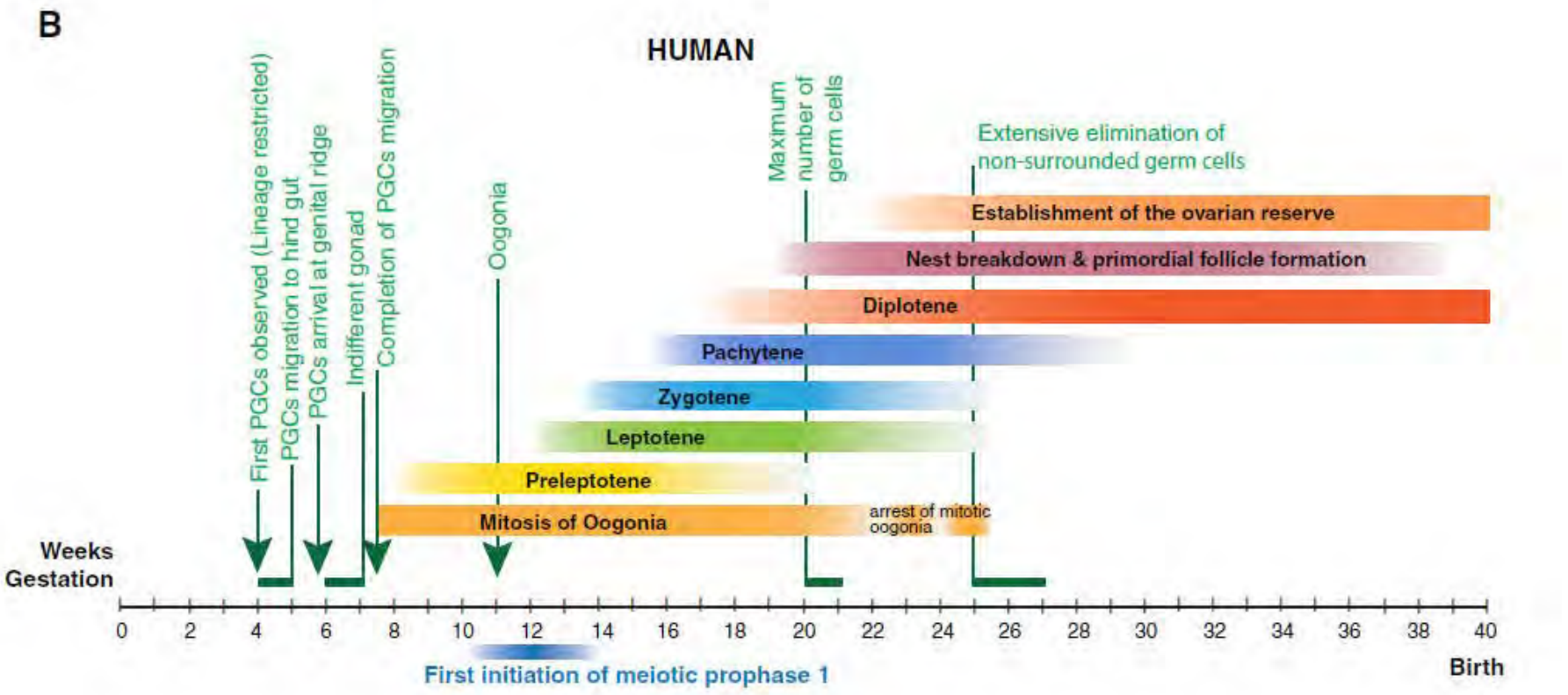
3.- Meiosis ovocito

BIOLOGY OF REPRODUCTION (2015) **93**(5):111, 1–7
Published online before print 30 September 2015.
DOI 10.1095/biolreprod.115.133652

Minireview

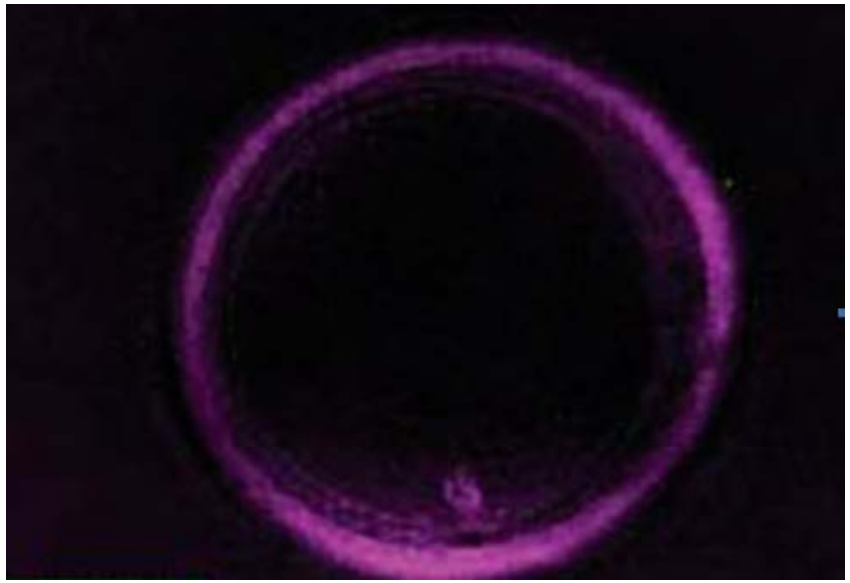
How Is the Number of Primordial Follicles in the Ovarian Reserve Established?[1]

John K. Findlay,[2,3,4,5] Karla J. Hutt,[3,6] Martha Hickey,[5] and Richard A. Anderson[7]



La meiosis en el ovocito es un proceso complejo, que no solo necesita una modificación sustancial del ciclo celular sino que también necesita de una maquinaria capaz de llevar a cabo la segregación de cromosomas con una mínima pérdida de citoplasma. Para ello, el ovocito desarrolla un diseño celular asimétrico y una posición periférica del huso meiótico. Este, dicta cuales son los planos de división de las divisiones meióticas justo debajo del oolema y de esta forma se alcanza la extrusión de los dos corpúsculos polares.

(Brunet and Verlhac, 2010; Yi et al., 2011).



Human Reproduction Update, Vol.23, No.6 pp. 706–722, 2017
Advanced Access publication on August 30, 2017 doi:10.1093/humupd/dmx026

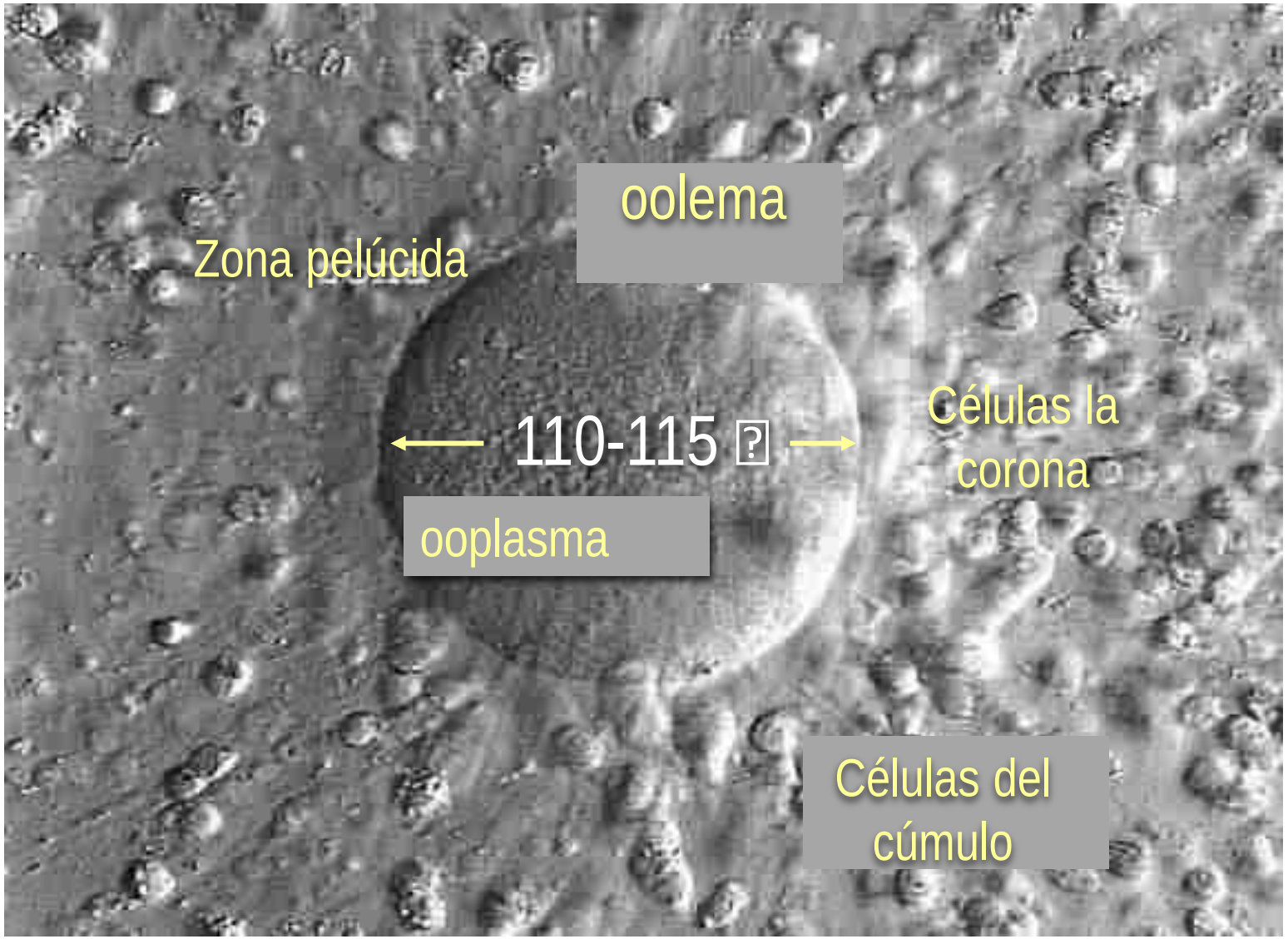
human reproduction update

Human female meiosis revised: new insights into the mechanisms of chromosome segregation and aneuploidies from advanced genomics and time-lapse imaging

Antonio Capalbo [1,2,*†], Eva R. Hoffmann[3,†], Danilo Cimadomo[1,4], Filippo Maria Ubaldi[1,2], and Laura Rienzi[1,2]

BACKGROUND: The unbalanced transmission of chromosomes in human gametes and early preimplantation embryos causes aneuploidy, which is a major cause of infertility and pregnancy failure. A baseline of 20% of human oocytes are estimated to be aneuploid and this increases exponentially from 30 to 35 years, reaching on average 80% by 42 years. As a result, reproductive senescence in human females is predominantly determined by the accelerated decline in genetic quality of oocytes from 30 years of age.

4. Estructura del ovocito



5.- Maduración ovocitaria

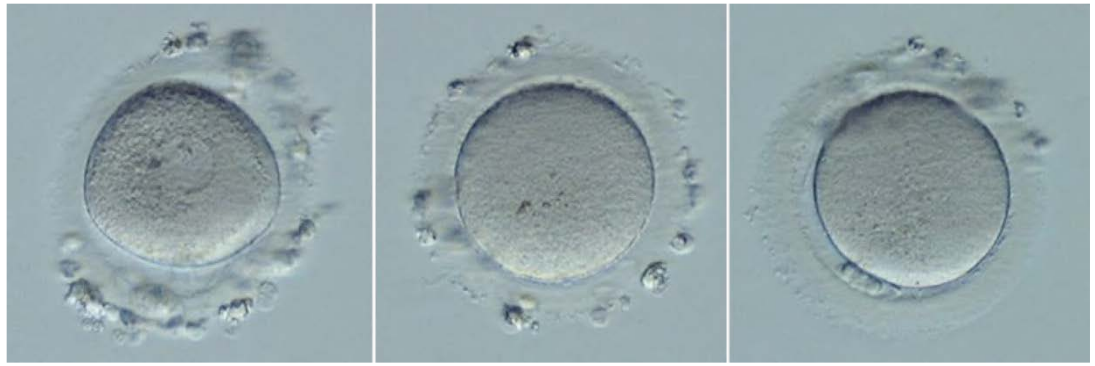
Proceso desde Dictiotena (Profase I) hasta Metafase II

Cambios celulares

-Desaparición VG
-Condensación cromosómica
-Formación huso
-Extrusión primer C.P.

Cambios moleculares

-Núcleo
-Citoplasma



5.- Maduración ovocitaria

a) Comunicación ovocito-cels. Somáticas
b) Mantenimiento del ovocito en meiosis
c) Reinicio de la meiosis
d) Cambios celulares
e) Cambios moleculares
f) Reorganización citoplasmática
g) Maduración citoplásmica

a. Comunicación intercelular entre granulosa y ovocito

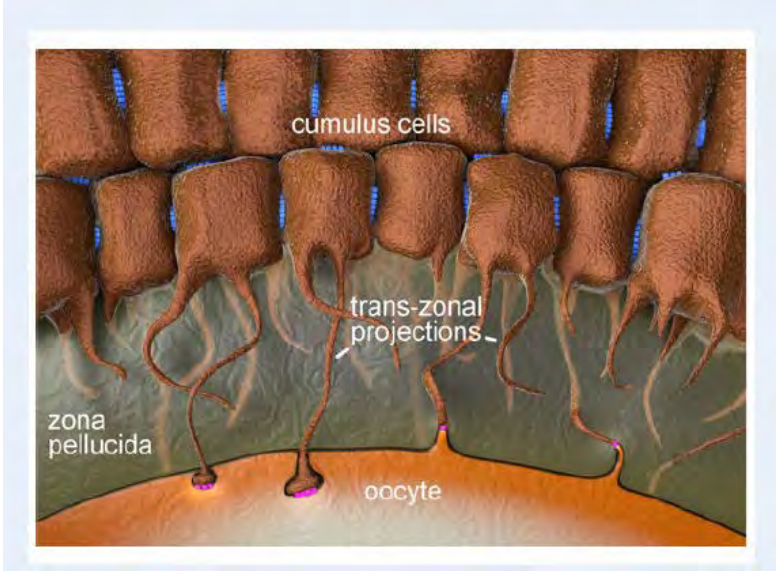
Human Reproduction Update, Vol.21, No.3 pp. 340–352, 2015
Advanced Access publication on February 9, 2015 doi:10.1093/humupd/dmv007

human reproduction update

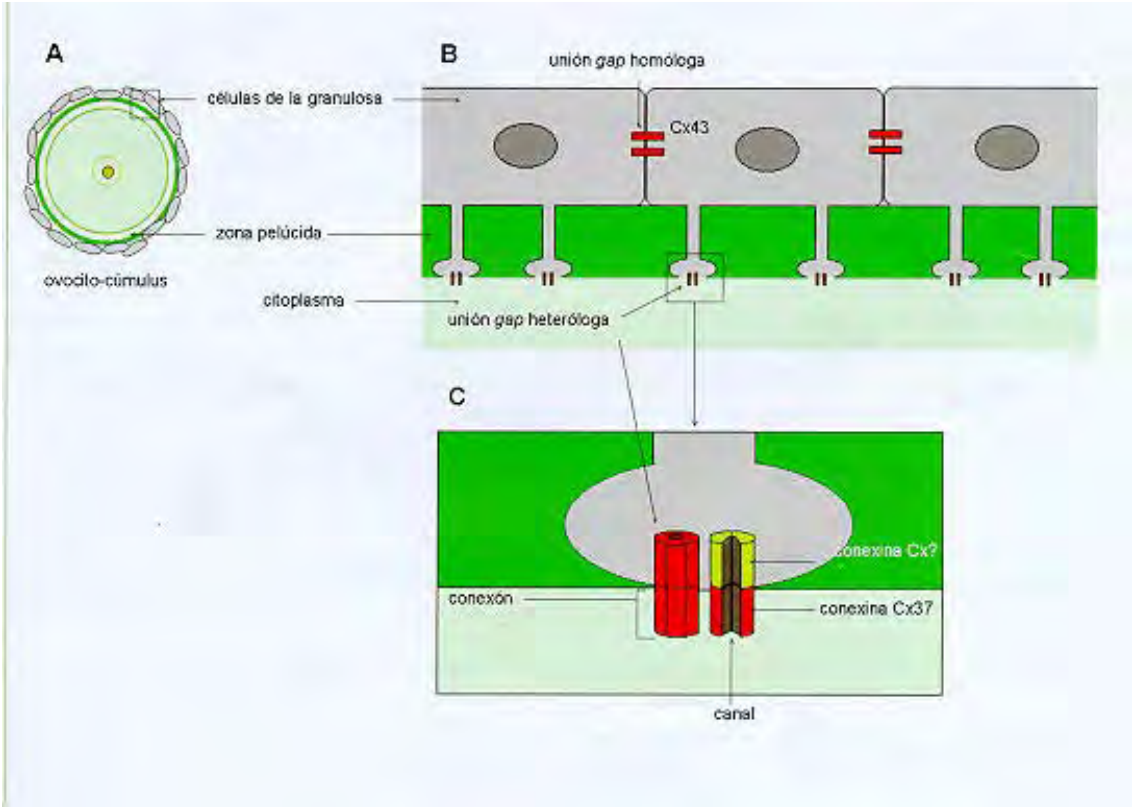
Gap junction connexins in female reproductive organs: implications for women's reproductive health

Elke Winterhager[1,*] and Gerald M. Kidder[2]

[1]Institute of Molecular Biology, University of Duisburg-Essen, University Clinics, 45211 Essen, Germany [2]Department of Physiology and Pharmacology, Schulich School of Medicine and Dentistry, The University of Western Ontario and Children's Health Research Institute, London, Ontario N6C 2V5, Canada



Nicholson y Bruzzone, 1997



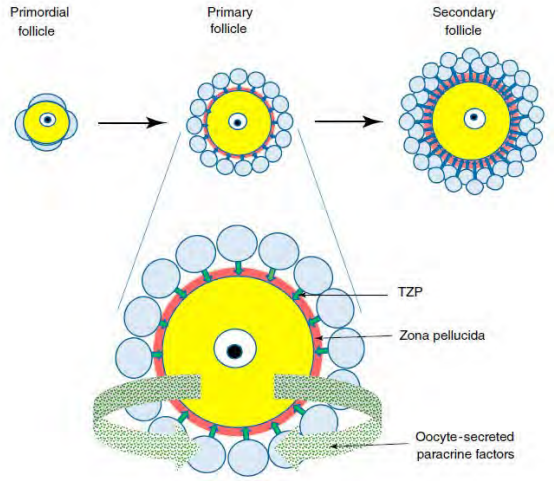
a. Comunicaciones ovocito-cels.somáticas

Reproduction: Oocytes Call, Granulosa Cells Connect

John J. Eppig
The Jackson Laboratory, Bar Harbor, ME 04609, USA
Correspondence: John.Eppig@jax.org
https://doi.org/10.1016/j.cub.2018.03.005

Making functional eggs requires a bidirectional conversation between oocytes and their companion somatic cells. Filopodia emanating from somatic cells carry crucial developmental information to oocytes, and a new study shows that oocytes signal elaboration of this key connection.

Current Biology 28, R342–R366, April 23, 2018

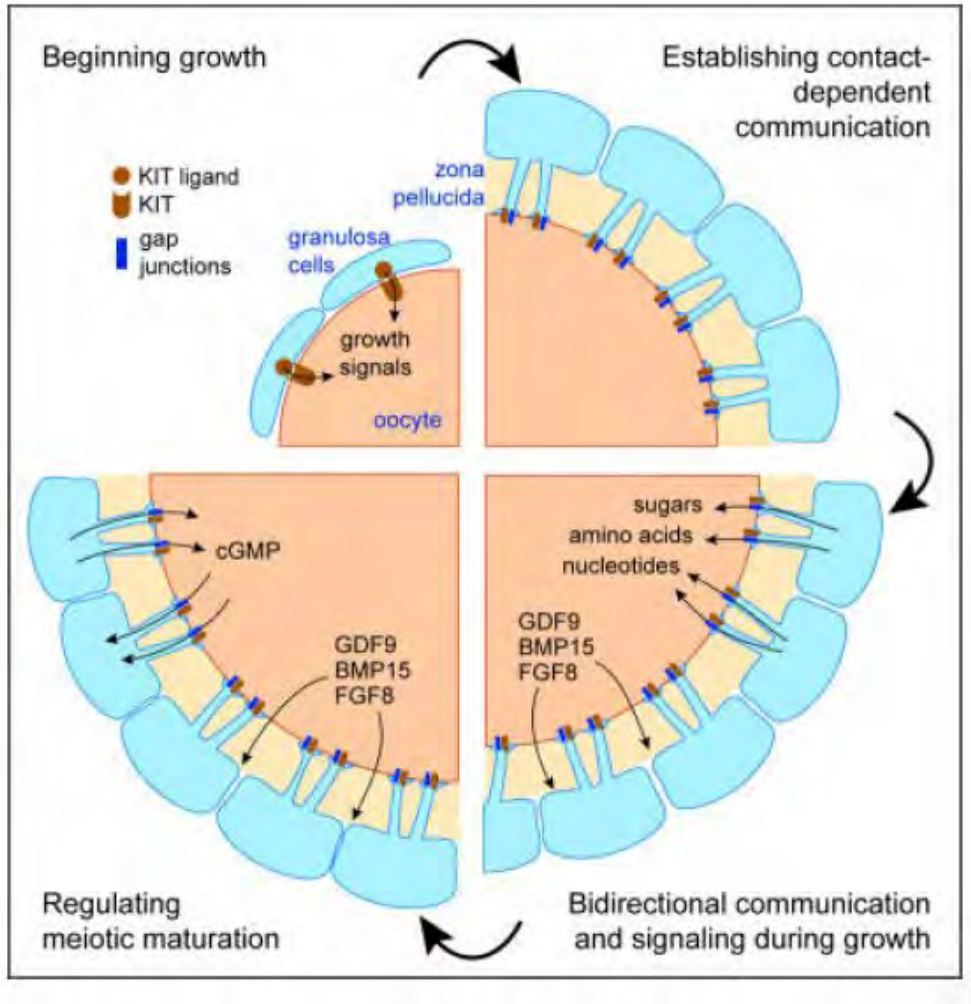


a. Comunicaciones ovocito-cels.somáticas

REGULATION OF GERM CELL DEVELOPMENT BY INTERCELLULAR SIGNALING IN THE MAMMALIAN OVARIAN FOLLICLE

Hugh J. Clarke

Todas las etapas del desarrollo de los ovocitos postnatales dependen de la comunicación con las células vecinas de la granulosa del folículo ovárico. Las señales enviadas por el ovocito también regulan la diferenciación de las células de la granulosa y aseguran que brinden un ambiente saludable para las células germinales.



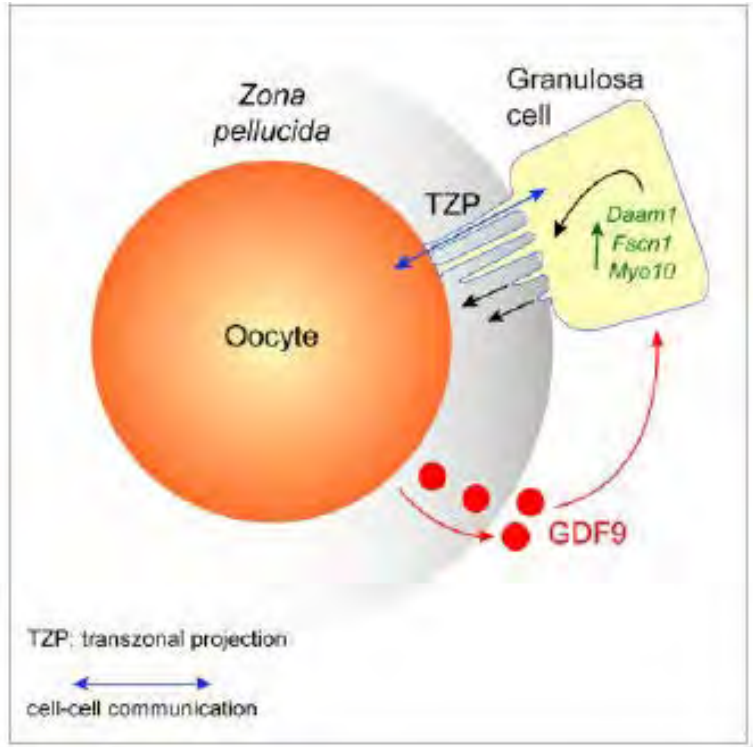
a. Comunicaciones ovocito-cels.somáticas

Curr Biol. 2018 April 02; 28(7): 1124–1131.e3. doi:10.1016/j.cub.2018.02.039.

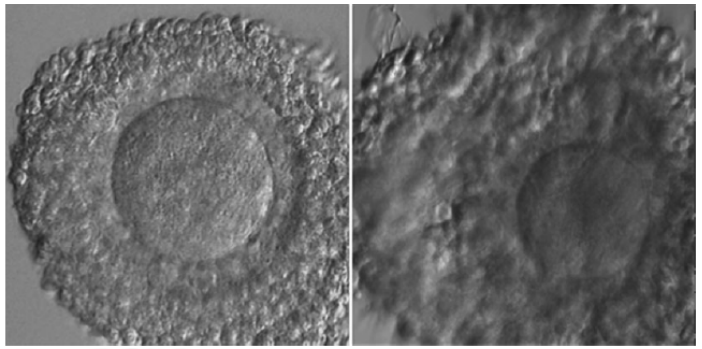
MAMMALIAN OOCYTES LOCALLY REMODEL FOLLICULAR ARCHITECTURE TO PROVIDE THE FOUNDATION FOR GERM LINE-SOMA COMMUNICATION

Stephany El-Hayek[1,2,4], **Qin Yang**[4], **Laleh Abbassi**[1,3,4], **Greg FitzHarris**[5], and **Hugh J. Clarke**[1,2,3,4]

GDF9 produced by the oocyte promotes generation of TZPs by granulosa cells



a. Comunicaciones ovocito-cels.somáticas



International Journal of *Molecular Sciences*

Int. J. Mol. Sci. **2019**,

Review

Extracellular Vesicles in Human Oogenesis and Implantation

Francesca Andronico [1], Rosalia Battaglia [1,*], Marco Ragusa [1,2], Davide Barbagallo [1], Michele Purrello [1] and Cinzia Di Pietro [1,*]

Las microvesículas y los exosomas, identificados en el líquido de los folículos ováricos durante la maduración del óvulo, intervienen en la comunicación entre el ovocito en desarrollo y las células foliculares somáticas.

b. Mantenimiento del ovocito en meiosis

Pan and Li *Reproductive Biology and Endocrinology* (2019) 17:8
https://doi.org/10.1186/s12958-018-0445-8

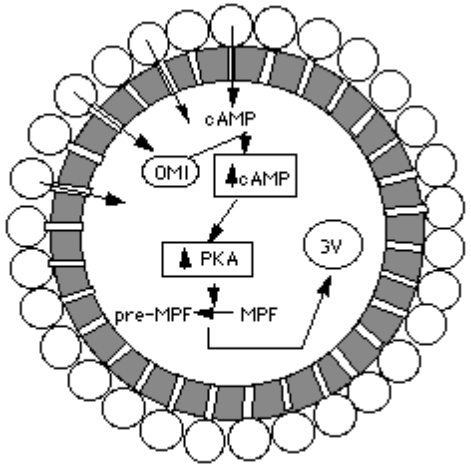
Reproductive Biology and Endocrinology

REVIEW Open Access

The art of oocyte meiotic arrest regulation

Bo Pan and Julang Li*

During Oocyte Growth and Before the LH Surge



- **OMI - Oocyte Maturation Inhibitor**
- **MPF - Maturation promoting factor**
- **GV - germinal vesicle**

Gap Junctions Allow Cell to Cell Communication!

