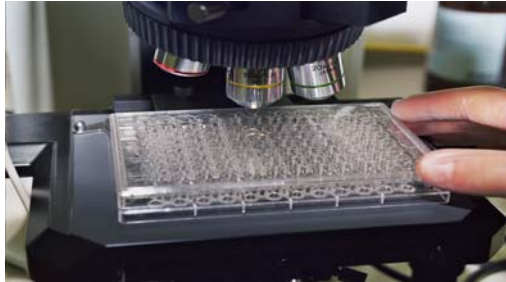




Safeguarding Reproductive Capacity



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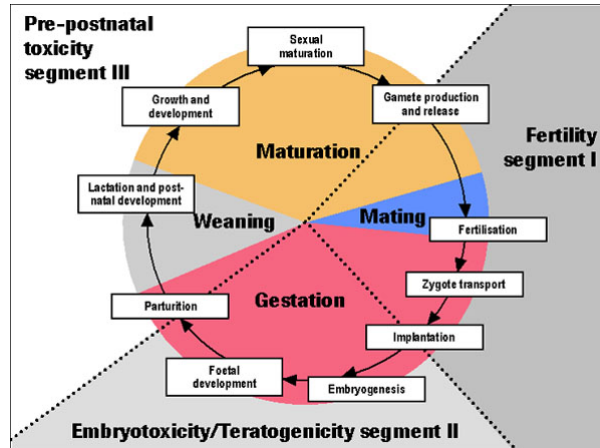


Centre of Excellence for Reproductive Function Testing
Focus on innovative in vitro bioassays