El nivel elevado de AMPc es necesario para la parada meiótica en profase. El propio ovocito adopta un sistema para generar suficiente AMPc endógeno, aunque es necesario el el GMPc de las células de la granulosa para mantener el AMPc elevado. Por lo tanto, el ovocito organiza la síntesis de cGMP en las células de la granulosa circundante, en colaboración con su propio cAMP antes del aumento de LH.

c. Reinicio de la meiosis

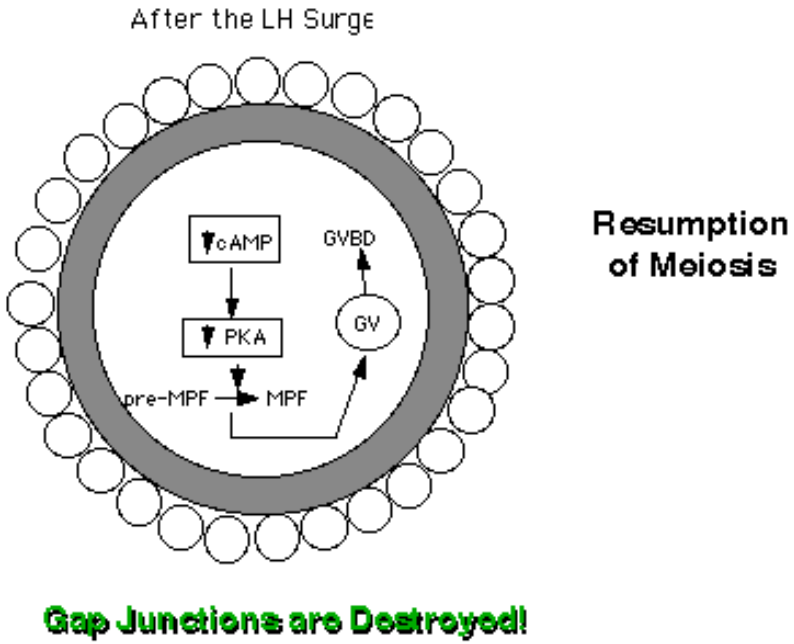

Pan and Li *Reproductive Biology and Endocrinology* (2019) 17:8
https://doi.org/10.1186/s12958-018-0445-8

Reproductive Biology and Endocrinology

REVIEW Open Access

The art of oocyte meiotic arrest regulation

Bo Pan and Julang Li*



Cuando se produce el aumento de LH, la señalización induce la desfosforilación e inactivación de NPR2, que resulta en una rápida caída de la concentración de cGMP en la célula de la granulosa y el ovocito en un orden secuencial a través de uniones gap.

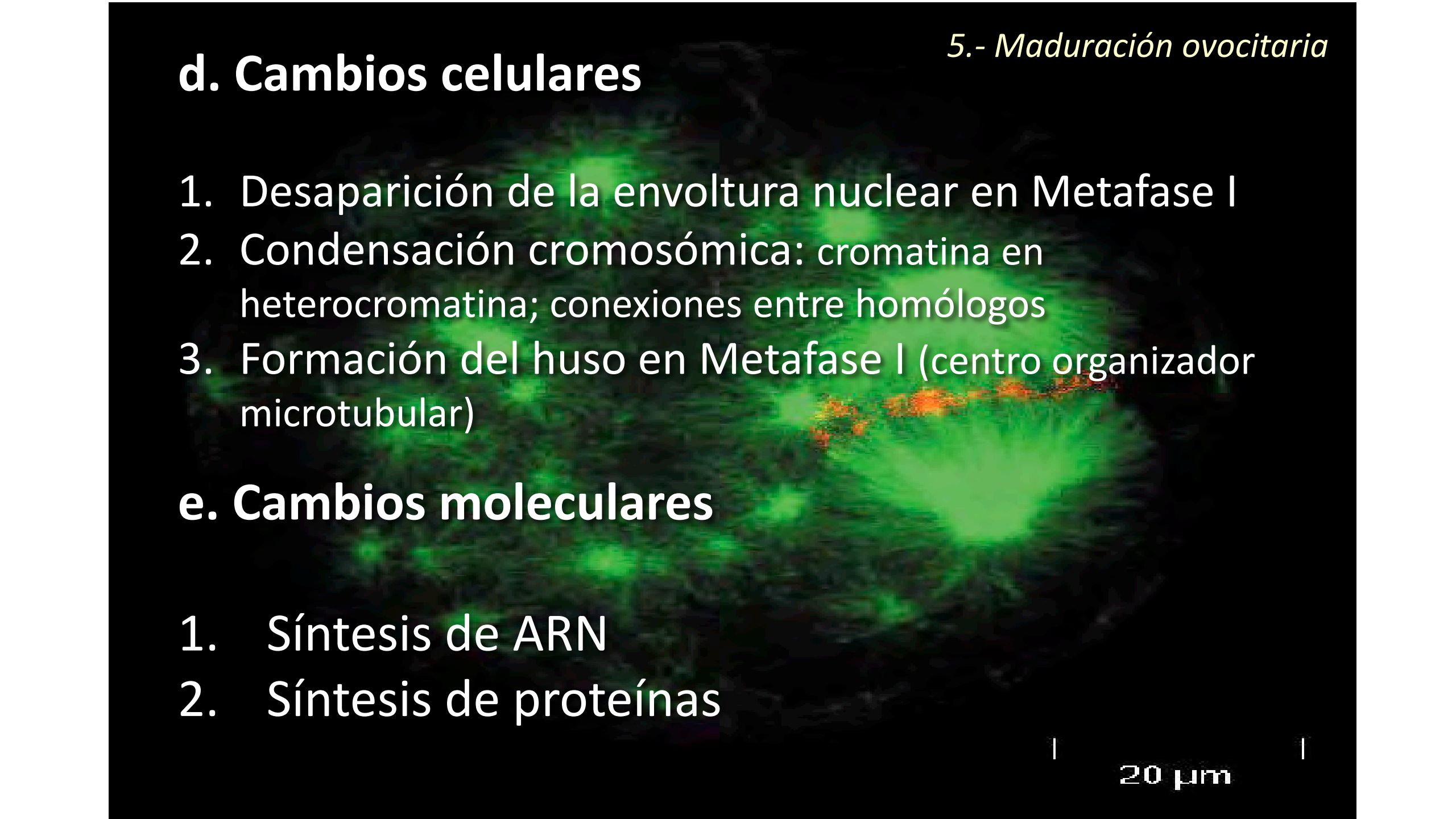
La LH interfiere entre las comunicaciones del cúmulo-ovocito-granulosa y la desconexión entre las cels del cúmulo y el ovocito hace que disminuya el flujo de sustancias inhibidoras de la meiosis.

d. Cambios celulares

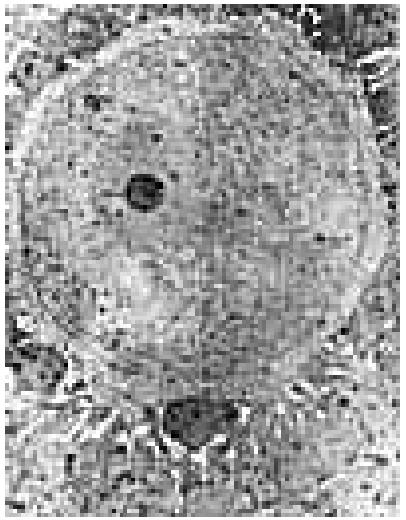
1. Desaparición de la envoltura nuclear en Metafase I
2. Condensación cromosómica: cromatina en heterocromatina; conexiones entre homólogos
3. Formación del huso en Metafase I (centro organizador microtubular)

e. Cambios moleculares

1. Síntesis de ARN
2. Síntesis de proteínas



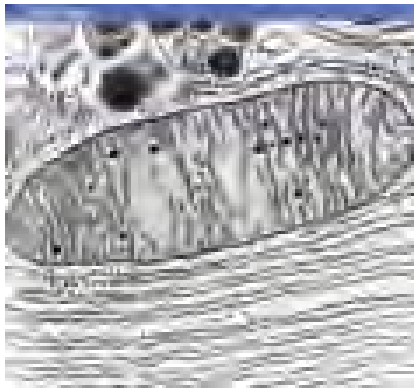
f. Reorganización citoplásmica



En las primeras etapas, orgánulos alrededor del núcleo: *corpúsculo de Balbiani.*

- **Núcleo**: aumenta de tamaño; intense actividad RNAasa. Falta de centriolos

-**Mitocondrias**: Cambian su estructura y el número. Pasan de ser ovaladas a redondeadas y dispersas. En cels. primordiales hay unas 10 por célula, en ovocito primario unas 10.000, y se multiplica por 10 durante el crecimiento folicular *(Jansen, 2000; Motta, 2000)*



- **Aparato de Golgi**: Almacenamiento de productos de secreción (glicoproteínas de la Z.P y gránulos corticales)

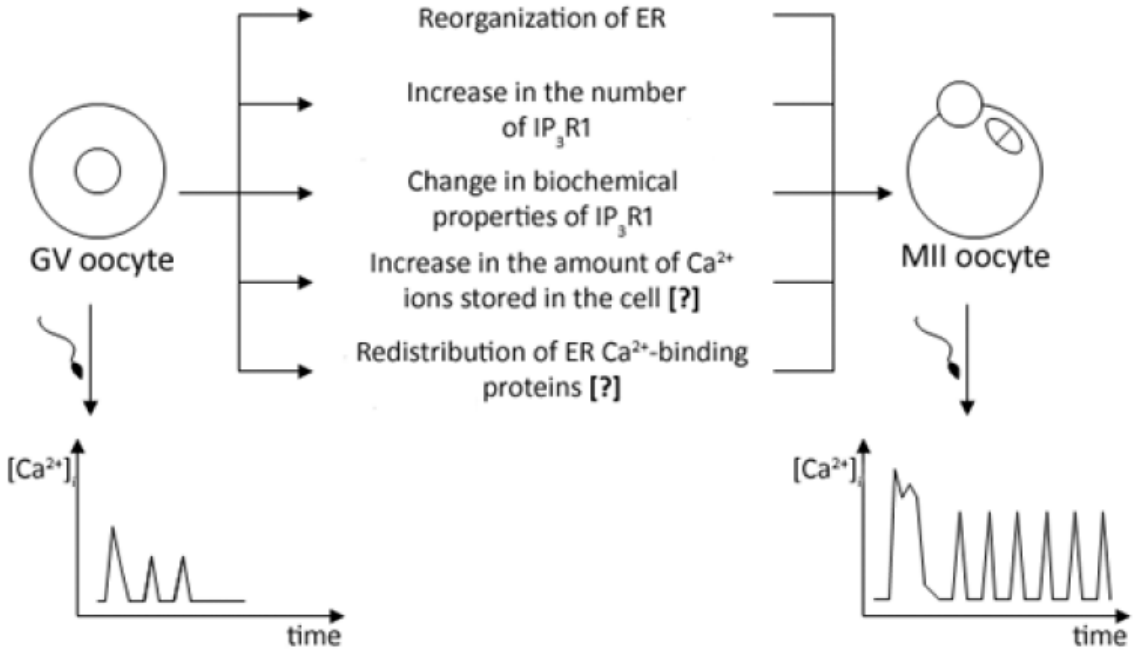
- **Retículo endoplásmico**: de dispersos por el citoplasma, a la superficie. Almacén de calcio.

- **Zona pelúcida**: imprescindible para la fecundación

g. Maduración citoplásmica

Todos los procesos que preparan al ovocito para la activación, formación de los pronúcleos y posterior desarrollo embrionario.

- Capacidad de descondensar la cromatina
- Liberar los iones calcio
- Liberación de gránulos corticales



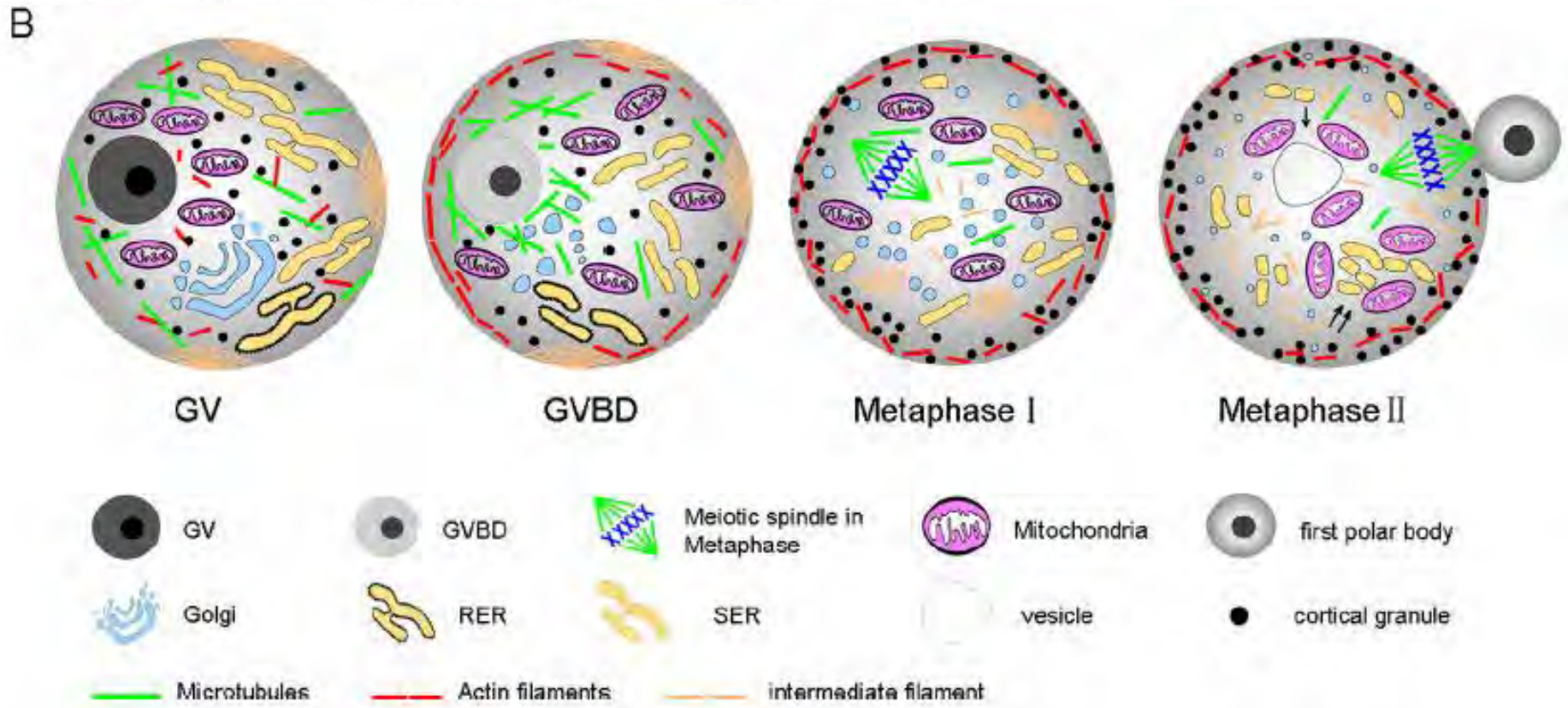
Reproductive Biology 2008 ***8*** *1:3-22.*

Reproductive BioMedicine Online (2014) 28, 284–299

REVIEW

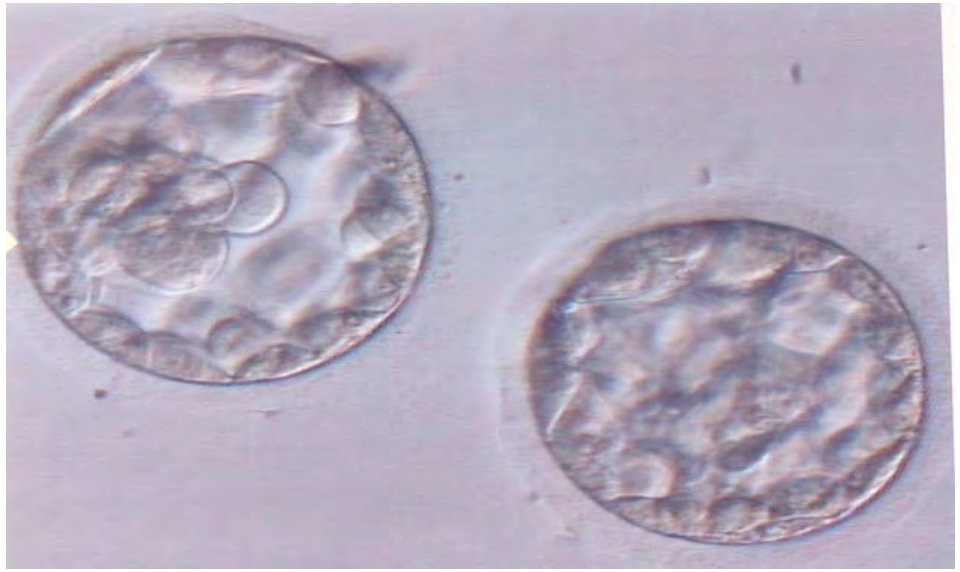
Behaviour of cytoplasmic organelles and cytoskeleton during oocyte maturation

Luna Mao [a], Hangying Lou [a], Yiyun Lou [a,c], Ning Wang [a], Fan Jin [a,b,*]



g. Maduración citoplásmica

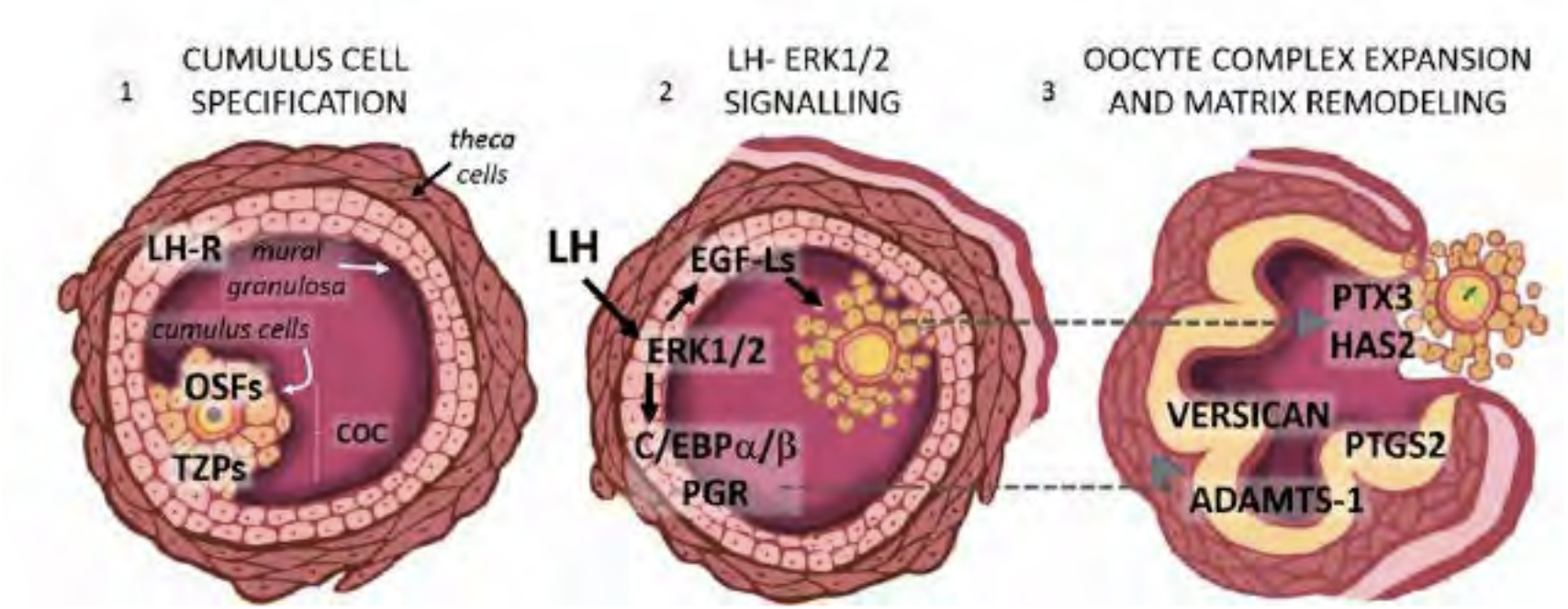
La capacidad de desarrollo hasta blastocisto es un indicador importante de la finalización de la maduración citoplásmica.



Coordination of Ovulation and Oocyte Maturation: A Good Egg at the Right Time

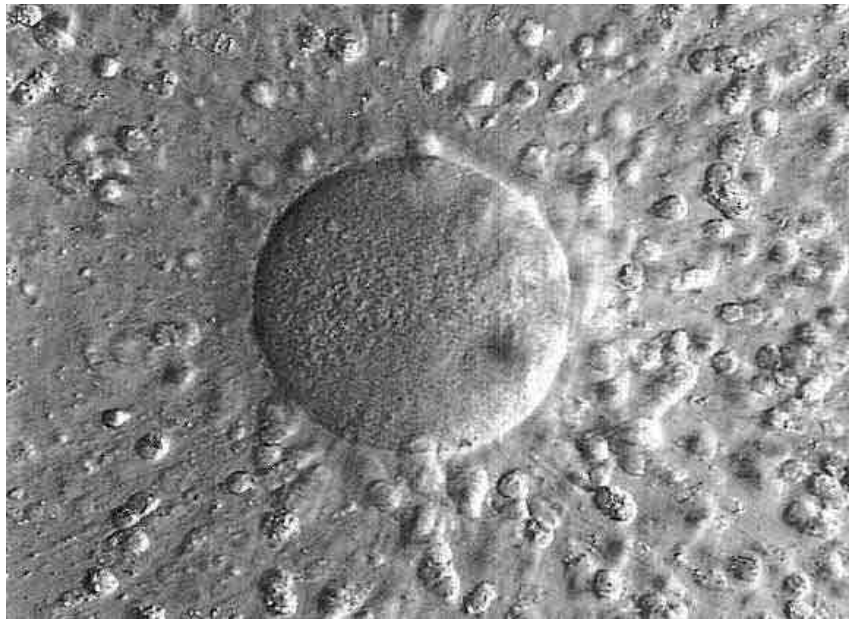
Rebecca L. Robker,[1] Jon D. Hennebold,[2,3] and Darryl L. Russell[1]

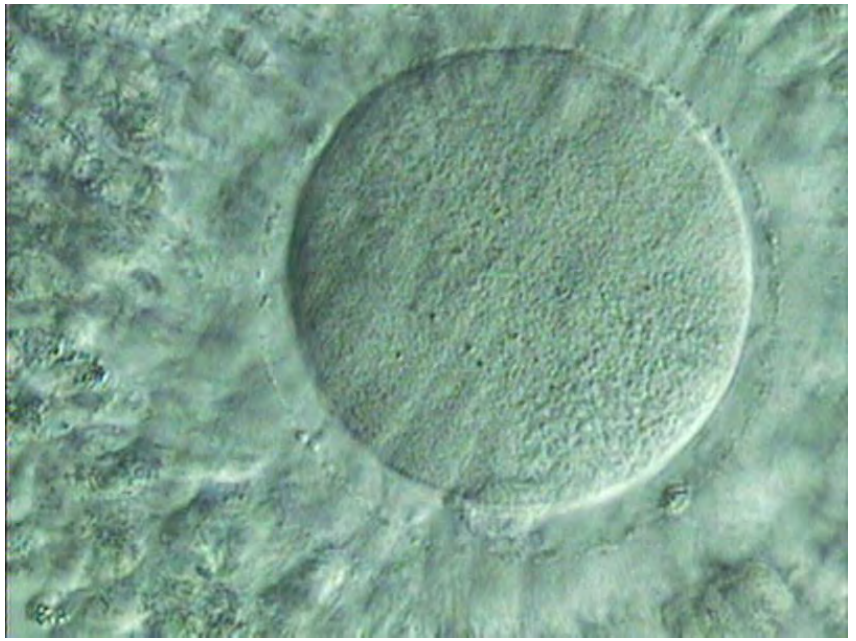
Endocrinology, September 2018, 159(9):3209–3218



Aspectos prácticos:

Ovocitos maduros:
Metafase II

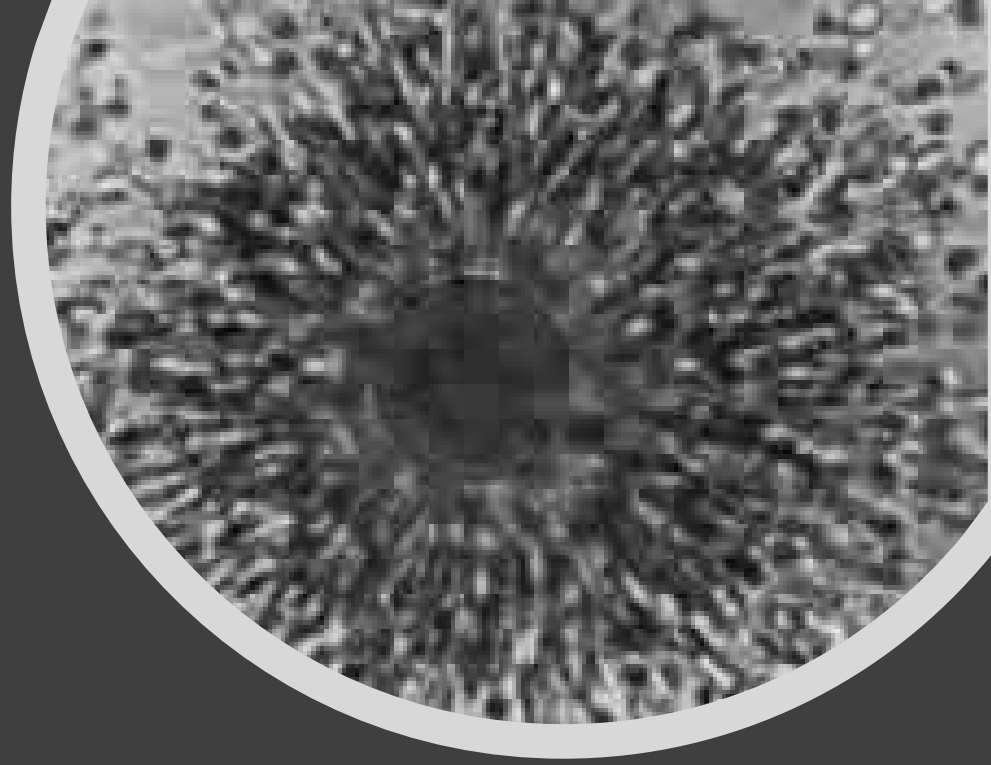




-Citoplasma claro
-Cúmulo expandido
-Corona clara
-Granularidad homogénea

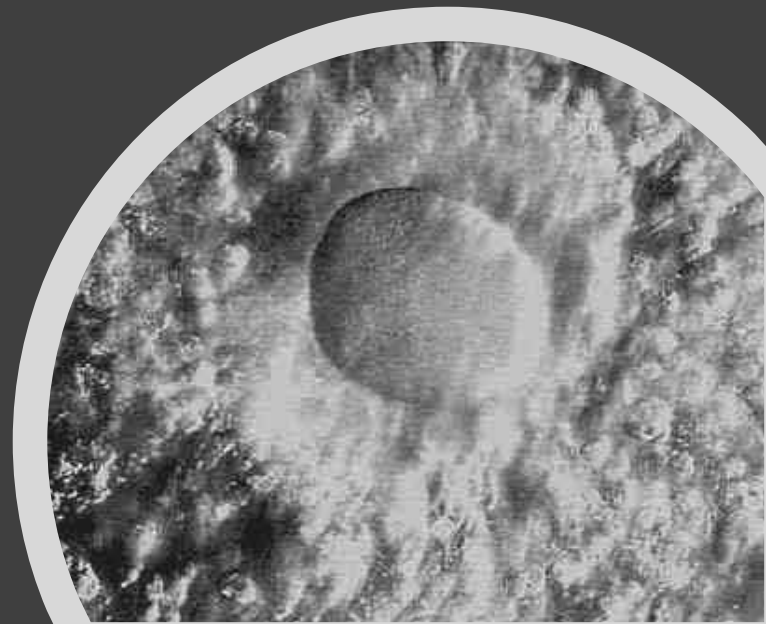
Inseminación o ICSI : 3-5 hrs post punción

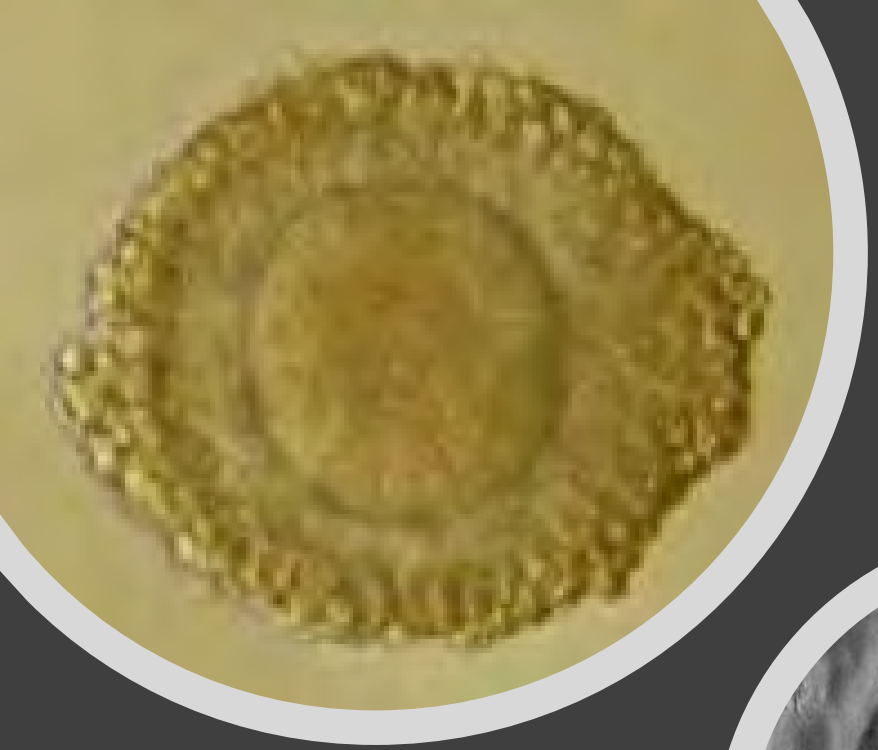
Ovocitos intermedios: Metafase I

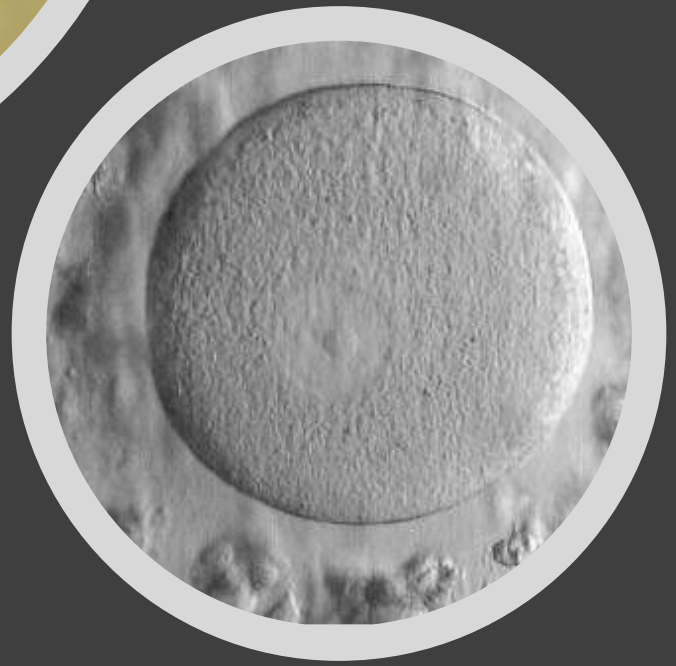


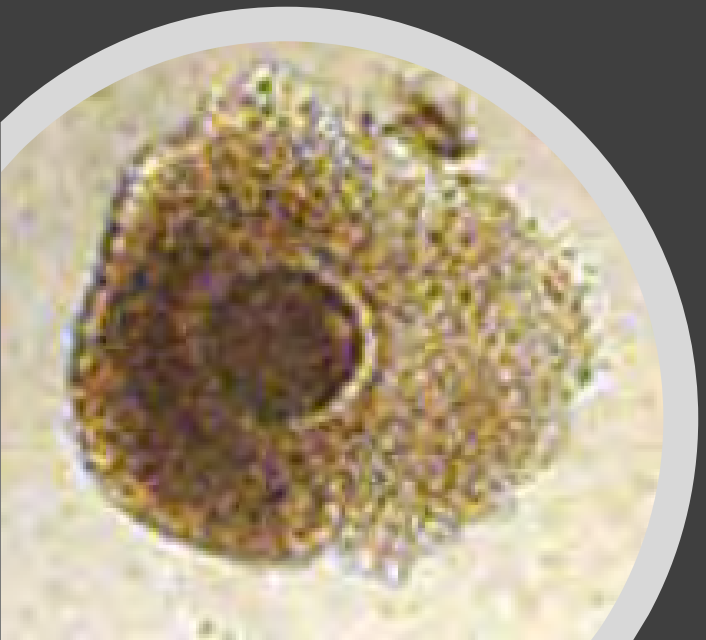
- -Ausencia de VG y CP
- -Citoplasma claro, con alguna granularidad
- -Cúmulos dispersos

-Necesitan de 1 a 24 hrs de cultivo antes de adquirir la madurez total









Ovocitos inmaduros: VG

- -VG en el citoplasma (si está en el centro indican parada madurativa)
- -Citoplasma oscuro y granular
- -Cúmulos compactos

- NO SE MICROINYECTAN

RBMO

ELSEVIER

ARTICLE

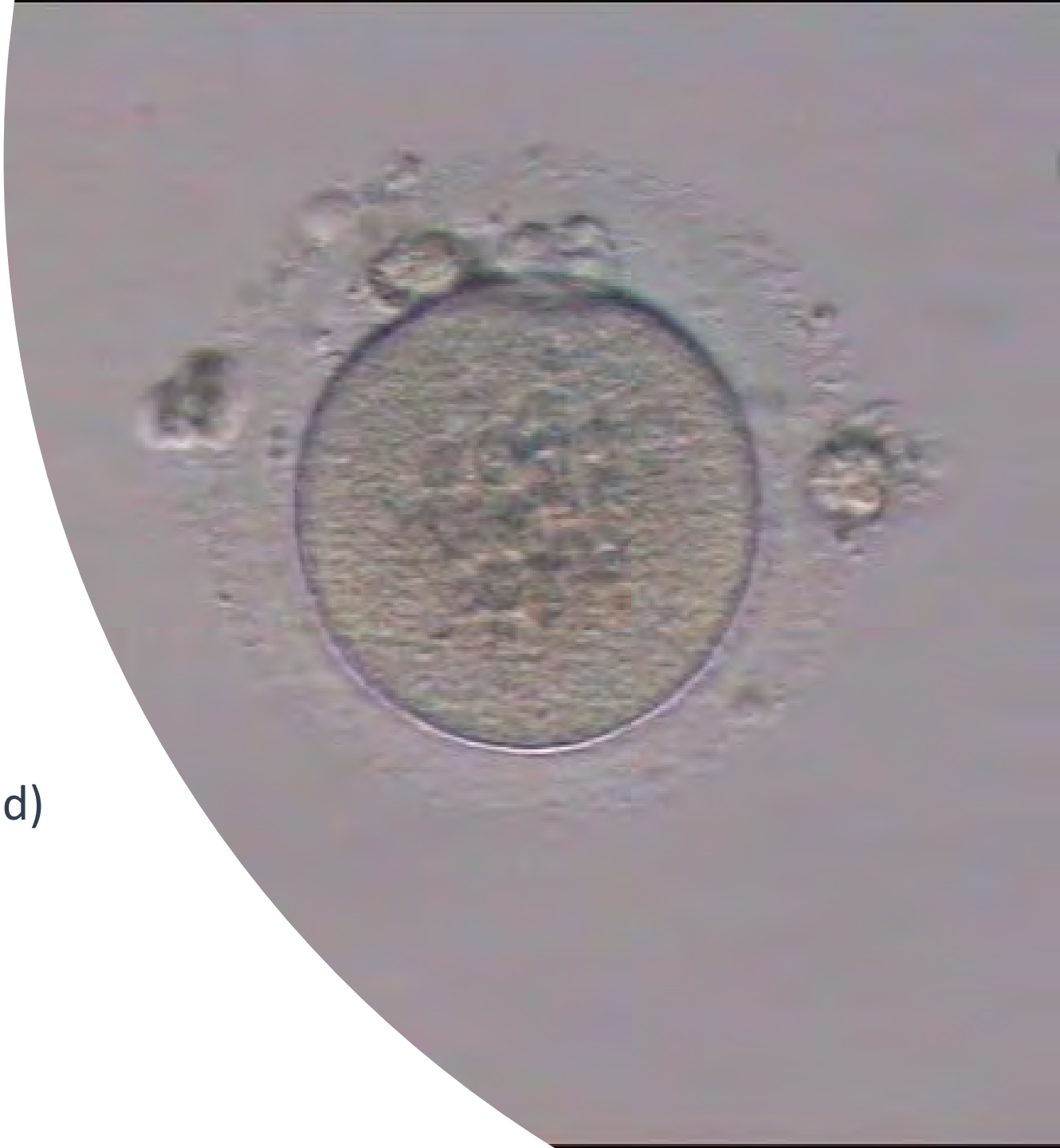
High proportion of immature oocytes in a cohort reduces fertilization, embryo development, pregnancy and live birth rates following ICSI

BIOGRAPHY

Alessandra Parrella earned a Master's degree in Biology from University of Sannio in 2015. She is a clinical embryologist with an academic faculty position at Weill Cornell Medicine. She is currently conducting several research projects on male infertility. One such project aims at measuring sperm chromatin fragmentation (SCF) from different levels of the male genital tract. In men with high SCF, Alessandra is isolating spermatozoa through a microfluidic device yielding the highest portion of progressively motile cells characterized by the highest genomic integrity. Using the Next-Generation Sequencing, she is currently assessing the gene expression profile of sperm RNA in man with idiopathic infertility.

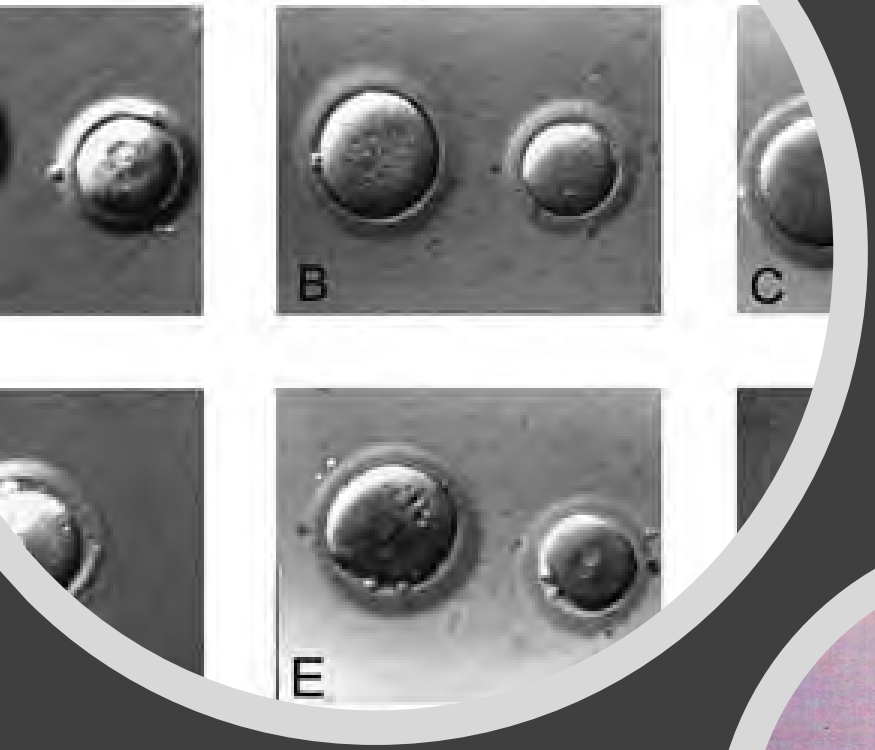
Alessandra Parrella[1], Mohamad Irani[1], Derek Keating, Stephen Chow, Zev Rosenwaks, Gianpiero D. Palermo*

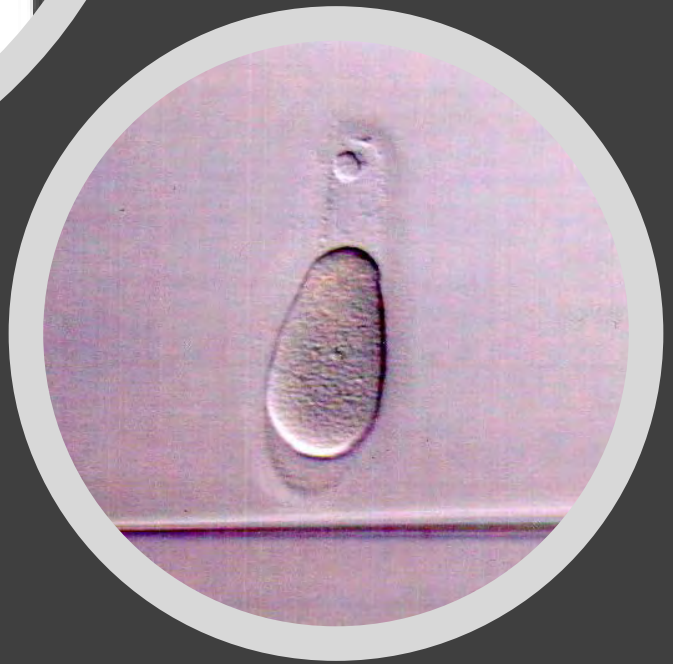
Importancia de la morfología del ovocito en los resultados de FIV-ICSI.

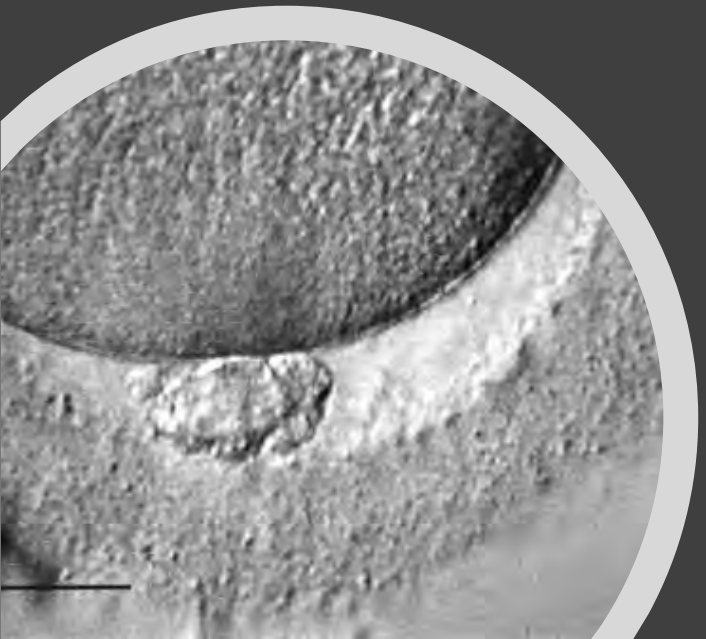


- Tamaño
- Forma
- Grosor de la Z.P.
- Espacio perivitelino
- Citoplasma (vacuolas, color, granularidad) apariencia del C. P.

Importancia de la morfología del ovocito en los resultados de FIV-ICSI.







Anomalías ovocitarias

1. *Ovocitos gigantes:*

Falta de citocinesis en la meiosis o fusión de ovogonias: dotación diploide

No microinyectarlos: zigotos poliploides

Pueden estar asociados a la estimulación *(Balakier, 2002)*

2. *Anomalías del corpúsculo polar:*

Proporciona información sobre la edad del ovocito, ya que permanecen intactos menos de 20 hrs post ovulación.

3. *Huso meiótico*:

Un alto grado de desalineación entre el huso y el primer C.P. predice un mayor riesgo de anomalías de fecundación.

4. *Citoplasma* (viscosidad, granularidad, vacuolas)
5. *Anomalías en la forma* (problemas en el hatching)

Received: 6 January 2018 | Accepted: 6 March 2018

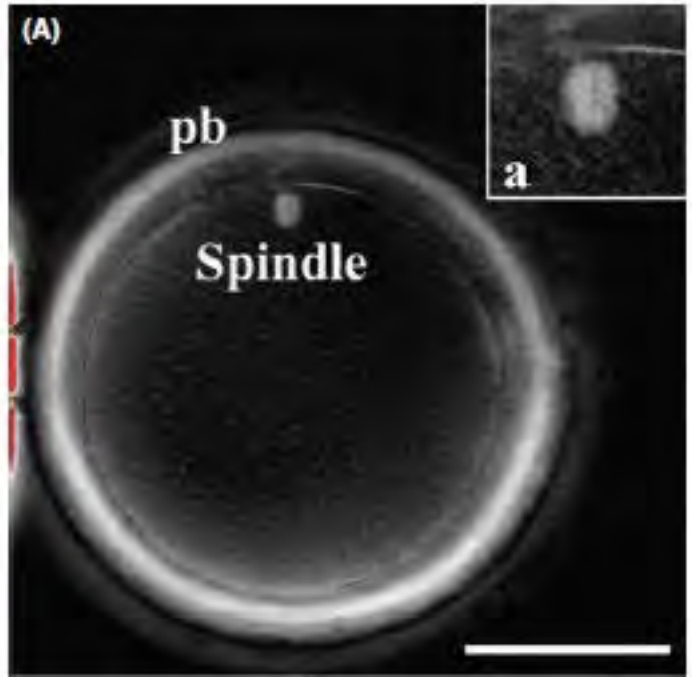
DOI: 10.1002/rmb2.12100

ORIGINAL ARTICLE

WILEY Reproductive Medicine and Biology

Meiotic spindle size is a strong indicator of human oocyte quality

Hiroyuki Tomari[1] | Ko Honjo[1] | Katsuko Kunitake[1] | Natsumi Aramaki[1] | Saori Kuhara[1] | Naomi Hidaka[1] | Kayoko Nishimura[1] | Yumi Nagata[1] | Toshitaka Horiuchi[2]



Human Reproduction, Vol.28, No.8 pp. 2111–2117, 2013
Advanced Access publication on May 21, 2013 doi:10.1093/humrep/det241

human reproduction ORIGINAL ARTICLE *Embryology*

Deliveries of normal healthy babies from embryos originating from oocytes showing the presence of smooth endoplasmic reticulum aggregates

I. Mateizel*, L. Van Landuyt, H. Tournaye, and G. Verheyen

Figure 1 Metaphase II oocyte displaying the SER dysporphism.

Anomalías originadas en la maduración temprana:

- Fusión ovogonias
- Granulaciones
- Fallos en la formación del huso

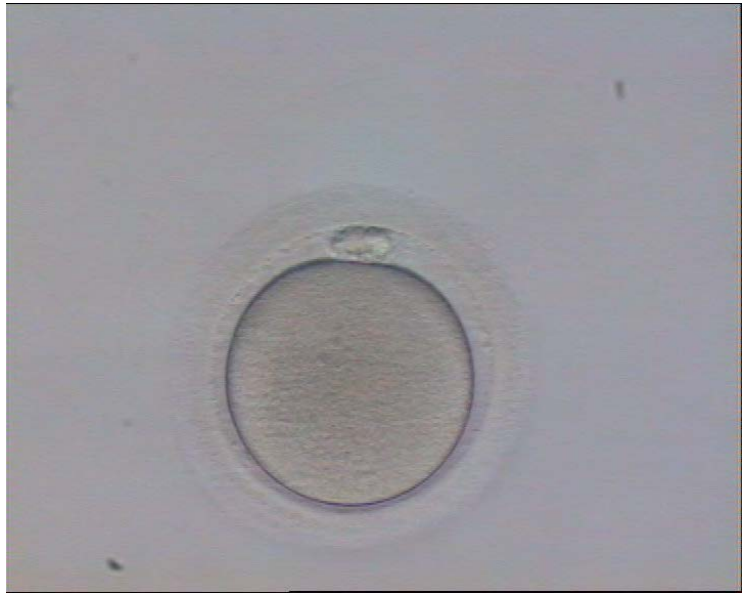
} -Fallos fecundación
-Aneuploidias

Anomalías originadas en las últimas etapas de la maduración:

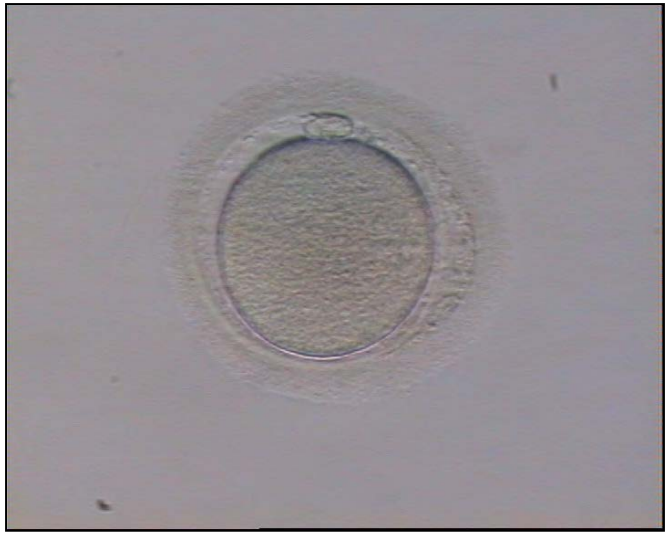
- Vacuolas
- Agregados de r.endoplásmico

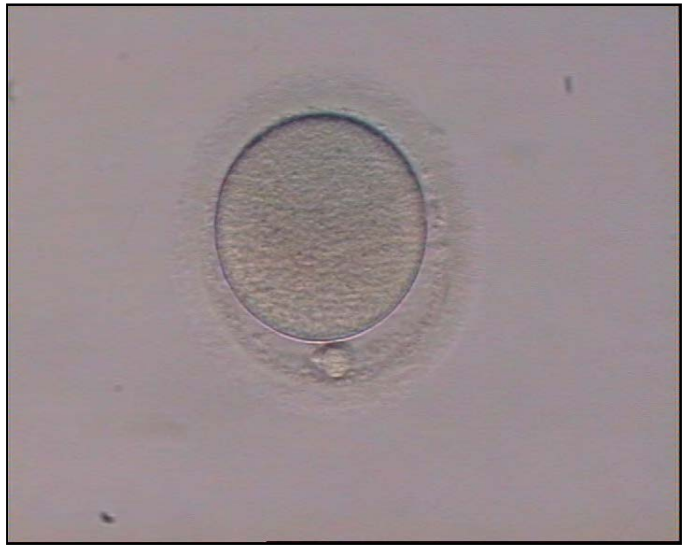
} Fallos de desarrollo

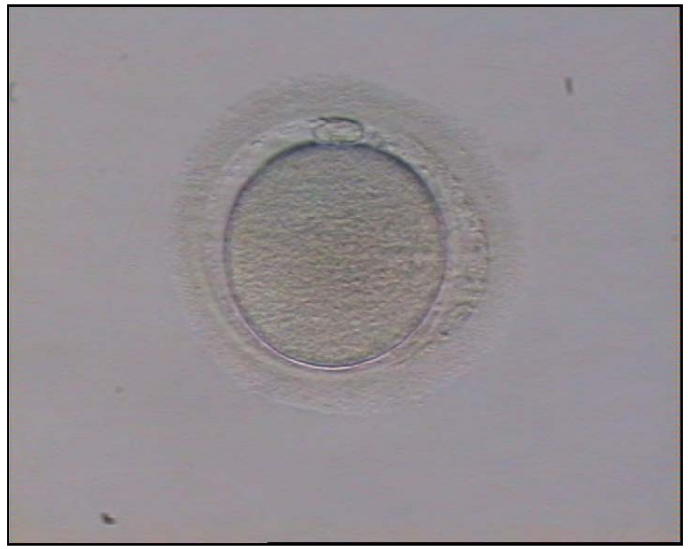
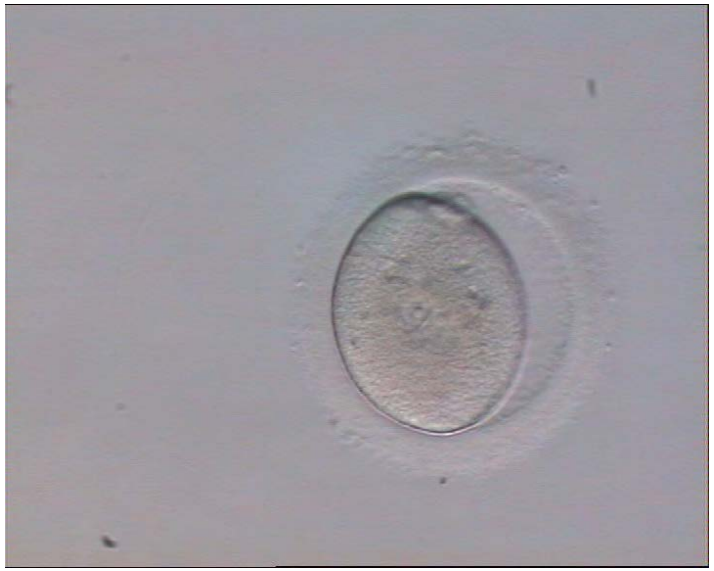
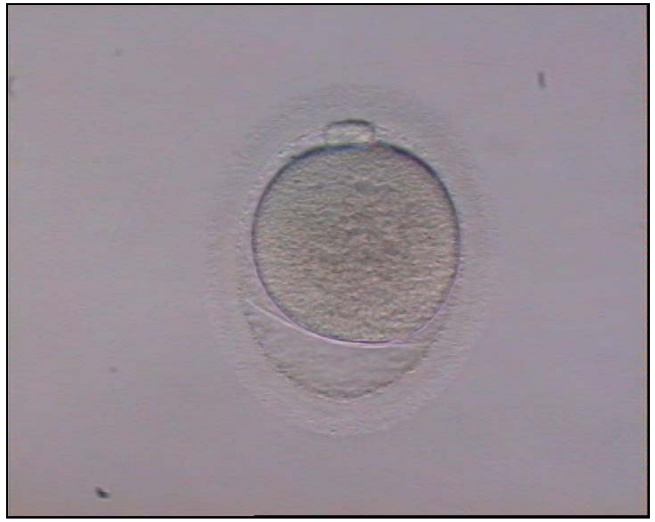
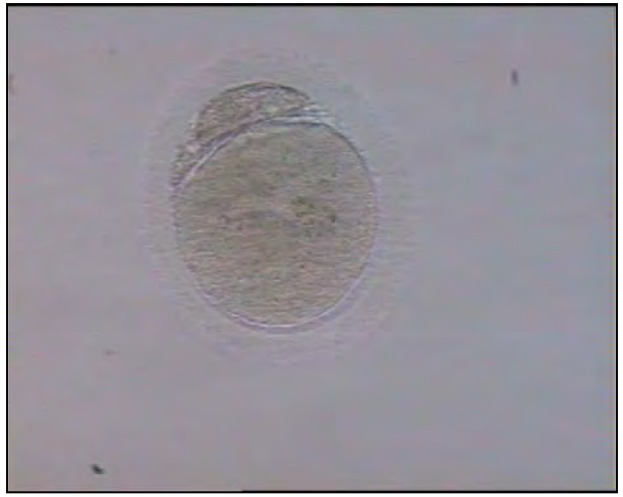
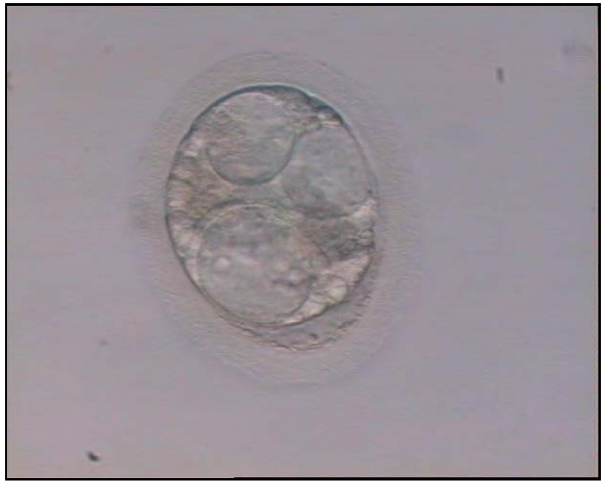
Ovocitos normales