Rita Cortvrindt



Innovation for Sustainable Production - Bruges 22-25 April 2008



Targets



Female

X

Male

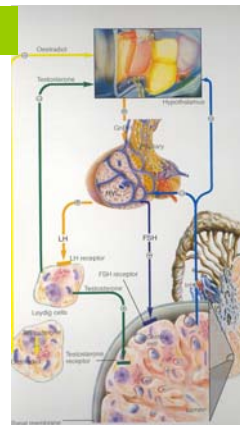
Embryo

Foetus

Offspring

Organ, cell , subcellular level

Complex dynamic systems



In Vitro Tools *for* Female Fertility assessment

ADULT FEMALE REPRODUCTIVE SYSTEM

Adults
Childbearing age

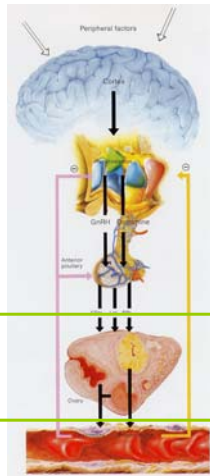
Target Organs

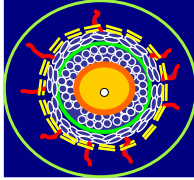
Hypothalamus

Pituitary

Ovary

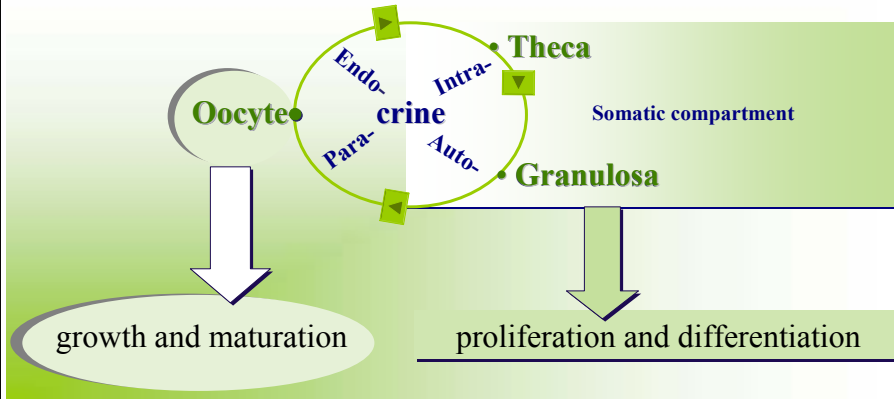
Uterus



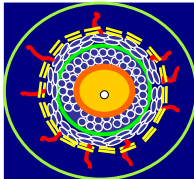


THE OVARIAN FOLLICLE

Functional unit within the ovary

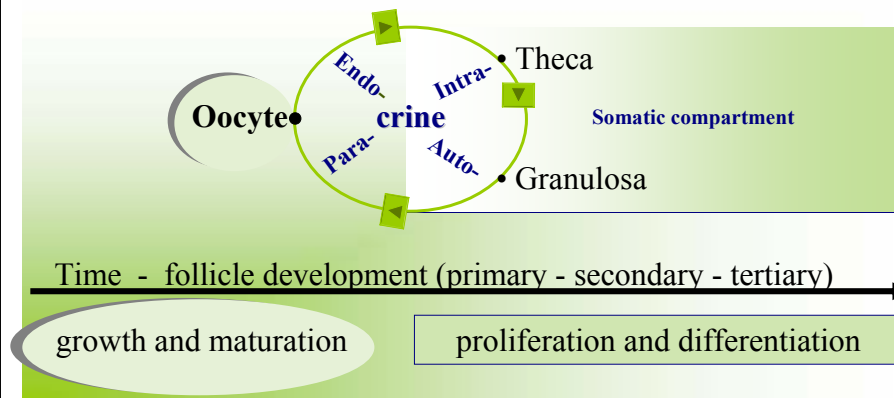


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THE OVARIAN FOLLICLE

Functional unit within the ovary



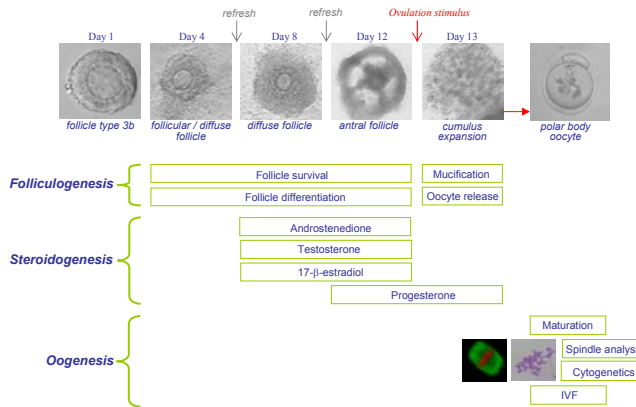
Folliculogenesis - Oogenesis - Steroidogenesis

FBA = Follicle Bioassay

- Follicle development -

- Steroidogenic pathway -

- Oocyte development -



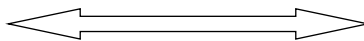
- Multiparametric assay for in vitro ovarian function evaluation -

* EggCentris NV holds the world wide exclusive licence of patent: WO 02/48316 A1

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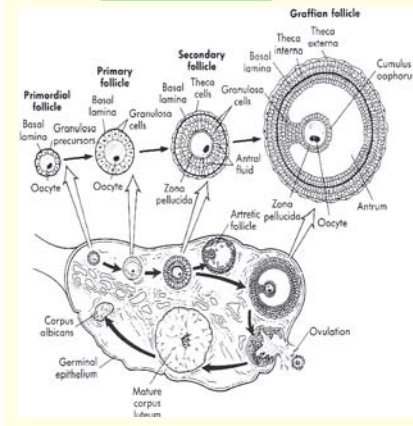
OVARY - Folliculogenesis

In Vivo



In Vitro

“chaotic”



synchronised

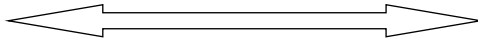


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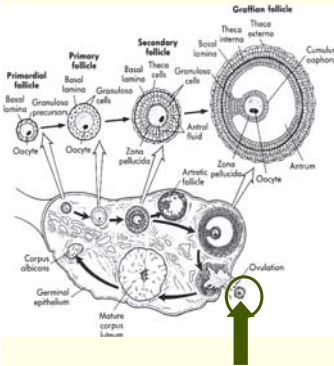


OVARY - OOGENESIS

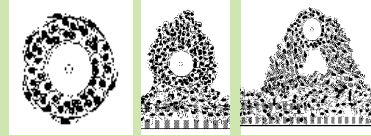
In Vivo



In Vitro



OOCYTE (only few)
not available for direct evaluation



OOCYTES (in large numbers)
AVAILABLE for direct evaluation



FOLLICLE CULTURE BIOASSAY

In vitro follicle growth mimics ovarian function

- all follicular cells are present
- normal granulosa-cell differentiation
- oocyte growth and nuclear arrest
- physiological steroid production pattern
- dependent on gonadotropins
 - follicle differentiation (FSH)
 - induction of meiosis (LH)
- strictly timed process

Requirements of a bioassay to be used as a test method



- Reproducibility?
- Relevant Endpoints?
- Sensitivity?
- Predictivity to in vivo /human?