Ovocitos anómalos





Human Reproduction Update Advance Access published July 16, 2010
Human Reproduction Update, Vol.00, No.0 pp. 1–12, 2010
doi:10.1093/humupd/dmq029

human reproduction update

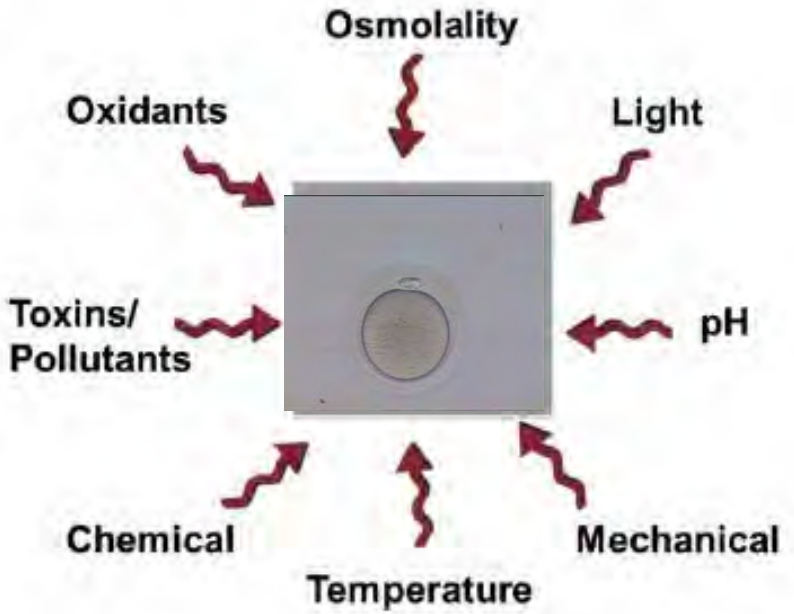
Predictive value of oocyte morphology in human IVF: a systematic review of the literature

Laura Rienzi [1,*], Gábor Vajta [2], and Filippo Ubaldi [1]

CONCLUSIONS: No clear tendency in recent publications to a general increase in predictive value of morphological features was found. These contradicting data underline the importance of more intensive and coordinated research to reach a consensus and fully exploit the predictive potential of morphological examination of human oocytes.

Factores que afectan al ovocito en el laboratorio

- *Transient cooling to room temperature can cause irreversible disruption of the meiotic spindle in the human oocyte.*
- *Pickering et al, Fertil Steril, 2000*



Received: 7 June 2018 | Revised: 7 August 2018 | Accepted: 9 August 2018
DOI: 10.1002/rmb2.12245

REVIEW ARTICLE

WILEY Reproductive Medicine and Biology

Updating the markers for oocyte quality evaluation: intracellular temperature as a new index

Yumi Hoshino

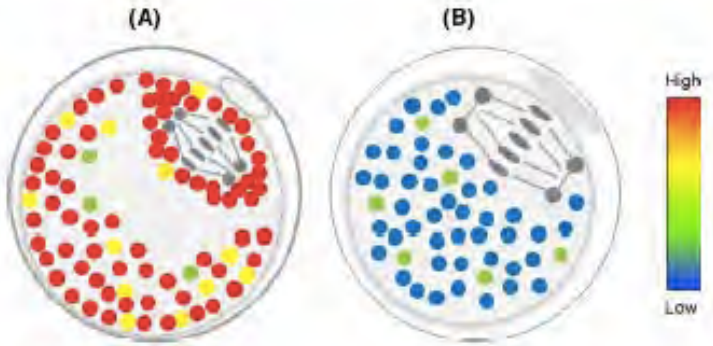
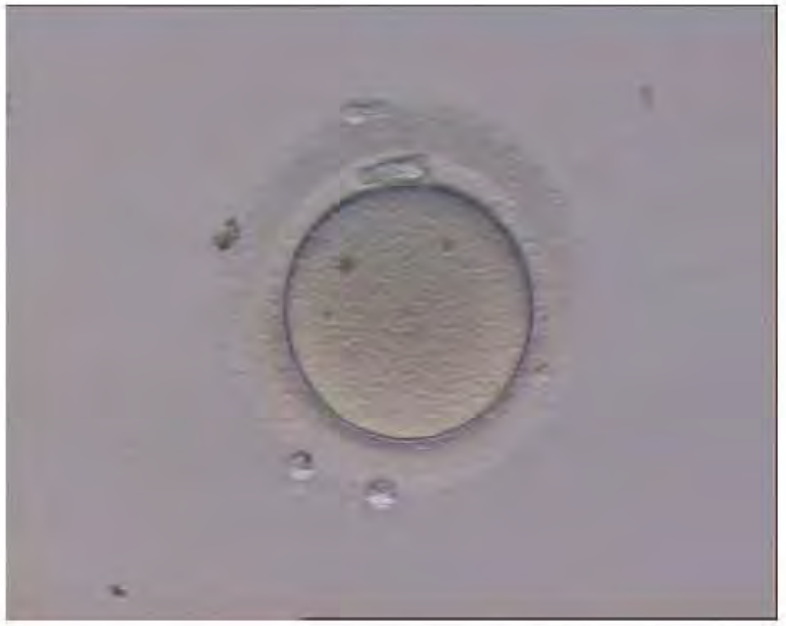


FIGURE 1 Schematic representation of intracellular temperature in matured oocytes. A, Fresh oocyte, and B, overmatured or aged oocyte. Fresh oocytes had high-temperature regions localized around the cell membrane and around the spindle. Red and yellow spots indicate high temperature, and blue and green spots indicate low temperature

¿Qué es lo que hace un buen ovocito?

EDAD

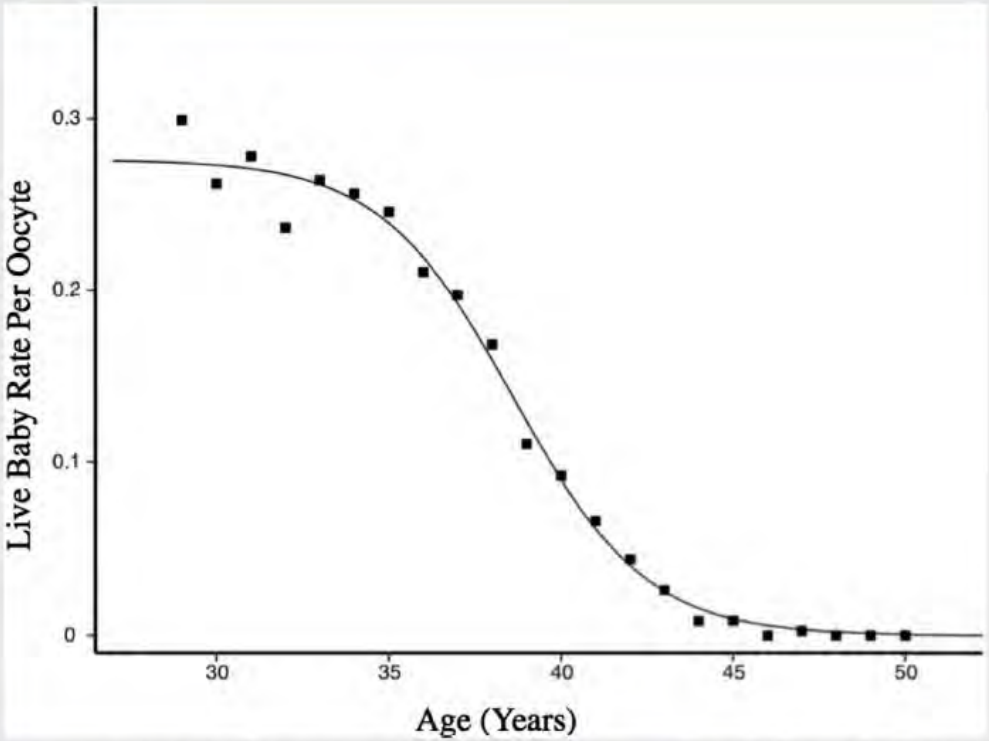
ESTIMULACIÓN



Intrinsic fertility of human oocytes

Sherman J. Silber, M.D.,[a] Keiichi Kato, M.D., Ph.D.,[b] Naoki Aoyama, M.Sc.,[b] Akiko Yabuuchi, Ph.D.,[b] Helen Skaletsky, Ph.D.,[c] Yuting Fan, M.D.,[c] Kazunori Shinohara, M.D.,[b] Noriyuki Yatabe, M.D., Ph.D.,[b] and Tamotsu Kobayashi, M.D.[b]

FIGURE 1



Fertility of the human oocyte related to age. We approximated the data with the simple logistic curve $r = 1/(a + \exp[b * (t - c)])$, where r is live baby rate per oocyte and t is age in years. The coefficients were evaluated using gradient method as implemented in statistical package R (version 3.2.5). The quality of the fit is very high and explains 99% of observed variation. The black squares depict empirical values (actual observations).

Silber. Intrinsic fertility of human oocytes. Fertil Steril 2017.

Something happens during stimulation

Fertility and Sterility® Vol. 105, No. 3, March 2016

VIEWS AND REVIEWS

Regimen of ovarian stimulation affects oocyte and therefore embryo quality

Ernesto Bosch, M.D.,[a] Elena Labarta, M.D.,[a] Efstratios Kolibianakis, M.D.,[b] Mitchell Rosen, M.D.,[c] and David Meldrum, M.D.[d]

Recent studies suggest that the use of high doses of gonadotropins as an independent factor correlates negatively with the probability of live birth, whereas a high ovarian response per se is associated with better cumulative pregnancy rates, owing to the availability of more euploid and good-quality embryos

Reproductive BioMedicine Online (2016) 32, 446–456

ELSEVIER

www.sciencedirect.com
www.rbmonline.com

ARTICLE

Oxidative stress in follicular fluid of young women with low response compared with fertile oocyte donors

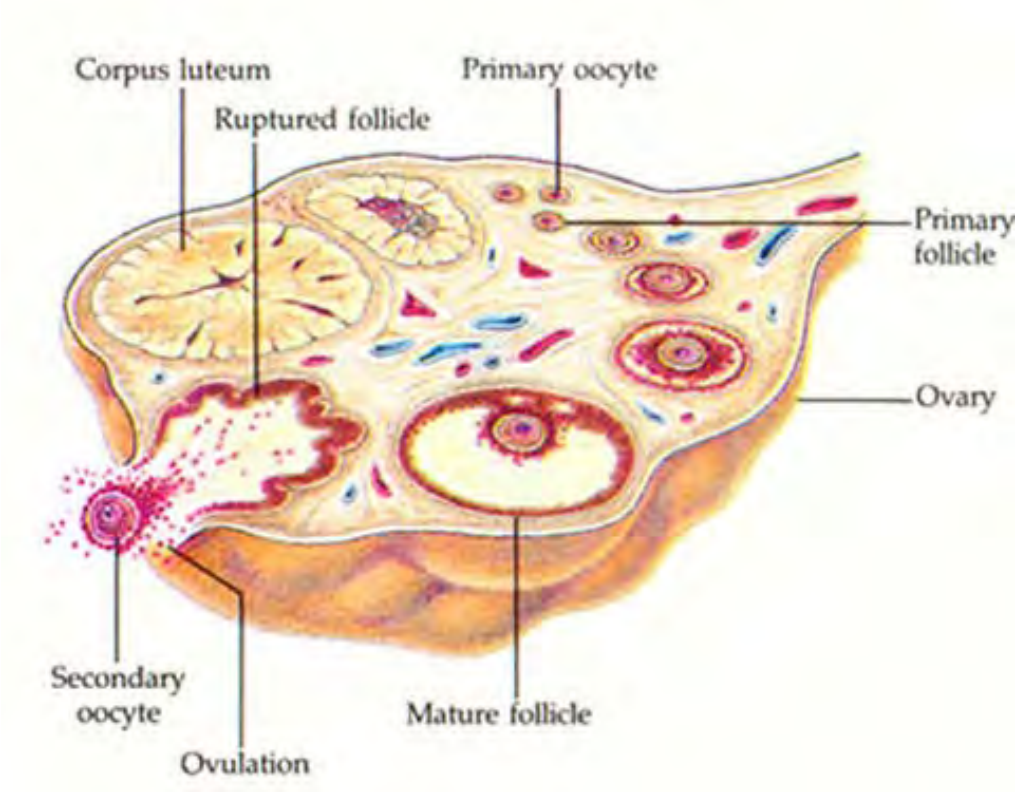
Rocío Nuñez-Calonge [a,*], Susana Cortés [a], Luis Miguel Gutierrez Gonzalez [b], Roman Kireev [b,c], Elena Vara [d], Leonor Ortega [a], Pedro Caballero [a], Lisa Rancan [b], Jesús Tresguerres [b]

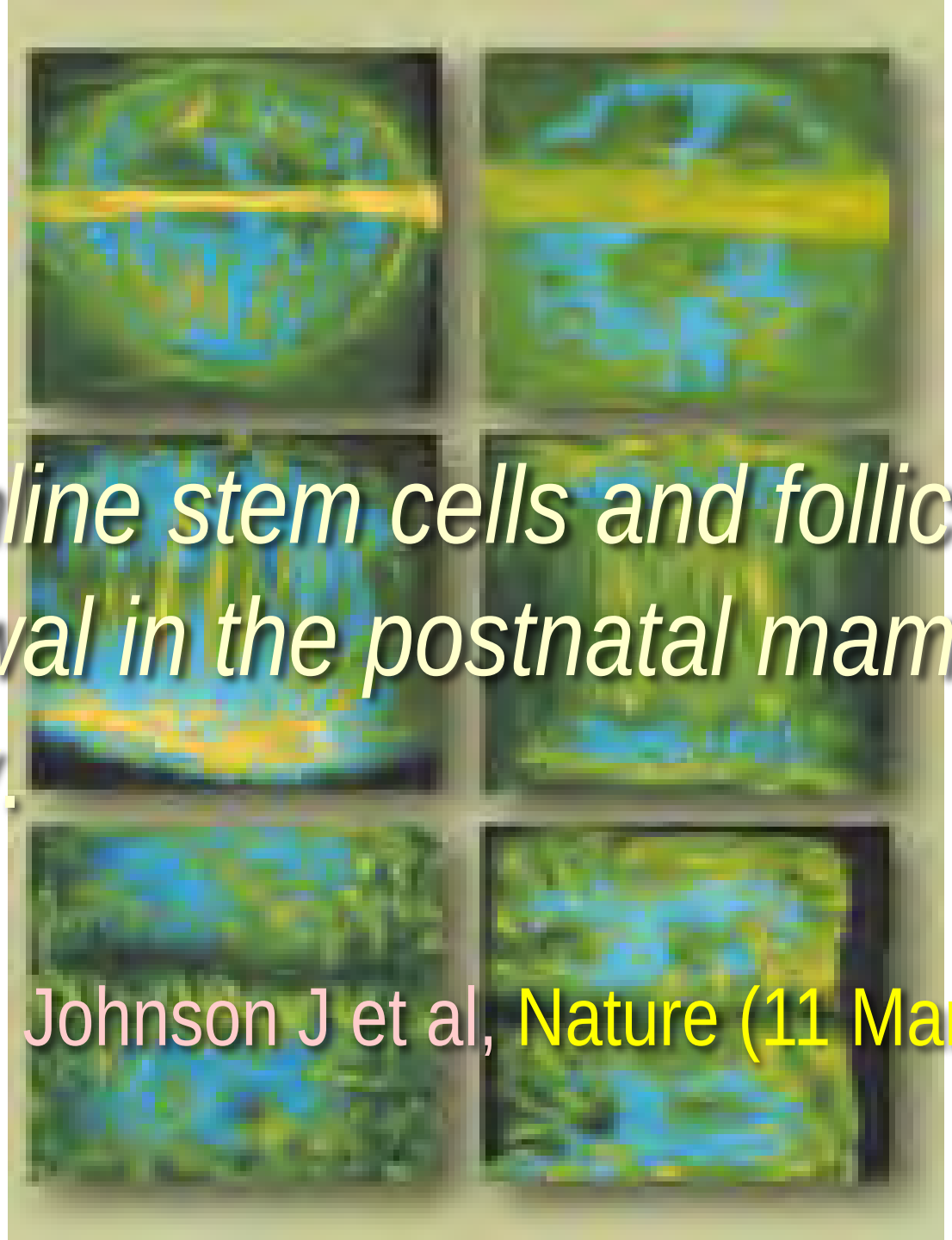
Weissmann A:

Die Continuitat des Keimplasmasah Grundlage einer The orie der Vereburg Jena: Fisher-Verlag; 1885.

Zuckerman (1951)

The number of oocytes in the mature ovary. Recent Progress in Hormone Research, 6, 63-109



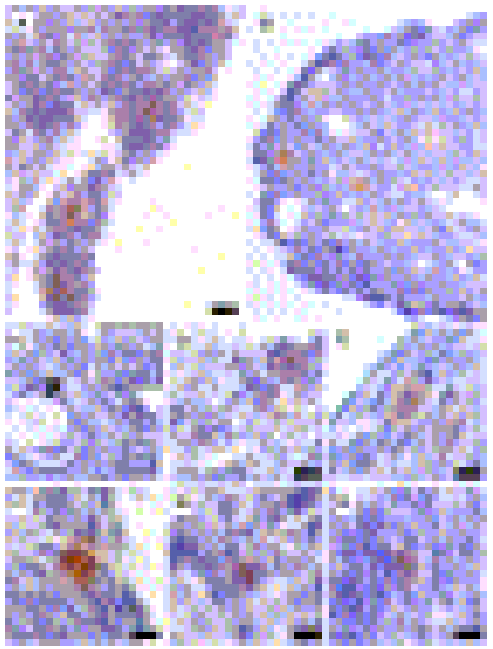


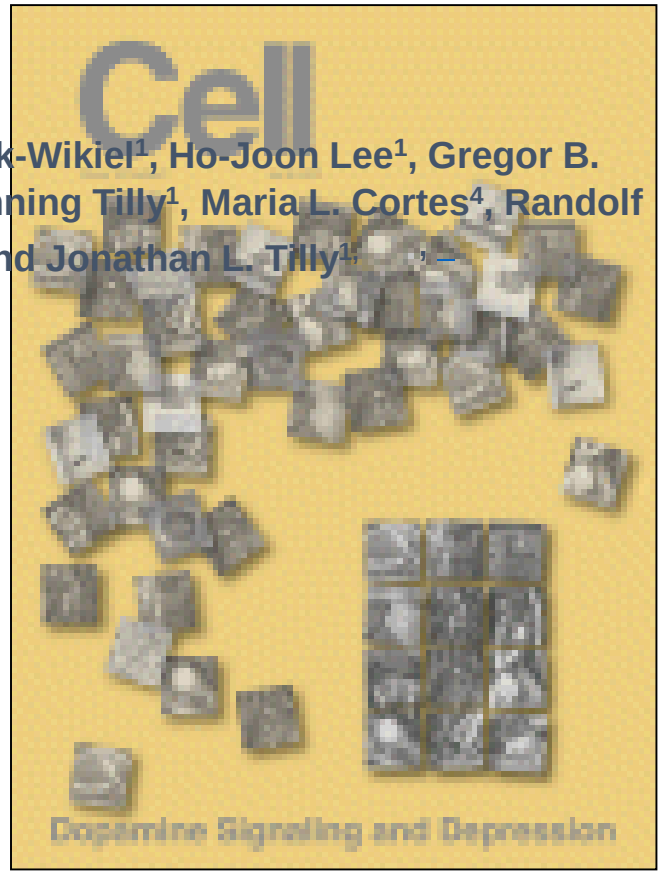
Germline stem cells and follicular renewal in the postnatal mammalian ovary.

Johnson J et al, Nature (11 Marzo 2004)

Oocyte Generation in Adult Mammalian Ovaries by Putative Germ Cells in Bone Marrow and Peripheral Blood

Joshua Johnson, Jessamyn Bagley, Malgorzata Skaznik-Wikiel[1], Ho-Joon Lee[1], Gregor B. Adams[3], Yuichi Niikura, Katherine S. Tschudy, Jacqueline Canning Tilly[1], Maria L. Cortes[4], Randolf Forkert, Thomas Spitzer, John Iacomini[2], David T. Scadden[3] and Jonathan L. Tilly[1,





cells

MDPI

Review

Implications and Current Limitations of Oogenesis from Female Germline or Oogonial Stem Cells in Adult Mammalian Ovaries

Jessica J. Martin, Dori C. Woods and Jonathan L. Tilly *

Laboratory of Aging and Infertility Research, Department of Biology, Northeastern University, Boston, MA 02115, USA; martin.je@husky.neu.edu (J.J.M.); d.woods@northeastern.edu (D.C.W.)

* Correspondence: j.tilly@northeastern.edu; Tel.: +1-617-373-2260

Received: 29 November 2018; Accepted: 16 January 2019; Published: 28 January 2019

CLIMACTERIC
2019, VOL. 22, NO. 1, 22–26
https://doi.org/10.1080/13697137.2018.1543264

REVIEW

OPEN

The existence and potential of germline stem cells in the adult mammalian ovary

E. E. Telfer[a] and R. A. Anderson[b]

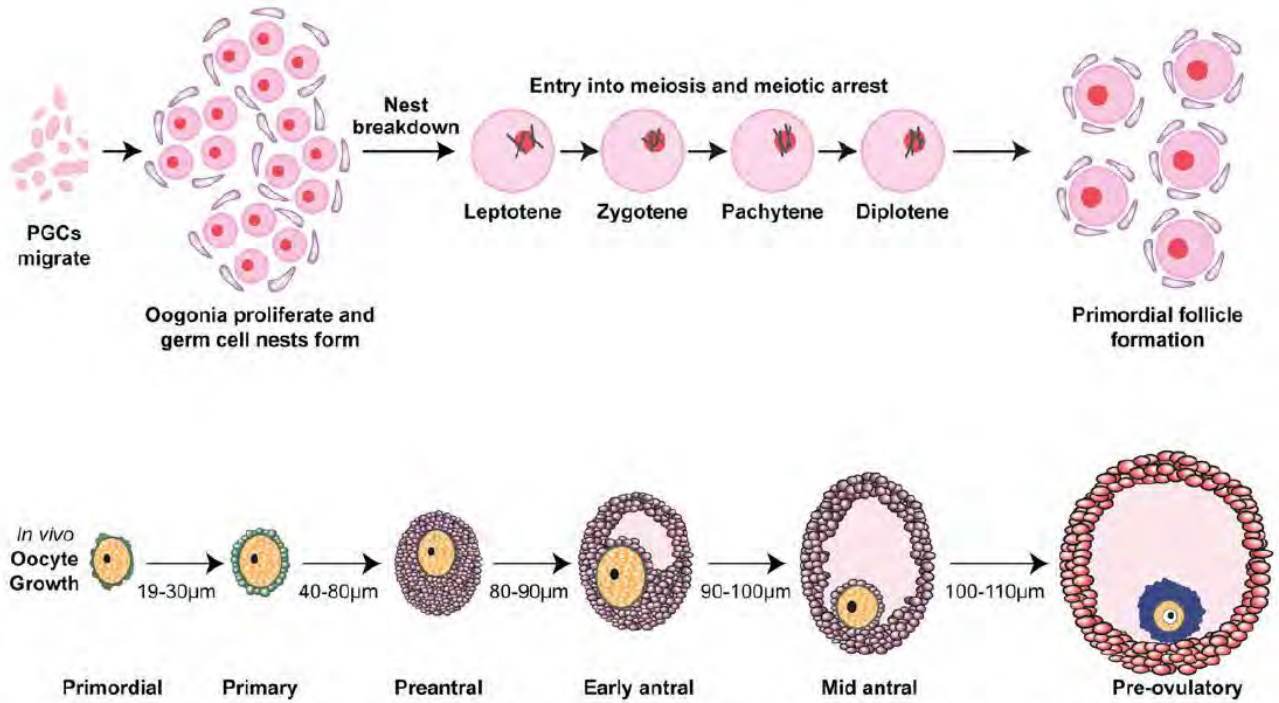
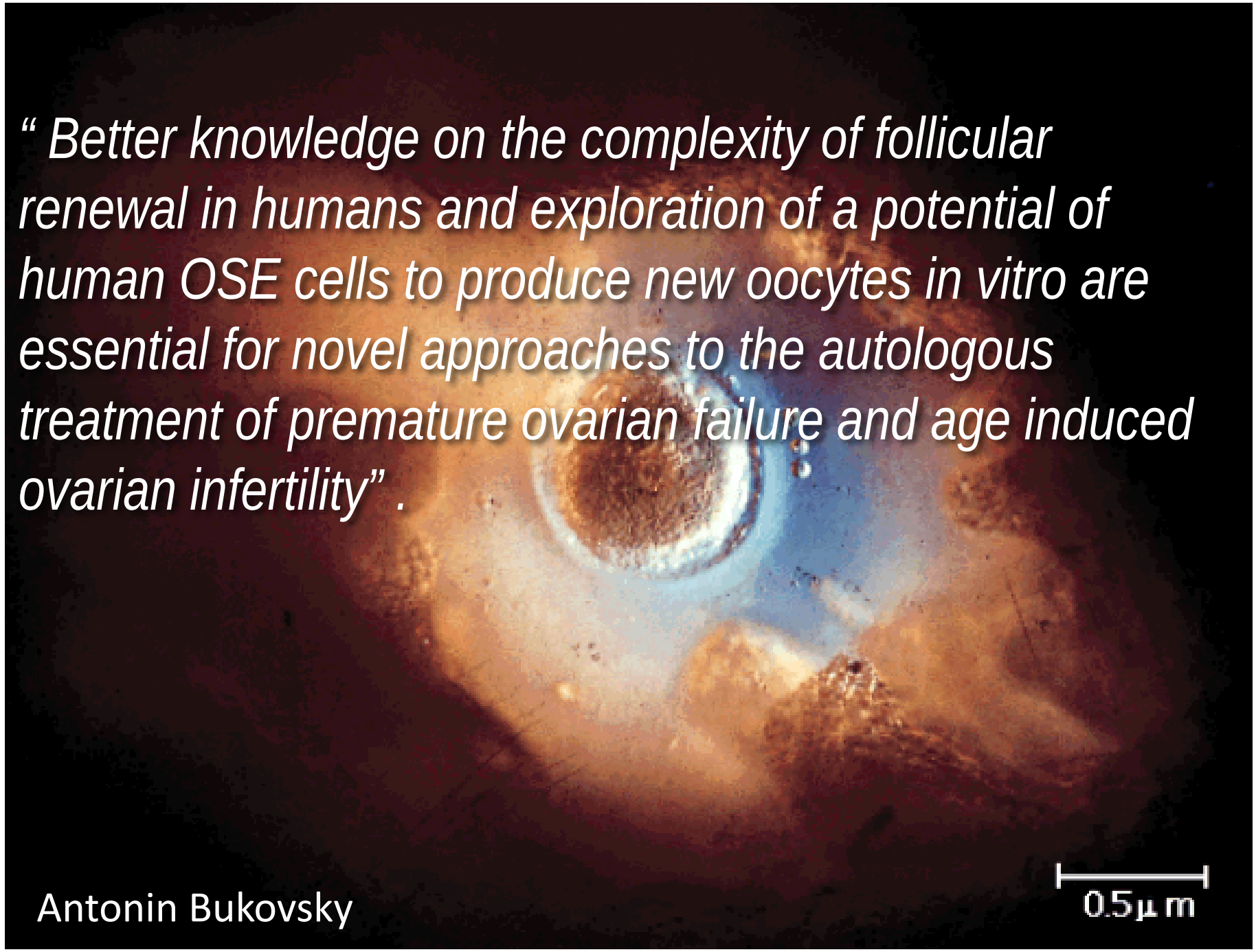


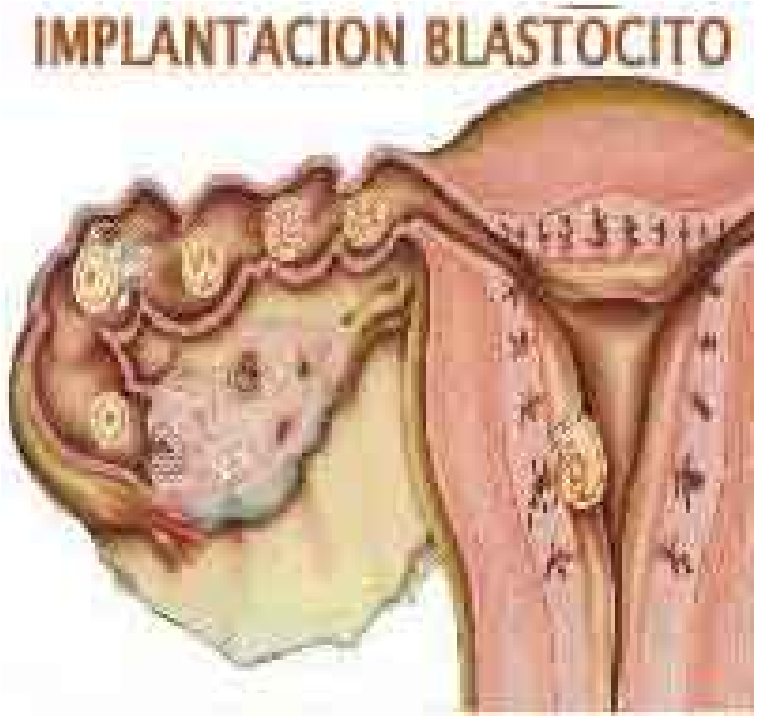
Figure 1. Schematic of the key stages of oocyte maturation. Upper panel: proliferative primordial germ cells (PGCs) form nests and then enter meiosis during fetal life. Nest breakdown results in the formation of primordial follicles. Lower panel: after growth activation, follicles progress through the stated phases, with the oocyte ultimately reentering meiosis and being released from the follicle. Sizes given are of the oocyte, not the follicle, showing how it also grows dramatically during this process. Reproduced from Anderson and Telfer[1] with permission.

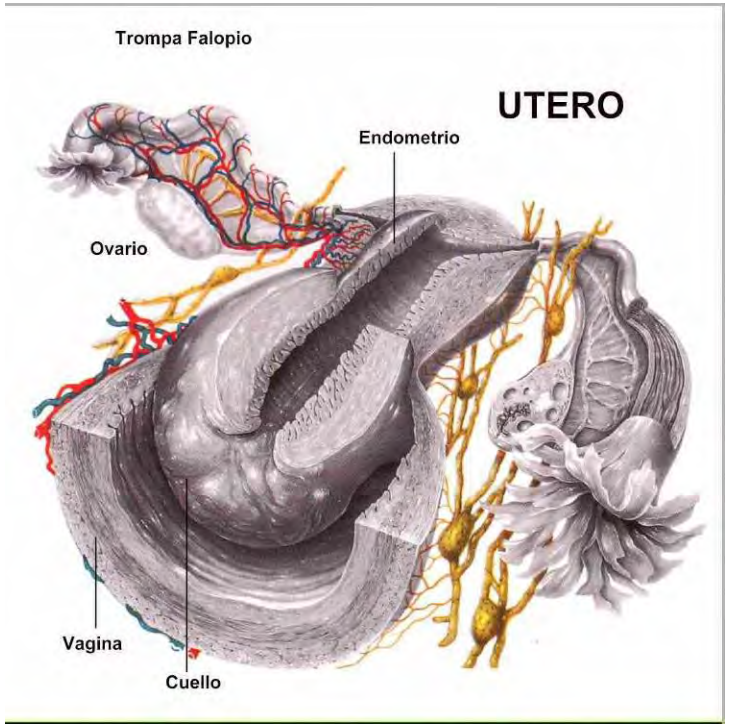

“ Better knowledge on the complexity of follicular renewal in humans and exploration of a potential of human OSE cells to produce new oocytes in vitro are essential for novel approaches to the autologous treatment of premature ovarian failure and age induced ovarian infertility” .
Antonin Bukovsky
0.5µm

Implantación embrionaria

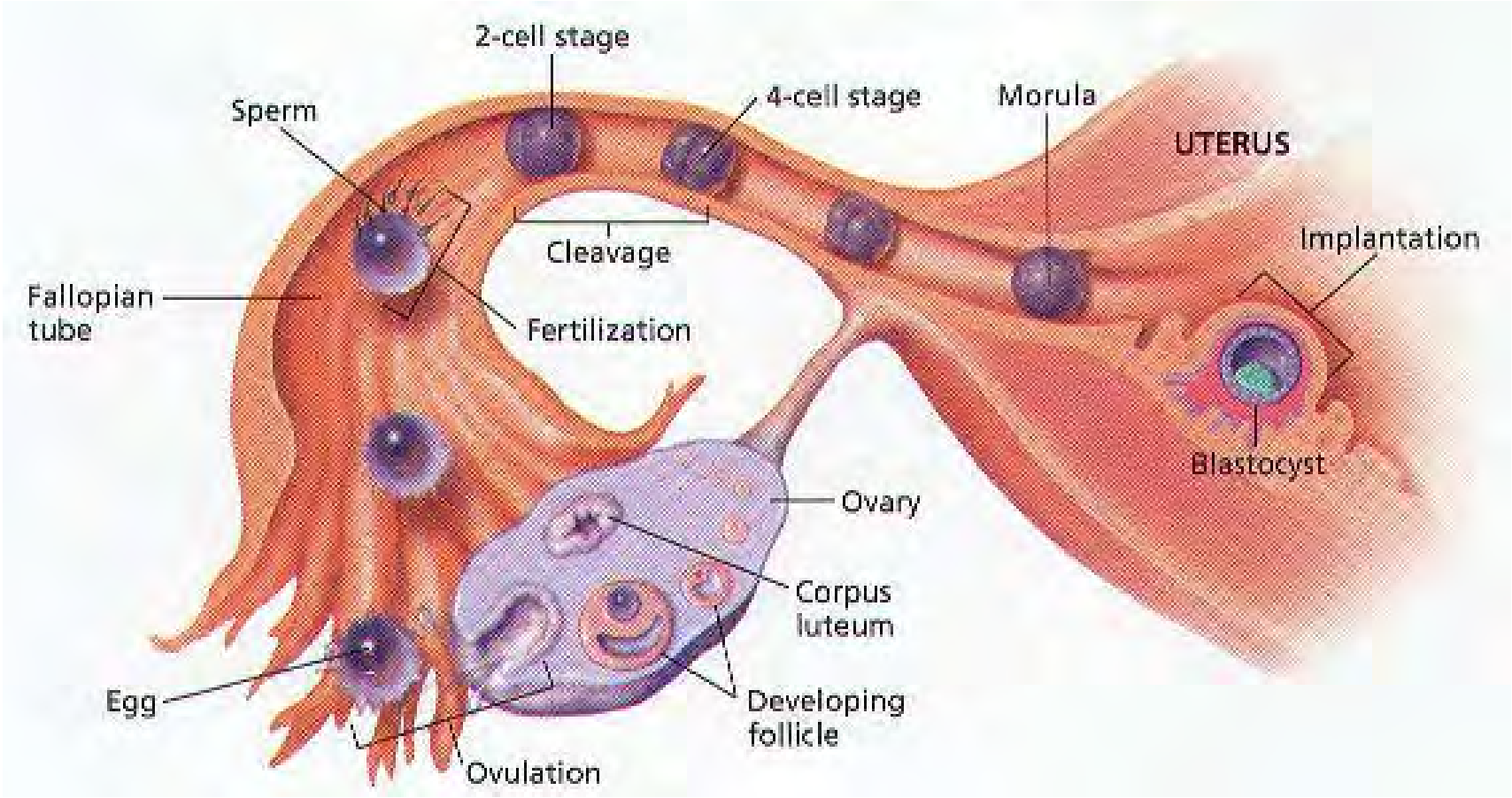

Implantación embrionaria es la fijación del embrión en estado de blastocisto al útero materno en fase receptiva

Se produce en el tercio medio y superior de la pared posterior del útero, 6-10 días post-ovulación (ventana de implantación)





Sincronización espacio temporal en la implantación



Fases de la implantación

- Preimplantatoria: -receptividad endometrial
  -crecimiento embrionario

- Implantatorio: -Aposición
  -Adhesión
  -Rotura membrana
  -Invasión

Hormonas esteroideas

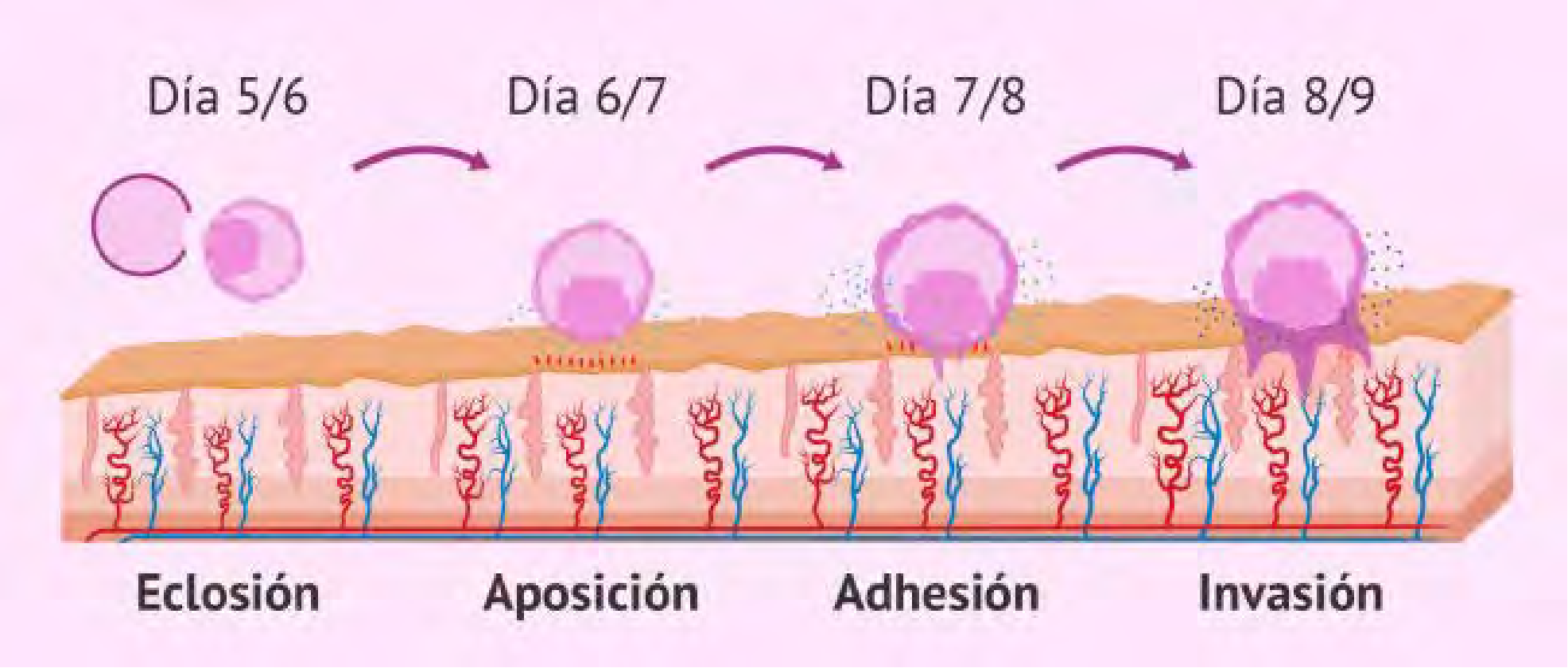
-Citoquinas ,Quimoquinas,Factores de crecimiento

-Moléculas de adhesión,Proteinasas

a) Comunicación epitelio-estroma

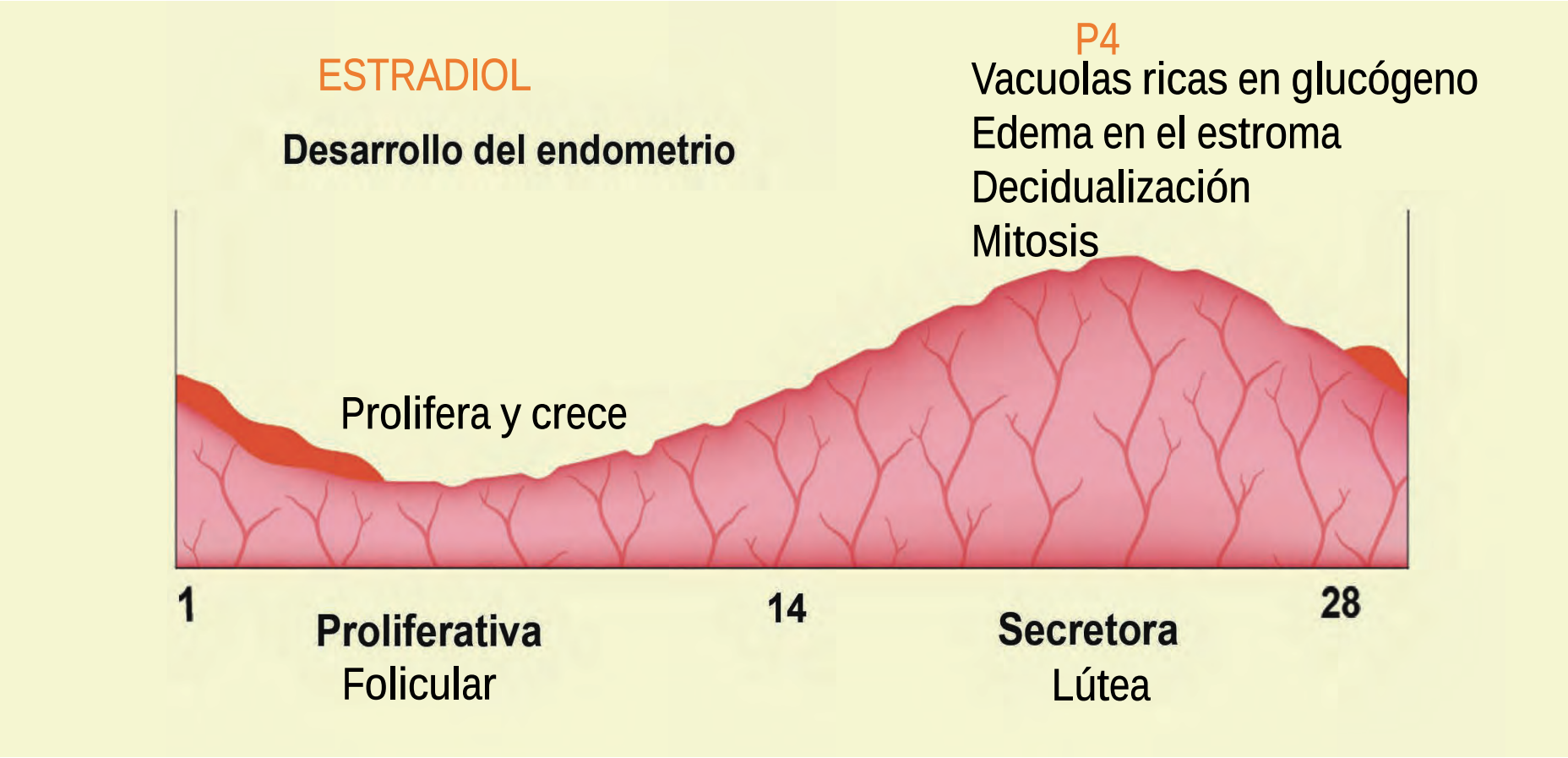
b) Interacción embrión-EE

c) Comunicación embrión-estroma

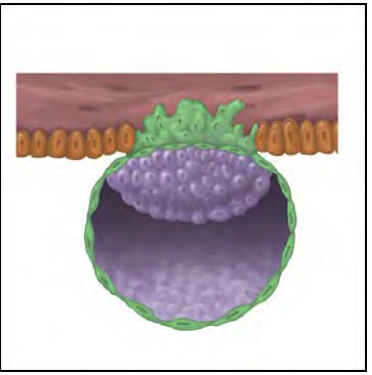


1. Fase preimplantatoria

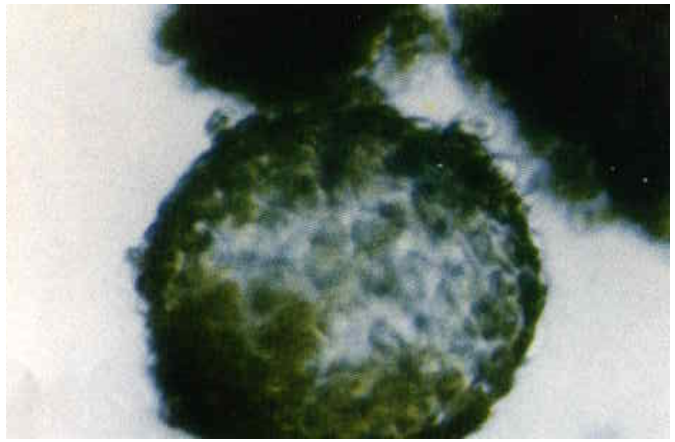
Adquisición de la receptividad endometrial



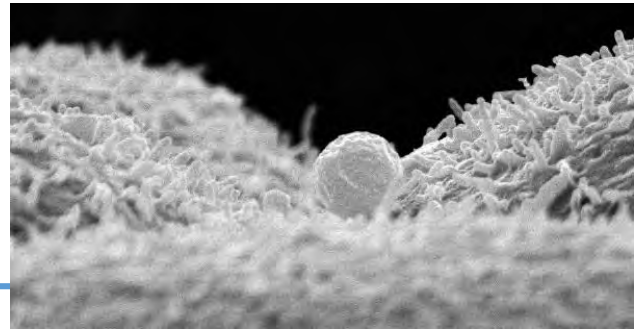
Epitelio endometrial



- Monocapa de células cuboidales polarizadas que tapizan el útero:
  Protección; Barrera; Permitir la implantación
- Controla el impacto del embrión sobre el estroma y los vasos endometriales
- Mediador del diálogo endometrio-embrión
- Primer contacto en el epitelio superficial
- Especialización apical de las céulas: microvellosidades (filamentos actina)
  - *Gap junctions: uniones intercelulares comunicantes*
  - *Tight junctions: adherencia íntima célula-célula*

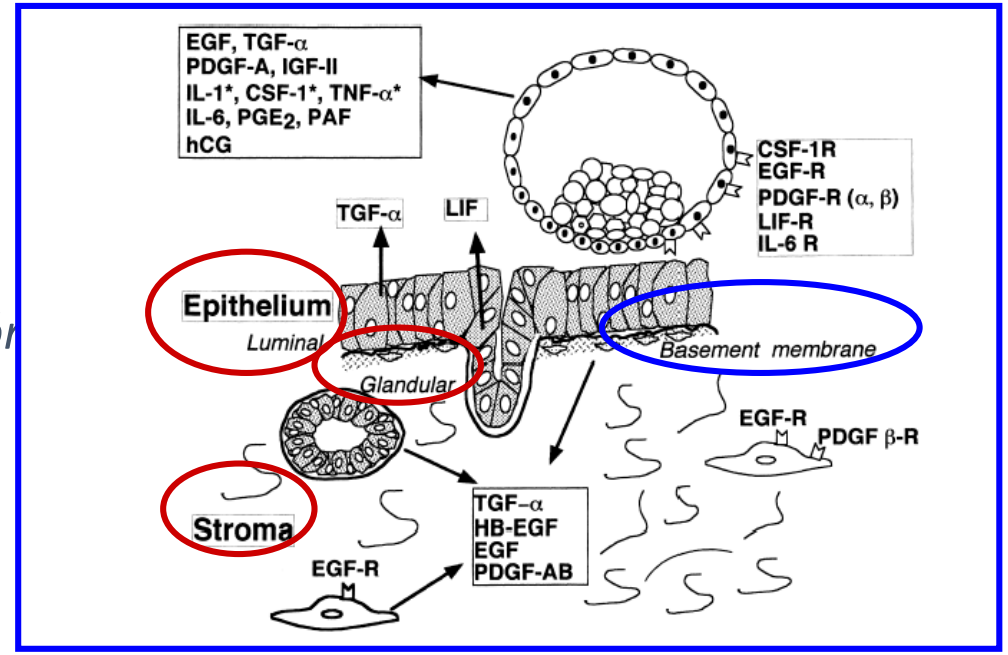


Epitelio endometrial



Modificaciones para hacer que el endometrio sea receptivo:

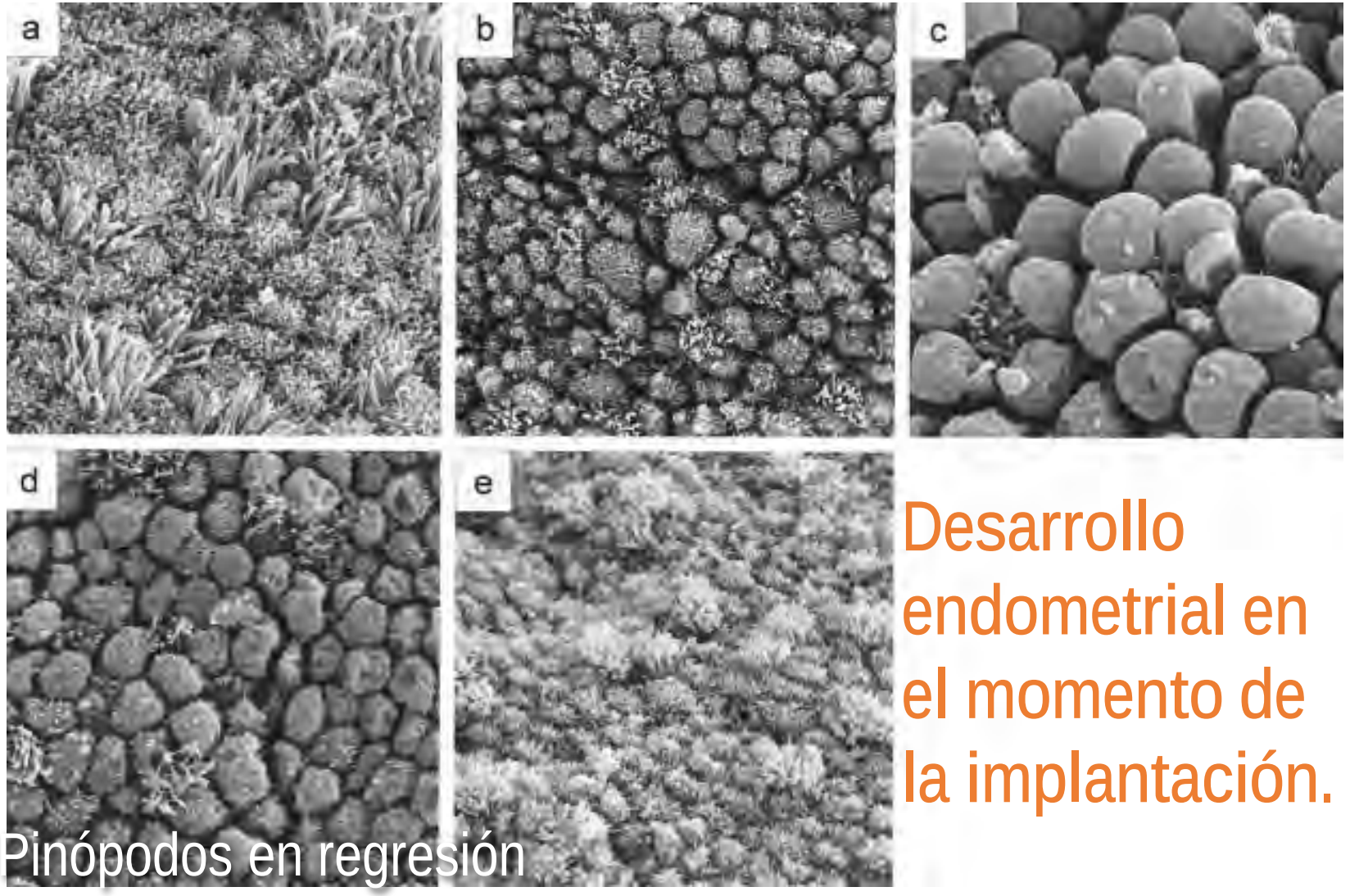
- Epitelio luminal: *contacto inicial*
- Epitelio glandular: *PP14*
- Células del estroma: *decidualización* *(síntesis y secreción* PRL)
- Compartimiento vascular *(aumento permeabilidad capilar)*



Antes del desarrollo de los pinópodos

Acortamiento de las microvellosidades

Pinópodos cubriendo la superficie



Pinópodos en regresión

Desarrollo endometrial en el momento de la implantación.

Stavreus-Evers,et al, Fertil Steril 76(4), 2001..