RePrTECT

Follicle Bioassay

Reproducibility

Parameter	Mean \pm SD	% CV
Follicle diameter (μm)	118 \pm 3	3
Preovulatory follicle (%)	96 \pm 7	7
Follicle survival (%)	99 \pm 3	3
LH-Responsiveness (%)	99 \pm 4	4
Polar body extrusion (%)	91 \pm 8	9

(n = 177)

Follicle Bioassay



Relevant endparameters – predictivity

Folliculogenesis

Follicle growth
Follicle differentiation
Follicle survival
Follicle responsiveness

Oogenesis

Oocyte growth
Oocyte survival
Oocyte nuclear maturation
Oocyte developmental capacity

Steroidogenesis

Androstenedione output
Testosterone output
Estradiol output
Progesterone output
.....

Follicle Bioassay



Relevant endparameters – predictivity

Folliculogenesis

Oogenesis

Steroidogenesis

Dose response levels

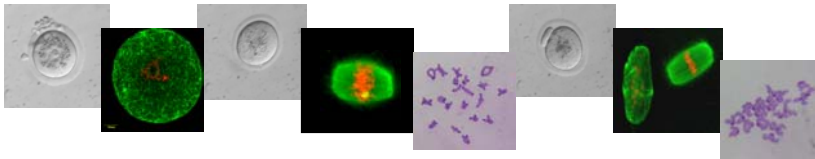
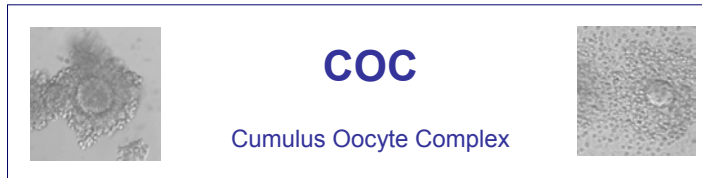
Integrated interpretation with knowledge of ovarian physiology

Dose related prediction

Cycle disturbances
Ovulation problems
Fertilisation problems
Conception problems
Endocrine disruption
.....