Molecular and Cellular Endocrinology
Available online 15 November 2019, 110644
In Press, Journal Pre-proof

Pinopodes: Recent advancements, current perspectives, and future directions

Kelsey E. Quinn, Brooke C. Matson, Margeaux Wetendorf, Kathleen M. Caron

Show more

https://doi.org/10.1016/j.mce.2019.110644

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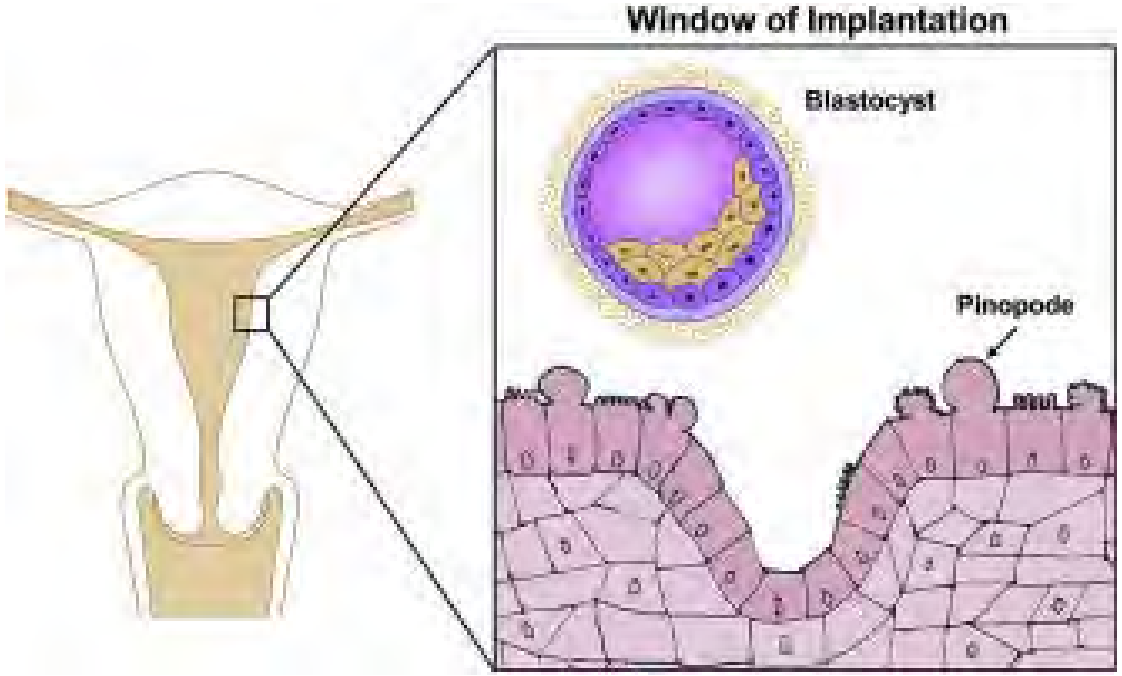
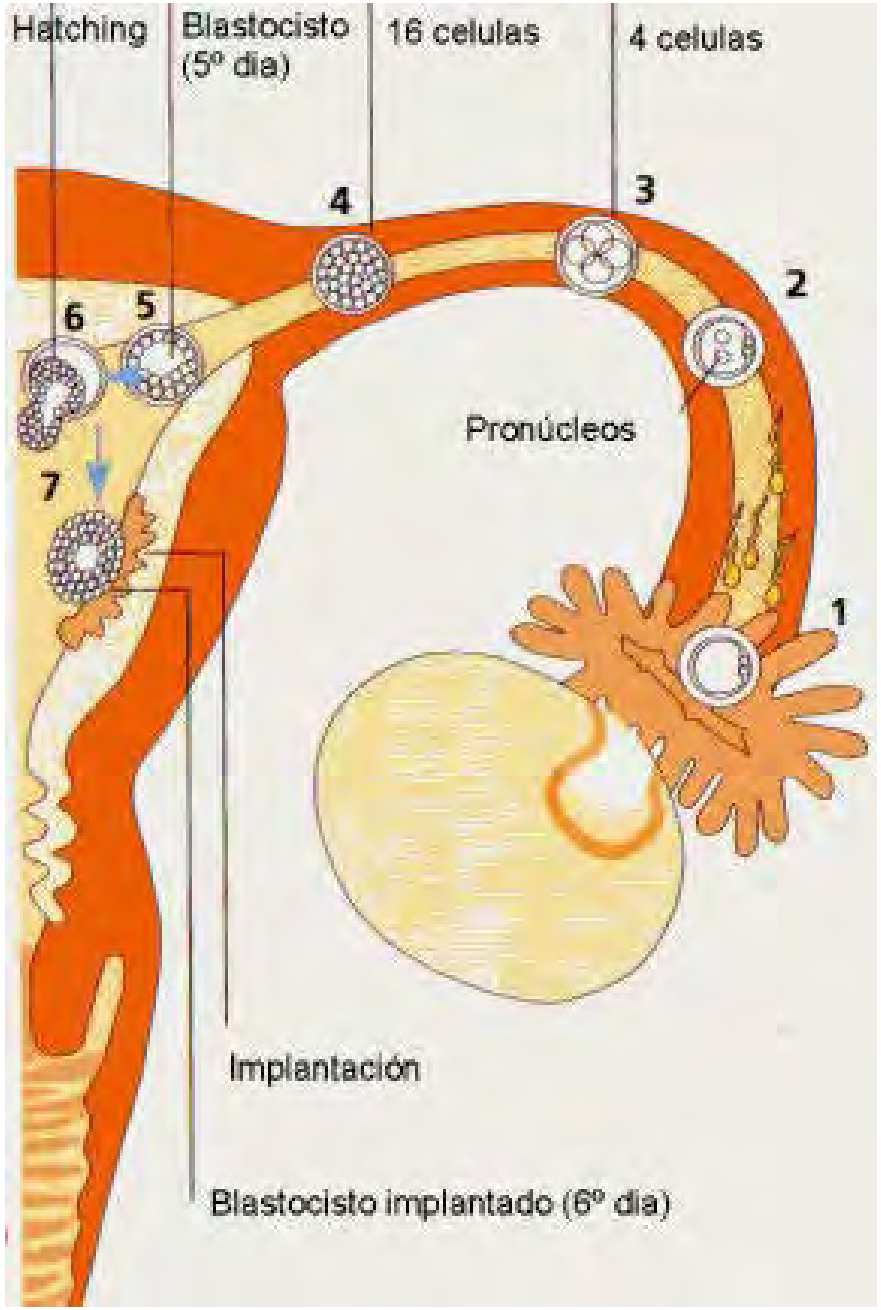
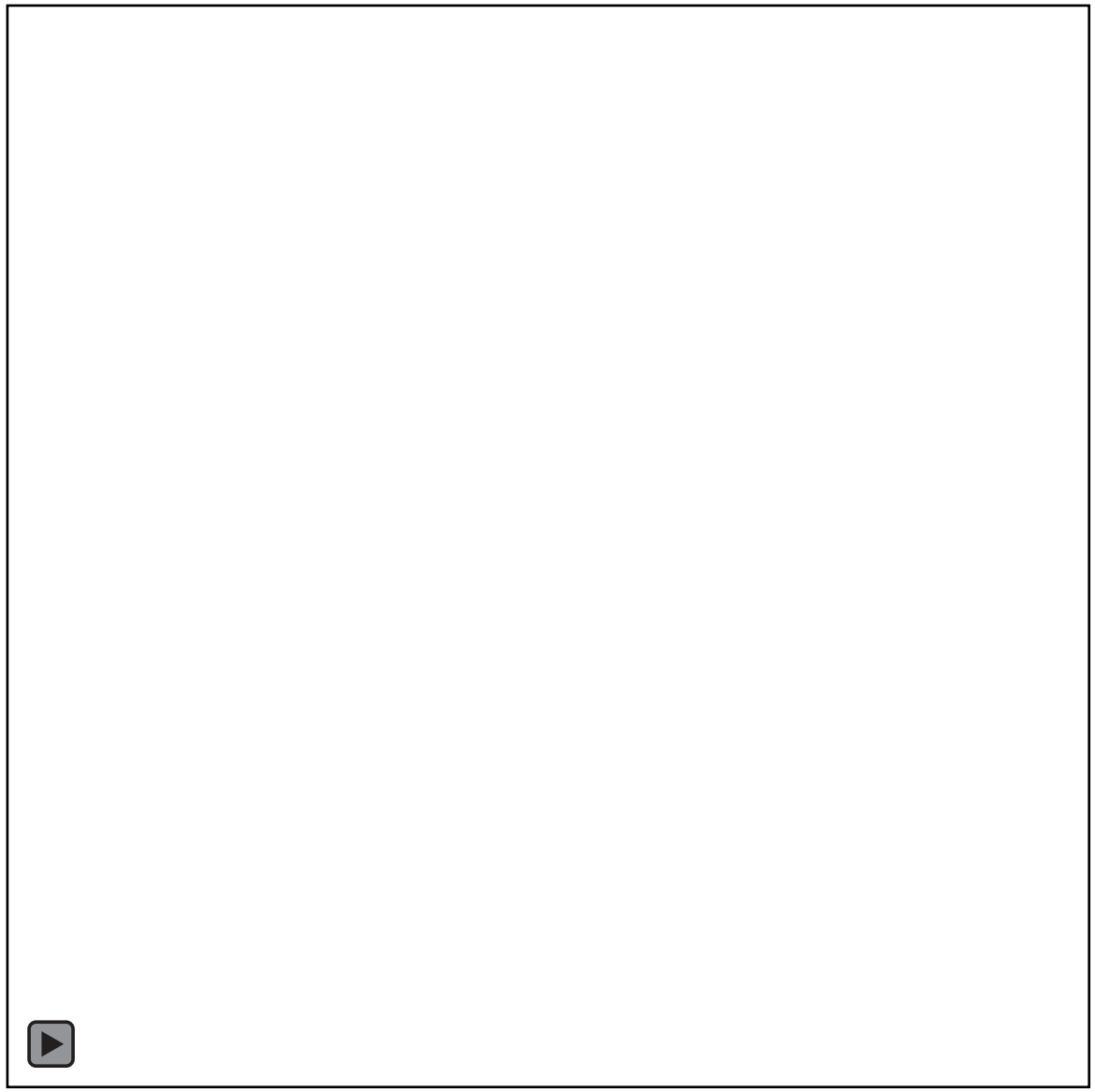
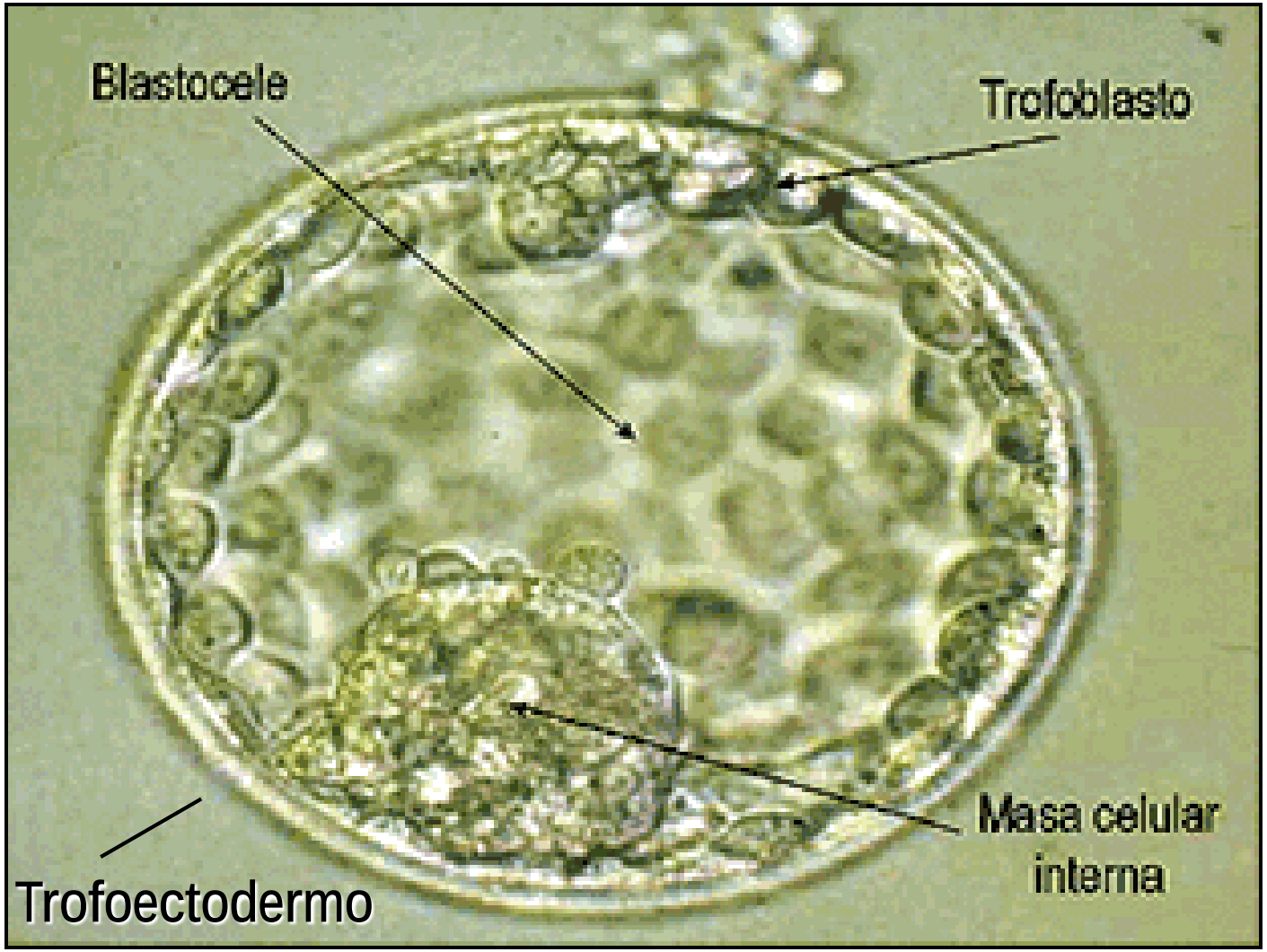




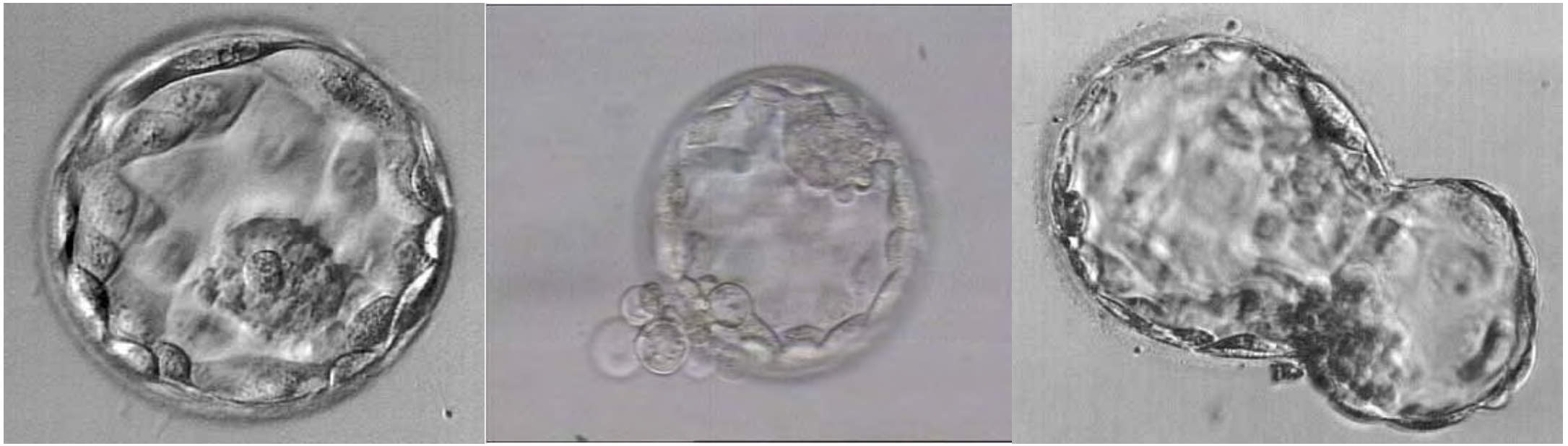
Desarrollo embrionario



Blastocisto



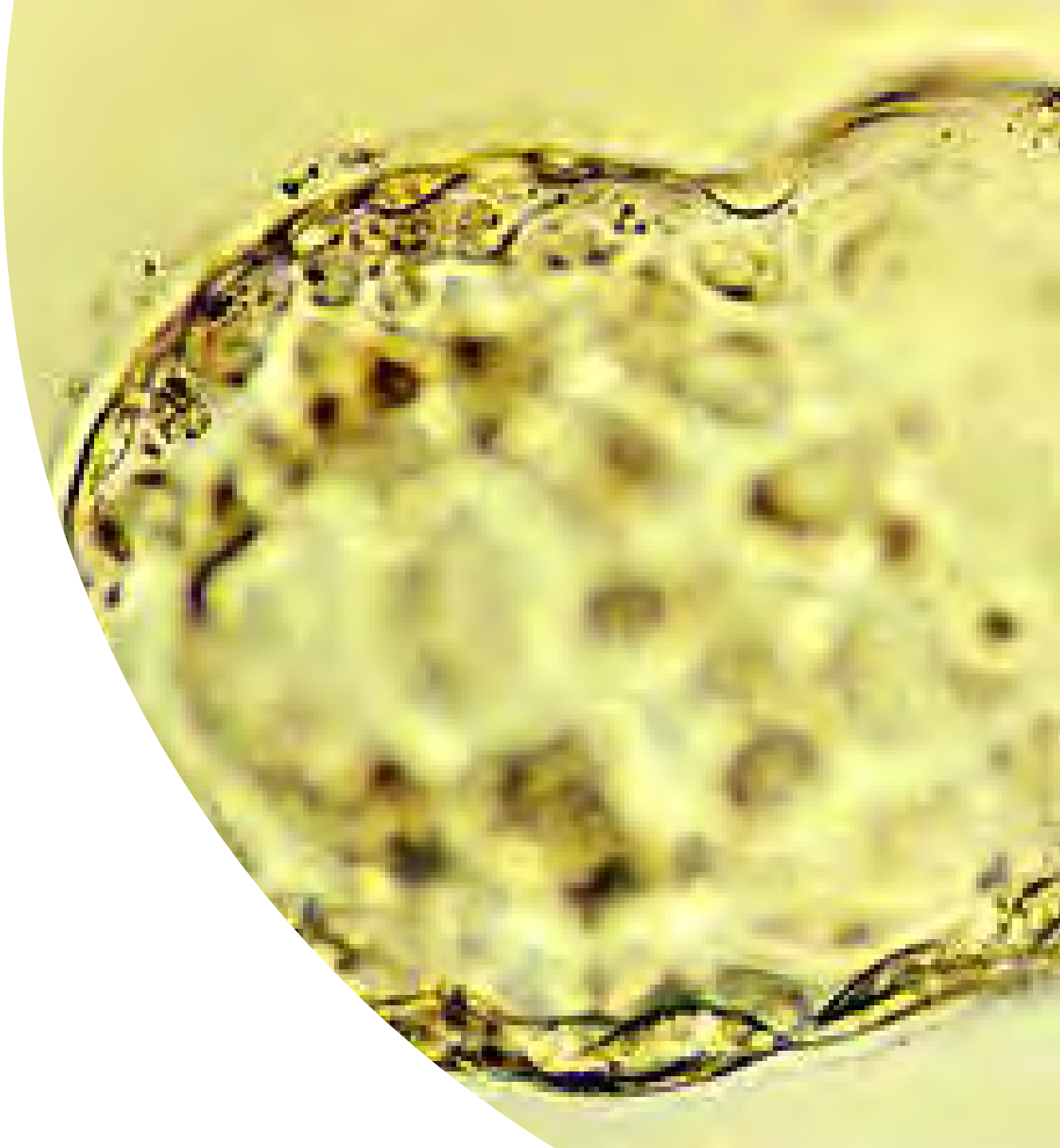
Blastocisto en “hatching”



a) *Mecánico*: el BT hace presión sobre la ZP, debilitándola
b) *Químico*: secreción de proteasas

Consideraciones bioquímicas

Señales procedentes del embrión preimplantatorio pueden inducir la producción de citoquinas o quimoquinas por el endometrio, que a su vez, activarían la expresión de las moléculas de adhesión (integrinas)

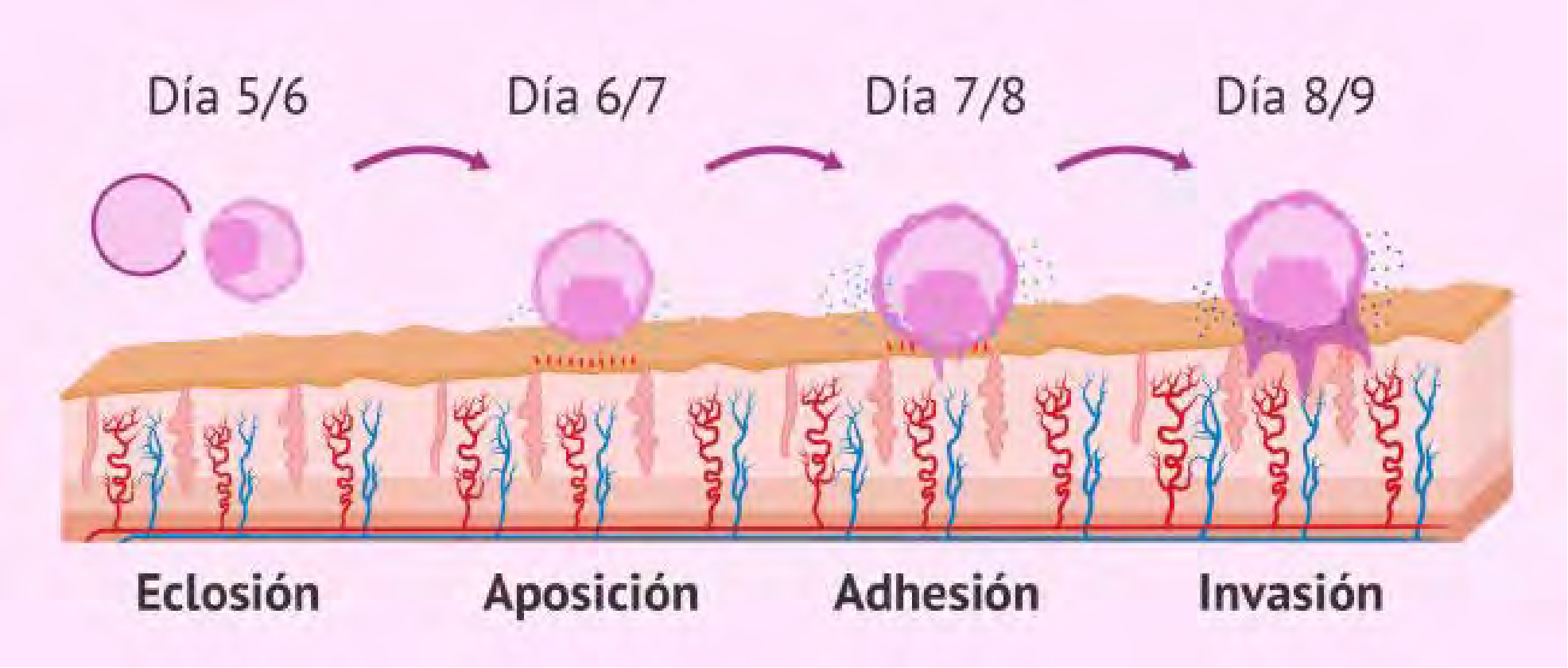


2. Fase implantatoria

a) Comunicación epitelio-estroma

b) Interacción embrión-EE

c) Comunicación embrión-estroma



a) Comunicación EE - estroma

Durante la adquisición de la receptividad y la decidualización.

Estrógenos → Epitelio endometrial

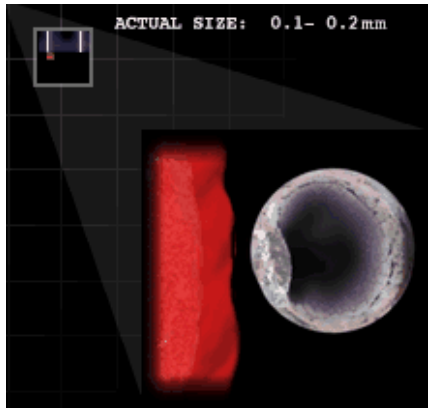
Efecto proliferativo

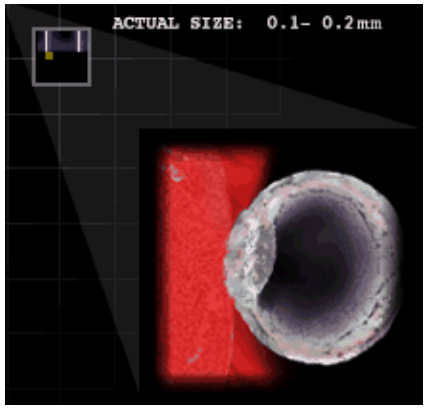
Ciclooxigenasa	*Calcitonina*
EGF	*Lactoferrina*
LIF	*IL-1*

Células del estroma

Proliferación
Secreción
Decidualización

b) Interacciones entre el embrión y el EE



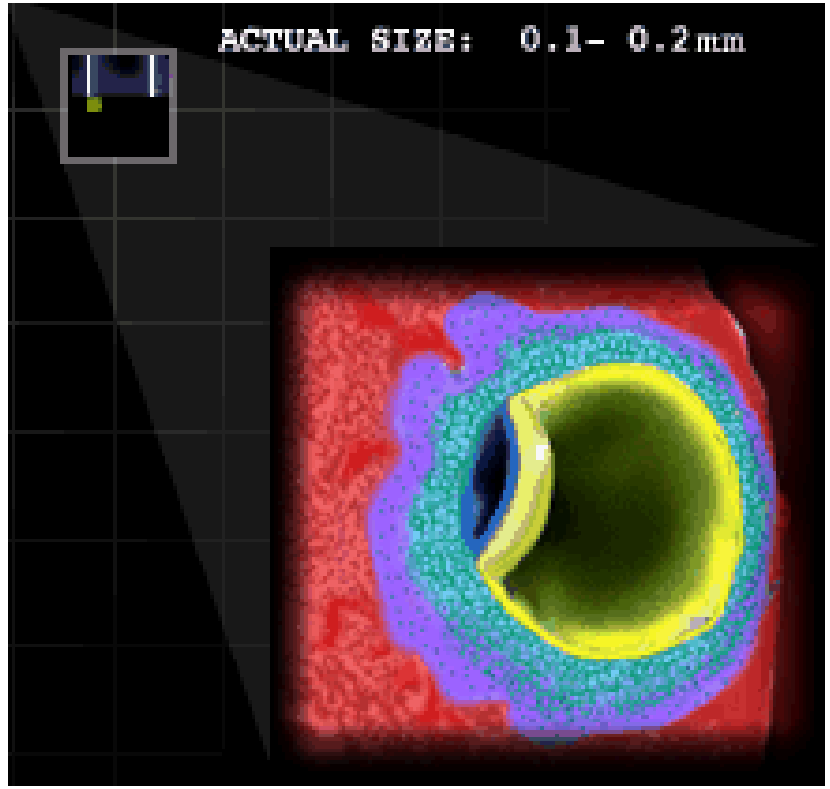


- Fase de aposición: el BT se posiciona en el fundus uterino. Esta fase va a determinar la localización de la placenta.
- Fase de adhesión: es el contacto directo entre el epitelio luminal y el trofoectodermo del BT
- Rotura de la barrera epitelial: se produce por apoptosis de las cél. epiteliales Inducida por el trofoblasto del embrión

c) Interacciones entre el embrión y el estroma

Fase de Invasión

Penetración del trofoblasto en el endometrio materno.
Las células trofoblásticas desplazan, disocian y sustituyen a las células epiteliales continuando la invasión a la membrana basal y al estroma.



Received: 12 April 2019 | Revised: 12 May 2019 | Accepted: 13 May 2019
DOI: 10.1002/rmb2.12280

MINI REVIEW

WILEY Reproductive Medicine and Biology

Uterine receptivity, embryo attachment, and embryo invasion: Multistep processes in embryo implantation

Yamato Fukui | Yasushi Hirota | Mitsunori Matsuo | Mona Gebril | Shun Akaeda | Takehiro Hiraoka | Yutaka Osuga

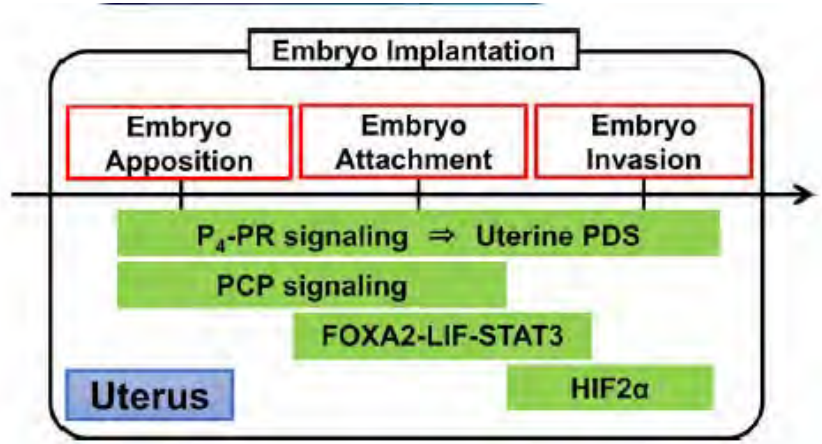
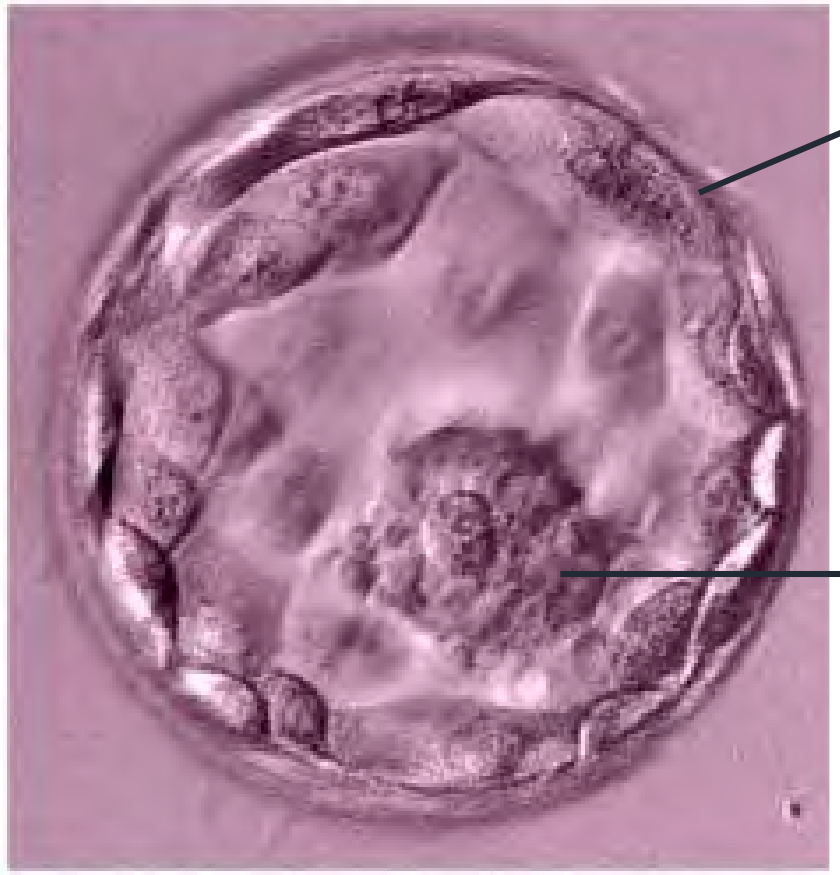


FIGURE 2 Key signals and pathways in the multistep processes of embryo implantation. Progesterone, P_4; progesterone receptor, PR; proliferation-differentiation switching, PDS; planar cell polarity, PCP; forkhead box protein A2, FOXA2; leukemia inhibitory factor, LIF; signal transducer and activator of transcription 3, STAT3; hypoxia-inducible factor 2α, HIF2α

Reconocimiento materno del blastocisto

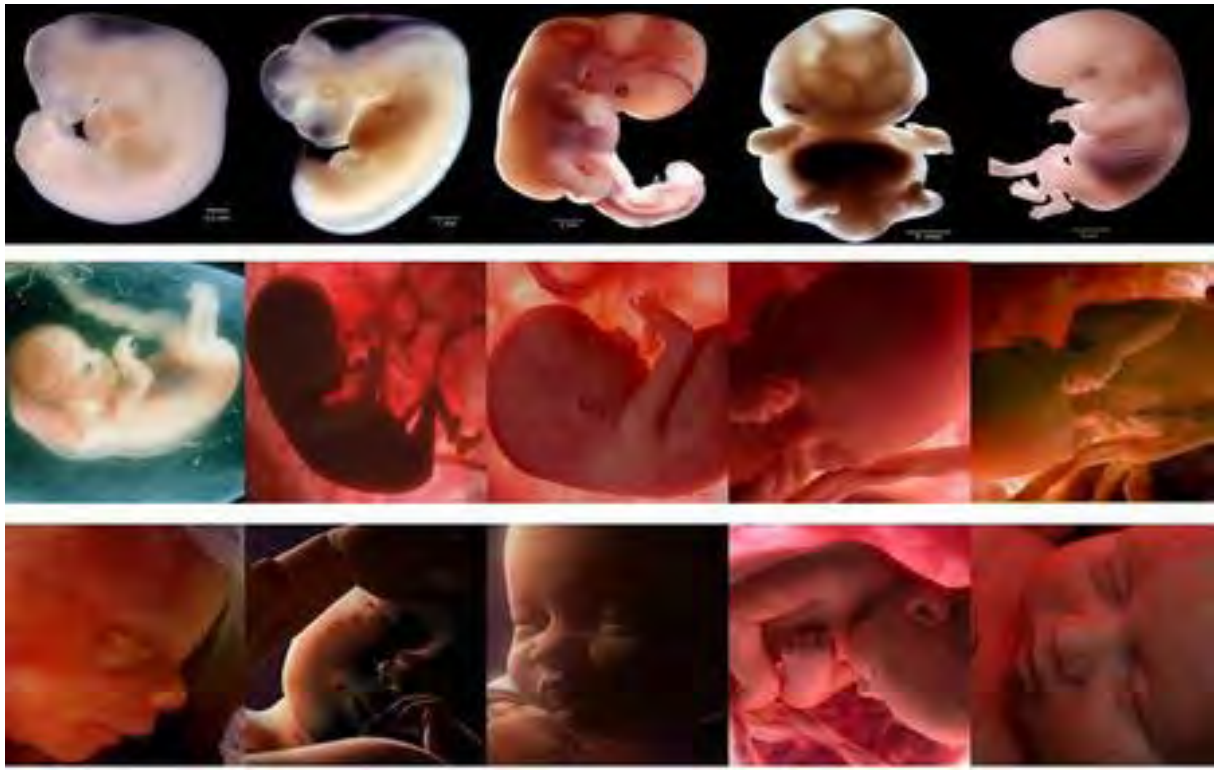
- El blastocisto estimula la producción de P4 y E2 hasta que la placenta toma el relevo (semana 10-15)
- El factor luteotrófico más importante es la hCG, sintetizada por el sincitiotrofoblasto y detectable entre los días 8 y 10 tras el pico de LH.
- Niveles máximos en la semana 10 y después se reduce.
- Se establece una placentación hemocorial: ni las células endoteliales ni la membrana basal interfiere entre el trofoblasto y la sangre materna.
- Las arterias espirales uterinas están constreñidas, y el embrión implanta en un ambiente hipotóxico. En la semana 10 de gestación las arterias se abren a la placenta con sangre materna que contiene nutrientes y oxígeno.



Placenta
Corion

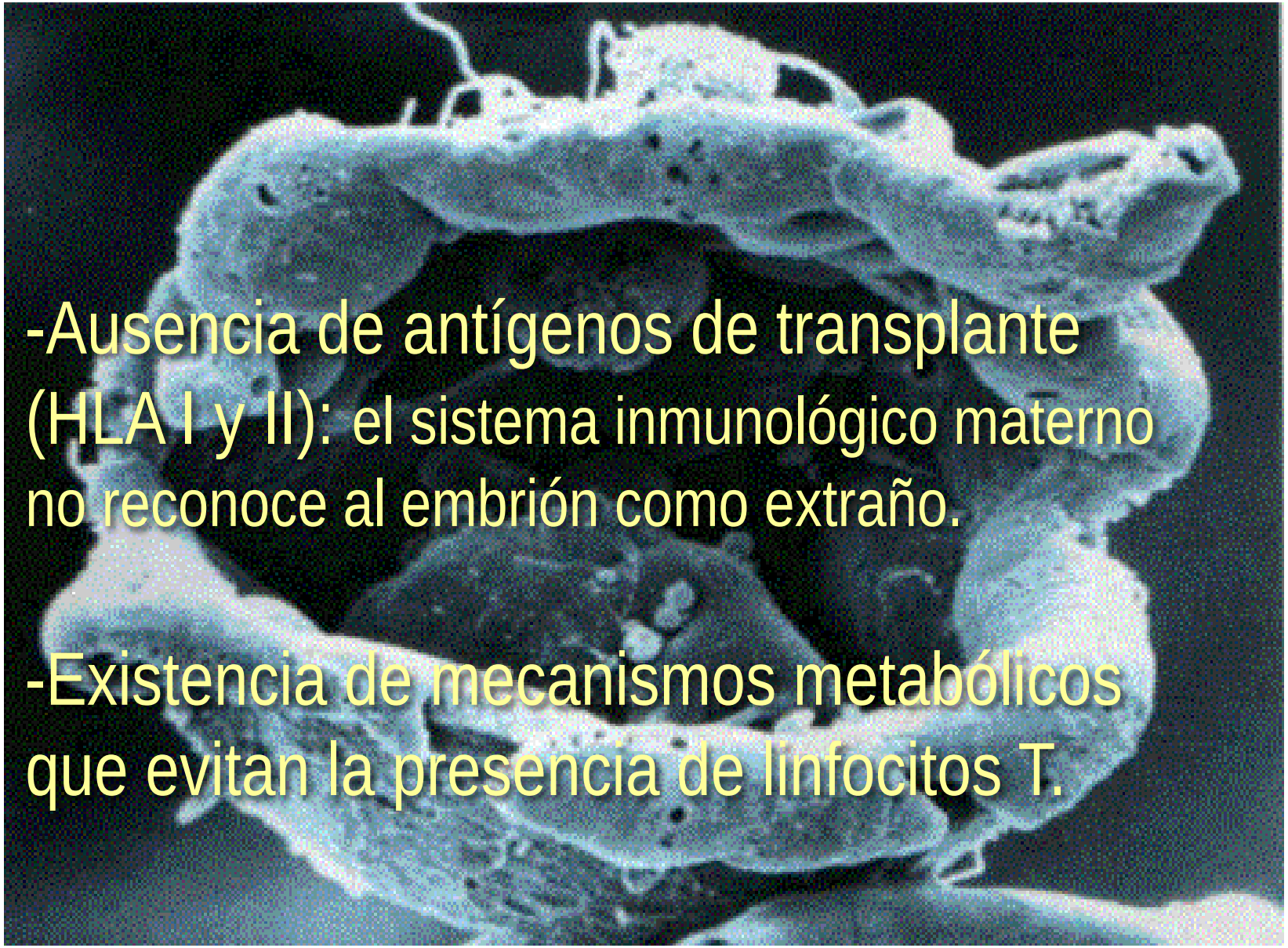
Feto
Amnios
Cels.mesenquimáticas

Aspectos inmunológicos de la implantación



- Madre y embrión poseen distinta dotación genética e inmunológica.
- Durante el embarazo, la gestante puede desarrollar una respuesta inmunológica ante antígenos extraños, incluyendo los fetales.

La clave está en el trofoblasto:



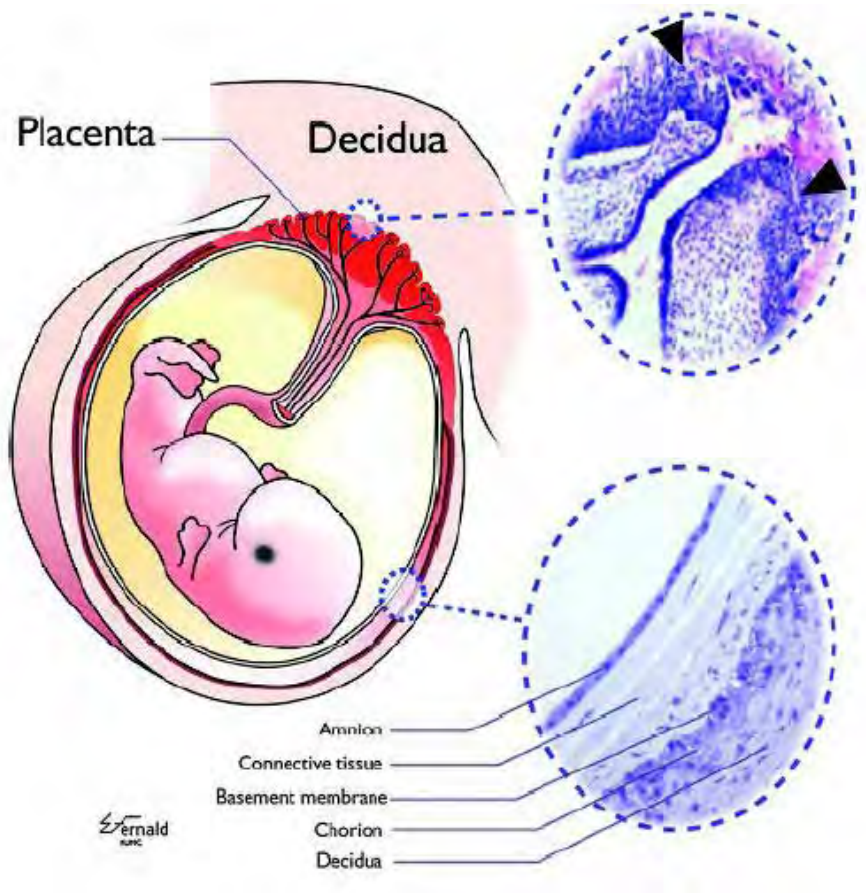
-Ausencia de antígenos de transplante (HLA I y II): el sistema inmunológico materno no reconoce al embrión como extraño.

-Existencia de mecanismos metabólicos que evitan la presencia de linfocitos T.

Stranger in a strange land

Joan S. Hunt
Department of Anatomy and Cell Biology, University of Kansas Medical Center, Kansas City, KS, USA.

Immunol Rev. Author manuscript; available in PMC 2006 November 16.



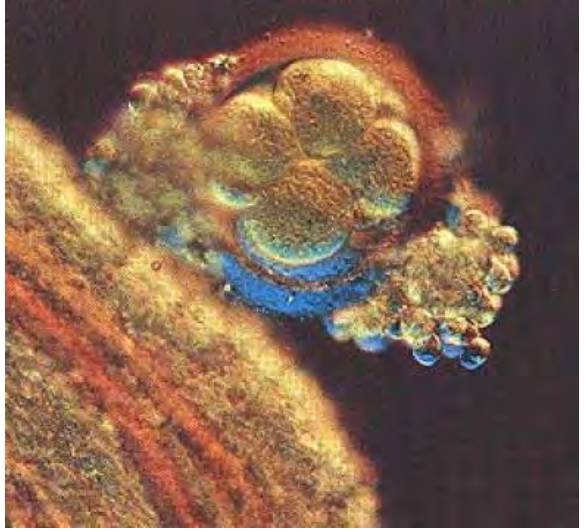
Aspectos clínicos de la implantación

En condiciones normales, solo el 33% de los ciclos fértiles acaba en gestación

30% embriones NUNCA implanta

30% embriones: implantación anómala

Alteraciones de la implantación



- *Fallo de implantación*: no gestación tras > 3 ciclos.
  Posible alteración genética.

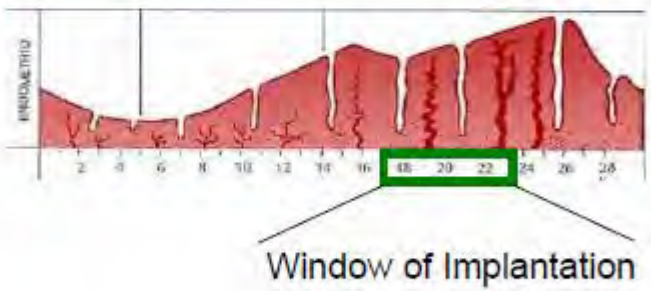
- *Pérdida gestacional precoz*: 31-36% ciclos naturales.
  40% en TRA

- *Preeclampsia*: alteración fase invasión (integrinas)

- *Acretismo/Percretismo placentario: invasión anómala de la placenta con inserción en el miometrio. Interacción defectuosa entre el trofoblasto y en endometrio.*

Key Factors Determining Clinical Outcomes

Identification/Modification of receptive endometrium



✓ 15% of cycles end in implantation failure of endometrial origin

Embryo Viability Identification

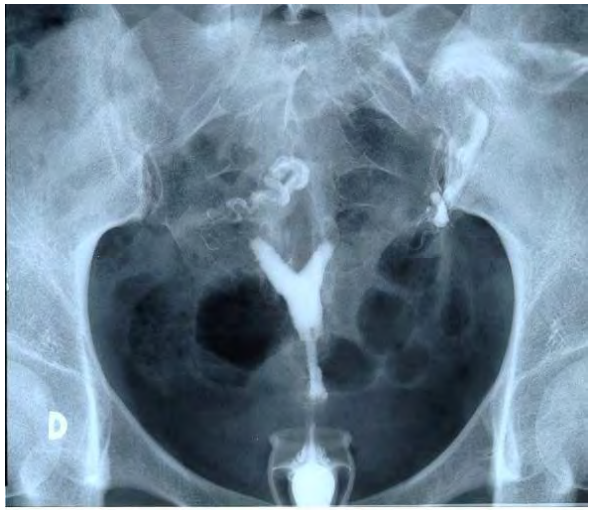
✓ 60%-90% of transferred embryos do not implant or die

Mejora de la implantación desde el punto de vista clínico

1. Diagnóstico previo correcto
2. Progesterona
3. Inducción de la ovulación
4. Mejora de la receptividad endometrial
5. Transferencia
6. Factores inmunológicos

Implantation failure: molecular mechanisms and clinical treatment

Hakan Cakmak and Hugh S. Taylor*



Human Reproduction Update, Vol.00, No.0 pp. 1–13, 2010

Table I Proposed mechanisms of implantation failure in gynecological diseases.

Gynecological disease	Proposed mechanism of implantation failure
Endometriosis	Reduced $\alpha_v\beta_3$ integrin and LIF expressions in the window of implantation Lack of IL-11 and IL-11Rα expressions in secretory phase Absence of HOXA10 and HOXA11 peak in secretory phase Elevated EMX2 expression Progesterone resistance Alteration in PR-A to PR-B ratio Decreased HOXA10 expression due to hypermethylation of its promoter region
Hydrosalpinx	Mechanical interference to apposition by bathing of endometrial lining with hydrosalpinx fluid intermittently Reduced $\alpha_v\beta_3$ integrin and LIF expressions Decreased HOXA10 expression
Leiomyoma	Distorting endometrial lining Obstructing the tubal ostia or cervical canal Decreased HOXA10 and BTEB1 expressions
Endometrial polyp	Mechanical interference with sperm transport and embryo implantation Low IGFBP-1 and osteopontin levels in secretory phase Low progesterone receptor levels in secretory phase
PCOS	Decreased $\alpha_v\beta_3$ integrin, HOXA-10 and IGFBP-1 during secretory phase Overexpression of androgen receptors Failure to downregulate estrogen receptor-α in the window of implantation Overexpression of the steroid receptor coactivators AIB1 and TIF2

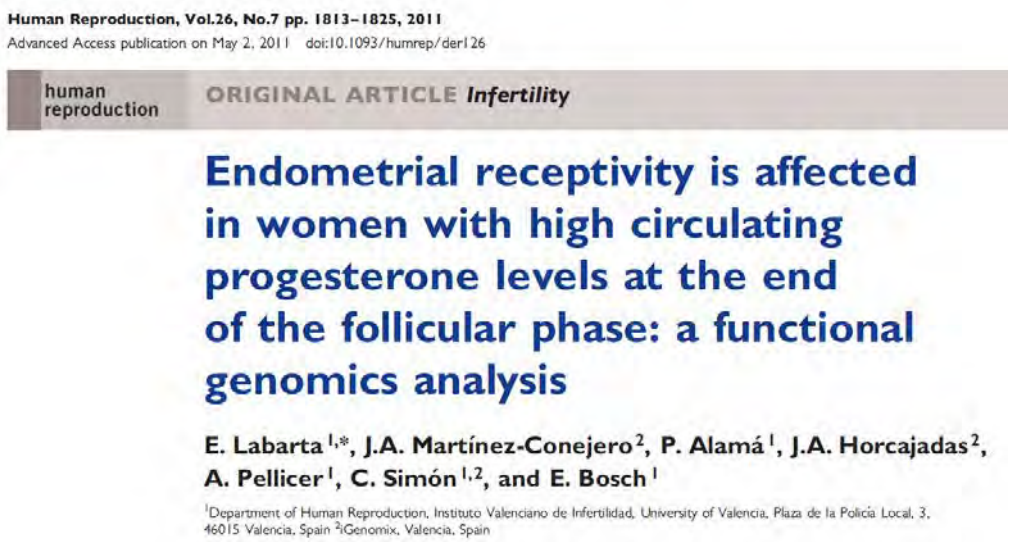
1.- Diagnóstico previo correcto

2.- Progesterona

- La iniciación de la receptividad endometrial parece depender de la regulación de los Rcs de estrógenos inducidos por progesterona.

- La suplementación de la fase lútea con P en FIV se realiza de rutina y está demostrada su utilidad. *(Soliman y col, 94)*

- Elevación de la progesterona



Human Reproduction, Vol.26, No.7 pp. 1813–1825, 2011
Advanced Access publication on May 2, 2011 doi:10.1093/humrep/der126

human reproduction ORIGINAL ARTICLE *Infertility*

Endometrial receptivity is affected in women with high circulating progesterone levels at the end of the follicular phase: a functional genomics analysis

E. Labarta[1,*], J.A. Martínez-Conejero[2], P. Alamá[1], J.A. Horcajadas[2], A. Pellicer[1], C. Simón[1,2], and E. Bosch[1]

[1]Department of Human Reproduction, Instituto Valenciano de Infertilidad, University of Valencia, Plaza de la Policía Local, 3, 46015 Valencia, Spain [2]iGenomix, Valencia, Spain

3.- Inducción de la ovulación

Something happens during stimulation

Fertility and Sterility® Vol. 105, No. 3, March 2016

VIEWS AND REVIEWS

Regimen of ovarian stimulation affects oocyte and therefore embryo quality

Ernesto Bosch, M.D.,[a] Elena Labarta, M.D.,[a] Efstratios Kolibianakis, M.D.,[b] Mitchell Rosen, M.D.,[c] and David Meldrum, M.D.[d]

Recent studies suggest that the use of high doses of gonadotropins as an independent factor correlates negatively with the probability of live birth, whereas a high ovarian response per se is associated with better cumulative pregnancy rates, owing to the availability of more euploid and good-quality embryos

4.- Mejora de la receptividad endometrial

ARTICLE IN PRESS

Reproductive BioMedicine Online (2012) xxx, xxx–xxx

ELSEVIER

www.sciencedirect.com
www.rbmonline.com

ARTICLE

Endometrial expression of selected genes in patients achieving pregnancy spontaneously or after ICSI and patients failing at least two ICSI cycles

Adolfo Allegra [a,*], Angelo Marino [a], Pedro Caballero Peregrin [b], Anna Lama [a], Áurea García-Segovia [b], Giusi Irma Forte [a], Rocío Núñez-Calonge [b], Cecilia Agueli [c], Sergio Mazzola [d], Aldo Volpes [a]

4.- Mejora de la receptividad endometrial

Implantation failure of endometrial origin: it is not pathology, but our failure to synchronize the developing embryo with a receptive endometrium

VOL. 108 NO. 1 / JULY 2017

M.S.,[a] and Carlos Simon, M.D., Ph.D.[a,b,c,d]

Repeated implantation failure (RIF) is an intriguing, massive failure of reproductive treatment in otherwise healthy women leading to the introduction of empirical adjuvant interventions that are costly, inefficient, and frustrating for our patients. In this article, we will try to convince the readers that RIF is neither a stigma nor a mysterious pathology but rather our failure to diagnose and properly synchronize the euploid blastocyst with the patient's personalized window of implantation. (Fertil Steril® 2017;108:15–8. ©2017 by Amer-

4.- Mejora de la receptividad endometrial

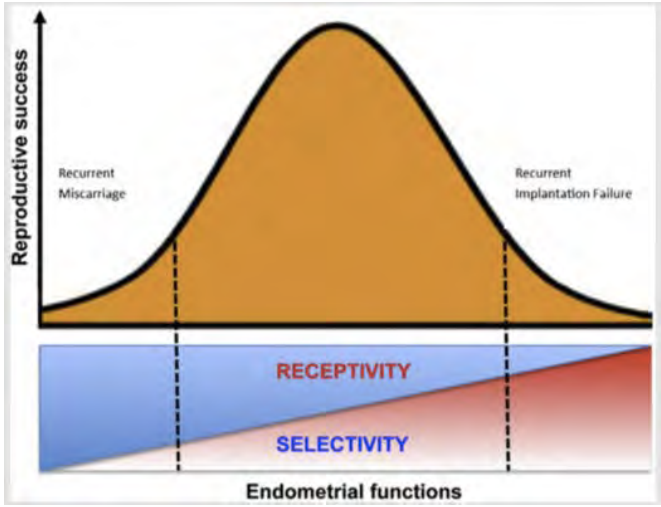
Recurrent implantation failure is a pathology with a specific transcriptomic signature

Nick Macklon, M.D., Ph.D.

Department of Obstetrics and Gynecology, Zealand University Hospital and University of Copenhagen, Roskilde, Denmark

VOL 108 NO. 1 / JULY 2017

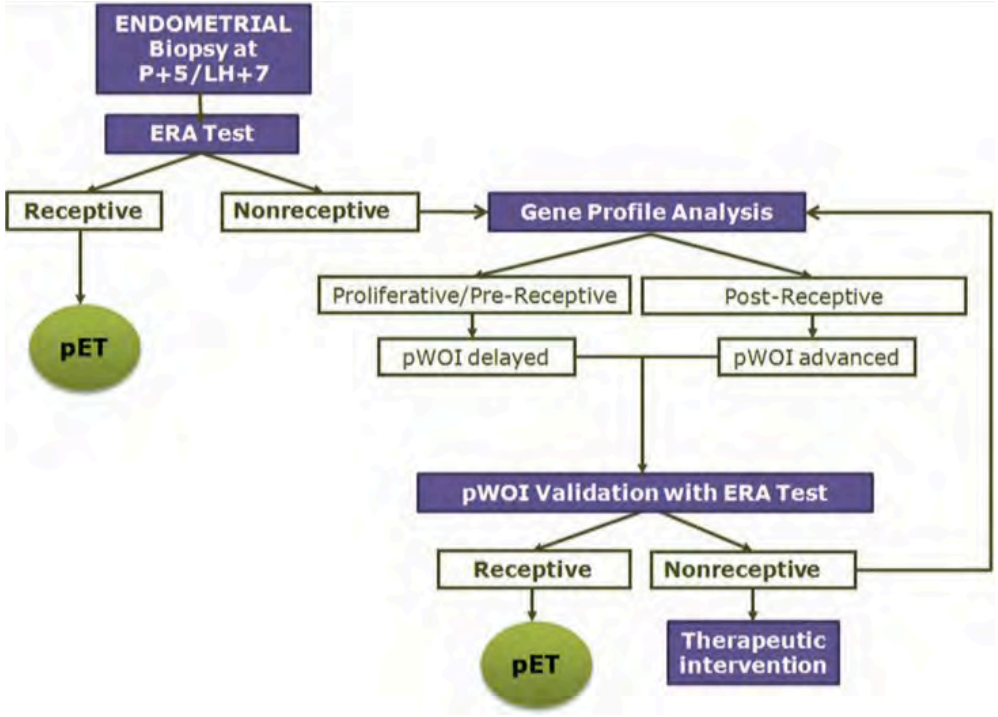
RECURRENT IMPLANTATION FAILURE REPRESENTS MORE THAN AYSNCHRONY



4.- Mejora de la receptividad endometrial

The endometrial receptivity array for diagnosis and personalized embryo transfer as a treatment for patients with repeated implantation failure

Maria Ruiz-Alonso, M.Sc.,[b] David Blesa, Ph.D.,[a,b] Patricia Díaz-Gimeno, Ph.D.,[a,c] Eva Gómez, M.Sc.,[a] Manuel Fernández-Sánchez, M.D.,[d] Francisco Carranza, M.D.,[d] Joan Carrera, M.D.,[e] Felip Vilella, Ph.D.,[a] Antonio Pellicer, M.D., Ph.D.,[a,b] and Carlos Simón, M.D., Ph.D.[a,b]



4.- Mejora de la receptividad endometrial

Human Reproduction Open, pp. 1–18, 2019
doi:10.1093/hropen/hoy025

human reproduction open

REVIEW

Endometrial scratching prior to IVF; does it help and for whom? A systematic review and meta-analysis

N.E. van Hoogenhuijze [1,*], J.C. Kasius[2], F.J.M. Broekmans[1], J. Bosteels[3], and H.L. Torrance[1]

4.- Mejora de la receptividad endometrial

Hindawi
Mediators of Inflammation
Volume 2019, Article ID 4893437, 10 pages
https://doi.org/10.1155/2019/4893437

Research Article

Characterization of Microbiota in Endometrial Fluid and Vaginal Secretions in Infertile Women with Repeated Implantation Failure

Kotaro Kitaya,[1] Yoko Nagai,[2] Wataru Arai,[2] Yoshiyuki Sakuraba,[2] and Tomomoto Ishikawa[1,3]

4.- Mejora de la receptividad endometrial

www.nature.com/scientificreports

SCIENTIFIC REPORTS

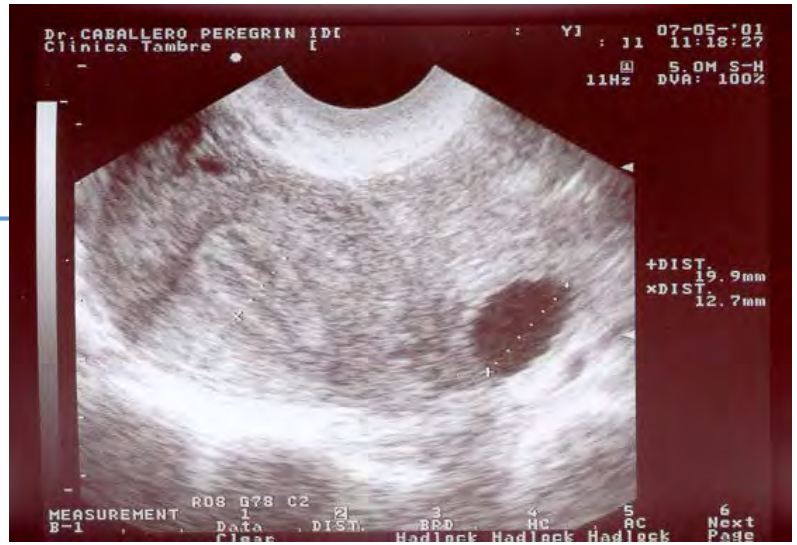
natureresearch

OPEN

Uterine SOX17: a key player in human endometrial receptivity and embryo implantation

Sophie Kinnear[1,2], Lois A. Salamonsen[1,3], Mathias Francois[1], Vincent Harley[1] & Jemma Evans[1,3*]

5.- Método de transferencia



- Habilidad y experiencia
- Catéter de transferencia
- Minimizar el trauma *(evitar el sangrado, contracciones uterinas y tenaculum)*
- Transferencia ecoguidada *(Coroleu y col, 2002)*

6.- Causas inmunológicas

ORIGINAL ARTICLE

Intravenous Immunoglobulin Treatment Increased Live Birth Rate in a Spanish Cohort of Women with Recurrent Reproductive Failure and Expanded CD56$^+$ Cells

Manuela Moraru[1,2], Javier Carbone[1], Diana Alecsandru[1], Marcela Castillo-Rama[1], Aurea García-Segovia[3], Juana Gil[1], Bárbara Alonso[1], Angel Aguarón[4], Rocío Ramos-Medina[1], Juan Martínez de María[3], Desamparados Oliver-Miñarro[1], Margarita Rodríguez-Mahou[1], Virginia Ortega[4], Pedro Caballero[3], Elena Meliá[5], Juan Vidal[5], Malena Cianchetta-Sivori[1], Carmen Esteban[1], Loreto Vargas-Henny[1], Jonathan Dale[1], Luis Ortiz-Quintana[4], Eduardo Fernández-Cruz[1], Silvia Sánchez-Ramón[1]

[1]Clinical Immunology Unit, Department of Immunology, Hospital General Universitario Gregorio Marañón, Madrid, Spain;
[2]Department of Immunology, Hospital Univesitario Puerta de Hierro Majadahonda, Madrid, Spain;
[3]Clínica Tambre, Madrid, Spain;
[4]Department of Obstetrics and Gynaecology, Hospital General Universitario Gregorio Marañón, Madrid, Spain;
[5]Unidad de la Mujer, Hospital Ruber Internacional, Madrid, Spain

American Journal of Reproductive Immunology (2012)

AJRI
American Journal of Reproductive Immunology

6.- Causas inmunológicas

Human Reproduction, Vol.30, No.7 pp. 1519–1525, 2015
Advanced Access publication on May 7, 2015 doi:10.1093/humrep/dev098

human reproduction DEBATE

First do no harm: uterine natural killer (NK) cells in assisted reproduction

Ashley Moffett[1,2,*] and Norman Shreeve[2,3]

[1]Department of Pathology, University of Cambridge, Cambridge, UK [2]Centre for Trophoblast Research, University of Cambridge, Cambridge, UK [3]Department of Obstetrics & Gynecology, University of Cambridge, Cambridge, UK

Contribution of immunology to implantation failure of euploid embryos

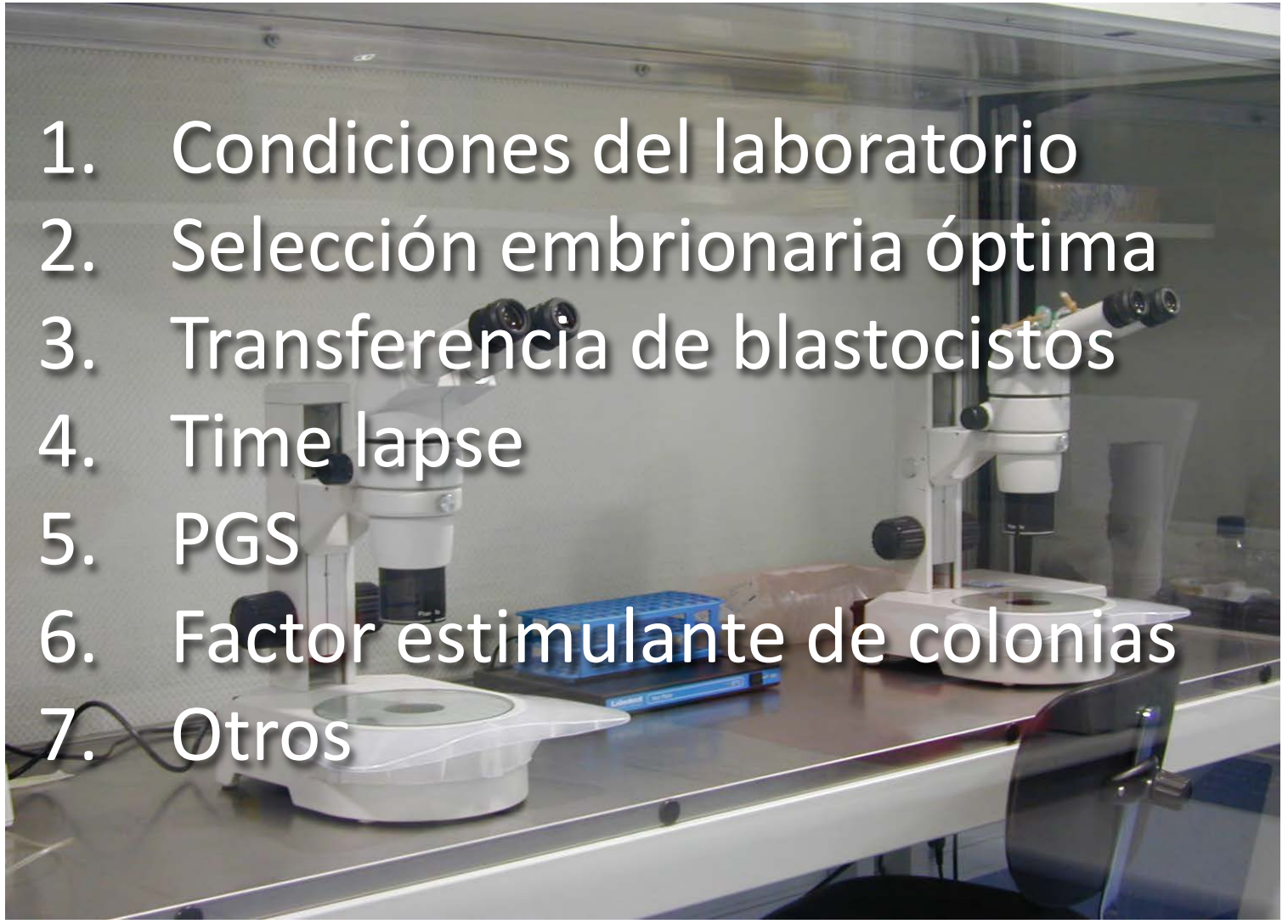
Jason M. Franasiak, M.D., T.S. (A.B.B.) and Richard T. Scott, M.D., H.C.L.D./A.L.D. (A.B.B.)

Reproductive Medicine Associates of New Jersey, Basking Ridge, New Jersey; and Thomas Jefferson University, Philadelphia, Pennsylvania

VOL. 107 NO. 6 / JUNE 2017

Aspectos biológicos en la mejora de la implantación

Estrategias en el laboratorio de FIV



1. Condiciones en el laboratorio

RBMO

ELSEVIER

REVIEW

Controversies in ART: can the IVF laboratory influence preimplantation embryo aneuploidy?

BIOGRAPHY

Jason E. Swain PhD, HCLD, is the Corporate Laboratory Director of the CCRM IVF Laboratory Network. He completed his BSc at Hillsdale College, his MSc at Purdue University and his PhD at the University of Michigan. His primary research interests include the pursuit of methods to improve in-vitro embryo culture conditions.

Jason E. Swain* PhD, HCLD

KEY MESSAGE

As reported, rates of embryo aneuploidy vary between IVF centres. Attention has focused on possible stressors in the IVF laboratory that may influence chromosome separation and segregation. Differences in blastocyst mosaicism rates could indicate laboratory causes of chromosomal errors. Possible mitotic stressors include pH, osmolality, temperature, oxygen tension and culture media.

2. Morfología embrionaria como parámetro de selección

Rock J, Menkin MF. In vitro fertilization and cleavage of human ovarian eggs. *Science* 1944; **100**:105–107.

One of these (embryo), when first seen in cleavage, consisted of one large blastomere and two smaller ones, each of the three containing a round, vesicular nucleus. The second egg from this same patient was in a similar stage, but part of the cytoplasm appeared fragmented, and soon proceeded to undergo rapid degenerative changes.

3. Transferencia de blastocistos

RBMO

ELSEVIER

ARTICLE

Fine-tuning blastocyst selection based on morphology: a multicentre analysis of 2461 single blastocyst transfers

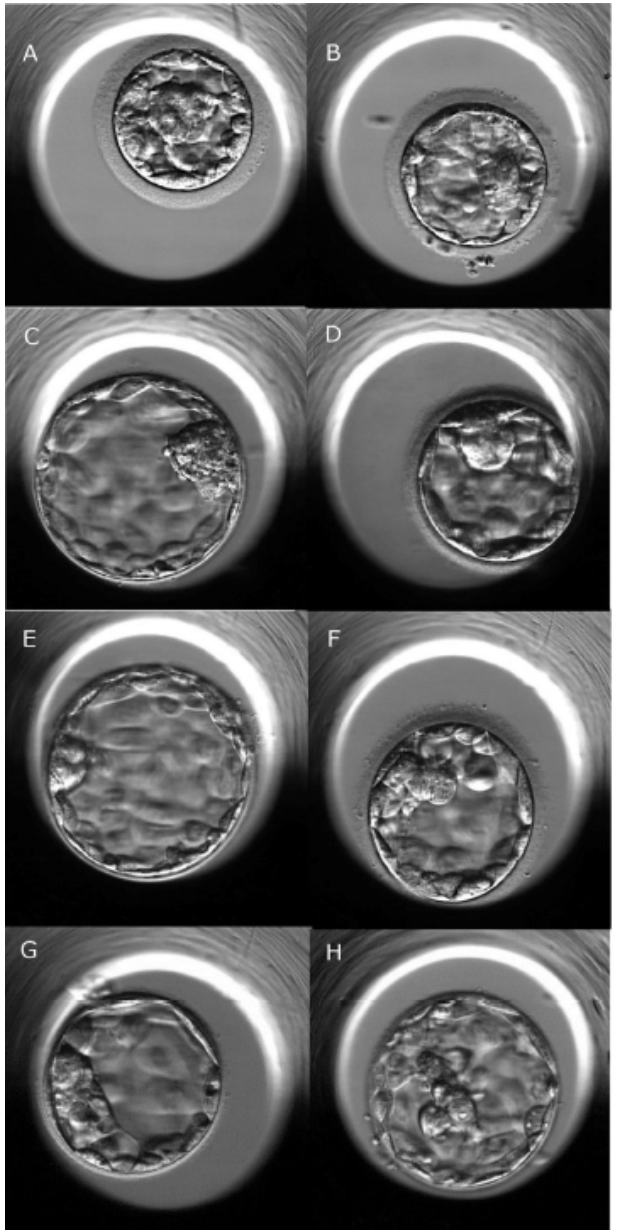
BIOGRAPHY

Ashleigh Storr is a senior clinical embryologist at Flinders Fertility in Adelaide, Australia. She has recently completed her PhD thesis with the University of New South Wales in Sydney, Australia, where her research interests include embryo selection and the use of time-lapse technology for the optimization of IVF outcome.

Ashleigh Storr[1,2,*], Esra Bilir[3], Simon Cooke[4], Don Garrett[4], Christos A. Venetis[4,5]

KEY MESSAGE

By controlling for the confounding effects of female age and endometrial receptivity for the first time in a single blastocyst transfer setting, this study suggests that developmental stage and trophectoderm grade are more important than inner cell mass grade as predictors of live birth when selecting a blastocyst for transfer.



4. Time-lapse

Fertility and Sterility® Vol. 105, No. 2, February 2016

Morphokinetic analysis and embryonic prediction for blastocyst formation through an integrated time-lapse system

Yamileth Motato, Ph.D., María José de los Santos, Ph.D., María José Escriba, Ph.D., Belén Aparicio Ruiz, Ph.D., José Remohi, M.D., and Marcos Meseguer, Ph.D.

Instituto Valenciano de Infertilidad, Universidad de V

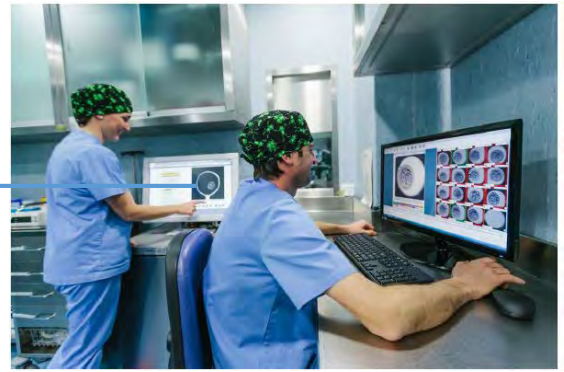
Fertility and Sterility® Vol. 105, No. 2, February 2016

Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial

Linnea R. Goodman, M.D., Jeffrey Goldberg, M.D., Tommaso Falcone, M.D., Cynthia Austin, M.D., and Nina Desai, Ph.D., H.C.L.D.

Department of Reproductive Endocrinology and Infertility, Cleveland Clinic, Beachwood, Ohio

4. Time-lapse



RBMO

ELSEVIER

ARTICLE

Embryo morphokinetics is potentially associated with clinical outcomes of single-embryo transfers in preimplantation genetic testing for aneuploidy cycles

BIOGRAPHY

Chun-I Lee is a PhD student at the Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan. His research interest is reproductive biology and the application of artificial intelligence in infertility. He was awarded an MD in 2008 from the National Defense Medical Center and completed his clinical training in reproductive medicine in 2016.

Chun-I Lee[1,2,3,†], Chien-Hong Chen[3,†], Chun-Chia Huang[3], En-Hui Cheng[3], Hsiu-Hui Chen[3], Su-Ting Ho[3], Pin-Yao Lin[1,3], Maw-Sheng Lee[1,2,3], Tsung-Hsien Lee[1,2,3,4,*]

KEY MESSAGE

Using high-resolution next-generation sequencing and time-lapse monitoring technologies, this study demonstrated varied developmental patterns corresponding to diploid–aneuploid mosaicism levels. In addition, the generally applicable KIDScore D5 algorithm was able during preimplantation development to distinguish euploid blastocysts with specific morphokinetic characteristics, potentially associated with clinical outcomes.

5. Screening genético preimplantacional

Human Reproduction, Vol.30, No.9 pp. 2097–2106, 2015
Advanced Access publication on July 5, 2015 doi:10.1093/humrep/dev139

human reproduction ORIGINAL ARTICLE *Gynaecology*

Reduction of multiple pregnancies in the advanced maternal age population after implementation of an elective single embryo transfer policy coupled with enhanced embryo selection: pre- and post-intervention study

Filippo Maria Ubaldi[1,*], Antonio Capalbo[1,2], Silvia Colamaria[1], Susanna Ferrero[1], Roberta Maggiulli[1], Gábor Vajta[3], Fabio Sapienza[1], Danilo Cimadomo[1,2], Maddalena Giuliani[1], Enrica Gravotta[1], Alberto Vaiarelli[1], and Laura Rienzi[1]

Outcomes of in vitro fertilization with preimplantation genetic diagnosis: an analysis of the United States Assisted Reproductive Technology Surveillance Data, 2011–2012

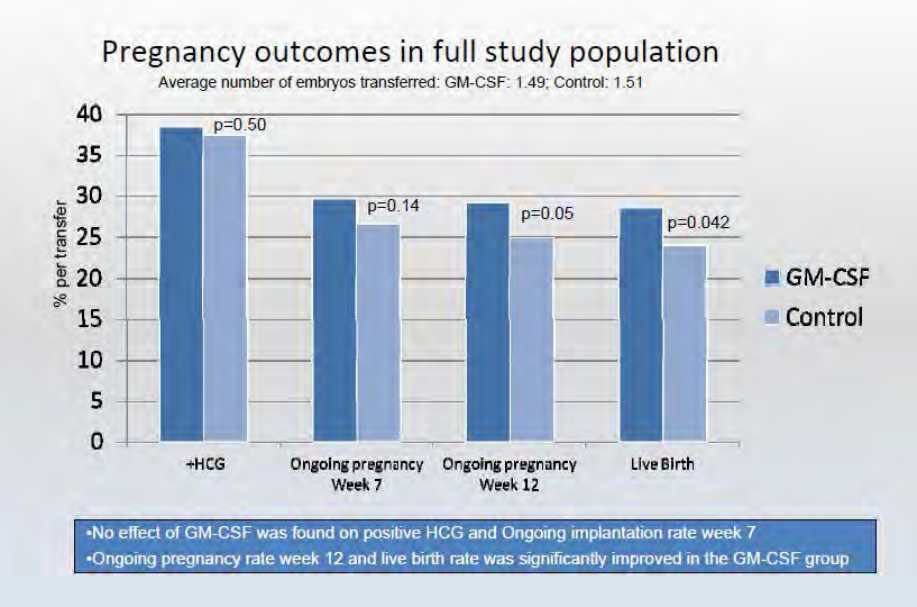
Jeani Chang, M.P.H., Sheree L. Boulet, Dr.P.H., Gary Jeng, Ph.D., Lisa Flowers, M.P.A., and Dmitry M. Kissin, M.D., M.P.H.

Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

Conclusion(s): Aneuploidy screening was the most common indication for PGD. Use of PGD was not observed to be associated with an increased odds of clinical pregnancy or live birth for women <35 years. PGD for aneuploidy was associated with a decreased odds of miscarriage for women >35 years, but an increased odds of a live-birth and a multiple live-birth delivery among women >37 years. (Fertil Steril® 2016;105:394–400. ©2016 by American Society for Reproductive Medicine.)

6. Factor estimulante de colonias

The effect of granulocyte-macrophage colony stimulating factor (GM-CSF) during in vitro culture of human embryos on subsequent implantation rates.



Int J Reprod BioMed Vol. 16. No. 5. pp: 299-304, May 2018

Original article

Granulocyte-colony stimulating factor may improve pregnancy outcome in patients with history of unexplained recurrent implantation failure: An RCT

Soheila Arefi[1, 2] M.D., Elham Fazeli[3] M.Sc., Manijeh Esfahani[1] M.Sc., Nasim Borhani[4] Ph.D., Nazila Yamini[5] Ph.D., Ahmad Hosseini[1] Ph.D., Fattaneh Farifteh[1, 6] Ph.D.

JBRA Assisted Reproduction 2019;**23**(3):250-254
doi: 10.5935/1518-0557.20190035

Original article

New therapeutic protocol for improvement of endometrial receptivity (PRIMER) for patients with recurrent implantation failure (RIF) - A pilot study

Felipe Dieamant[1,2], Laura D. Vagnini[2], Claudia G. Petersen[1,2], Ana L. Mauri[1,2], Adriana Renzi[2], Bruna Petersen[1,2], Mariana C. Mattila[1], Andreia Nicoletti[1,2], João Batista A. Oliveira[1,2], Ricardo Baruffi[1,2], Jose G. Franco Jr[1,2]

7. Nuevas estrategias

New strategy for diagnosing embryo implantation potential

Fertility and Sterility® Vol. 105, No. 1, January 2016

MicroRNAs in culture mediu from trophecto can be explor embryo reproc competence a

Antonio Capalbo, Ph.D.,[a,b] Filippo Maria Uba
Yakoub Khalaf, M.D., M.Sc.,[c] Alessio Farcom

Liu et al. Reproductive Biology and Endocrinology (2019) 17:54
https://doi.org/10.1186/s12958-019-0495-6

Reproductive Biology and Endocrinology

RESEARCH Open Access

Cell-free mitochondrial DNA in human follicular fluid: a promising bio-marker of blastocyst developmental potential in women undergoing assisted reproductive technology

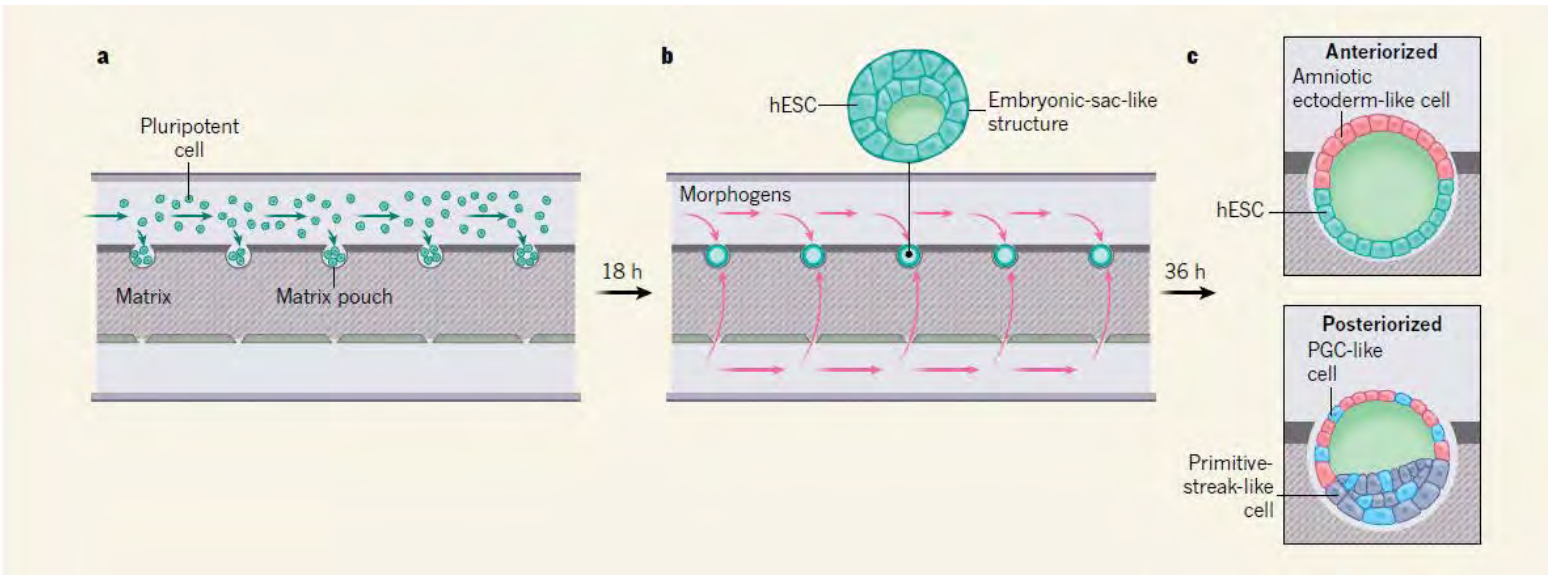
Yu Liu[1], Qiuzi Shen[1], Xue Zhao[1], Min Zou[1], Shumin Shao[1], Jiao Li[1], Xinling Ren[2] and Ling Zhang[1*]

DEVELOPMENTAL BIOLOGY

A model of human embryo implantation

An innovative microfluidic device has enabled the modelling of the events that occur in human embryos when they implant in the wall of the uterus. It could be used to help understand early pregnancy loss. SEE LETTER P.421

| NATURE | VOL 573 | 19 SEPTEMBER 2019



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