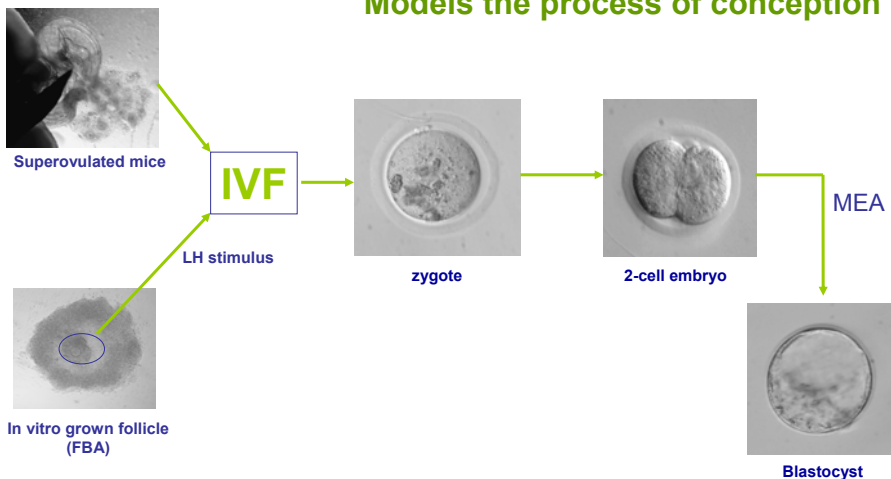
IVM = In Vitro Maturation

Models the Meiotic Process at Ovulation



IVF = In Vitro Fertilisation

Models the process of conception

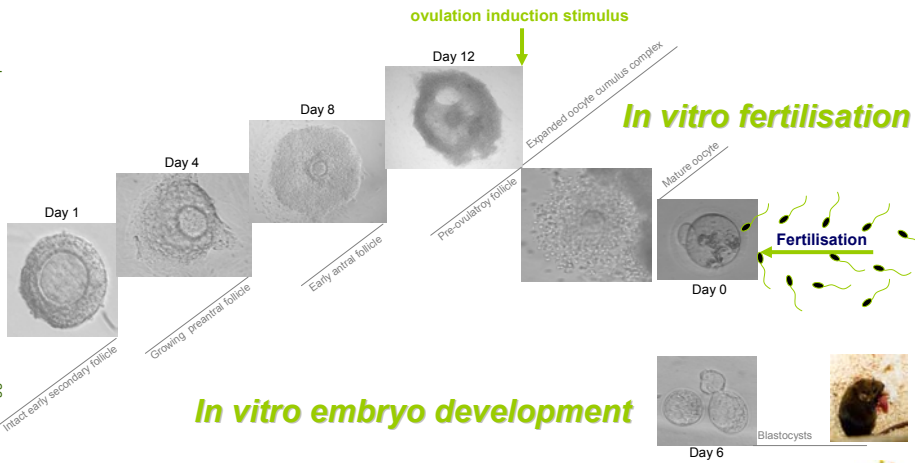


An in vitro battery for female fertility assessment



The Follicle Bioassay*

* EggCentris NV holds the world wide exclusive licence of patent: WO 02/48316 A1



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EggCentris
Proactive Female Reproduction Testing

In Vitro Tools

for

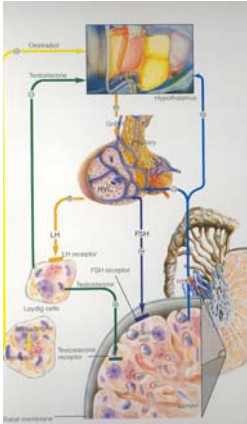
Male Fertility assessment

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ADULT MALE REPRODUCTIVE SYSTEM

Target Organs



Sperm Motility Assay (SMA)



Sperm survival and motility parameters

Functional assessment in IVF assay

Sertoli cells

Leydig cells



In Vitro Tools

for

Embryo Toxicity Assessment

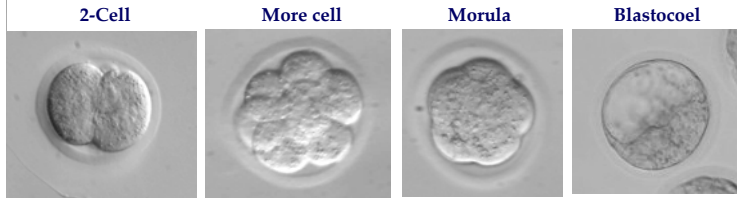


Mouse Embryo Peri-implantation Assay (MEPA)

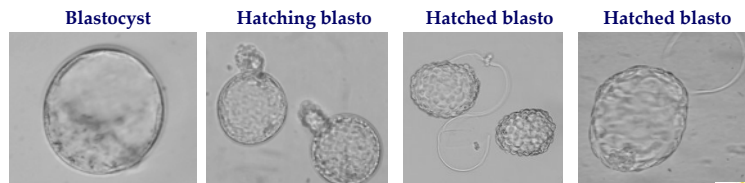


Zygote

Pre - implantation development



Peri-implantation development

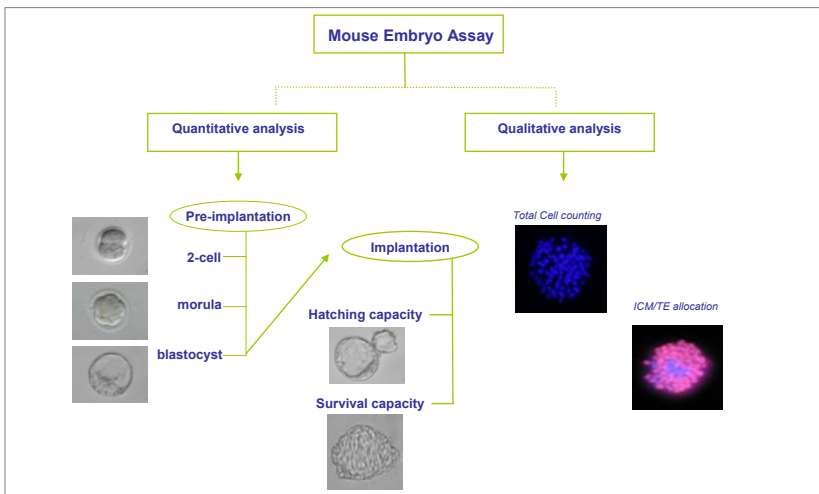


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MEPA

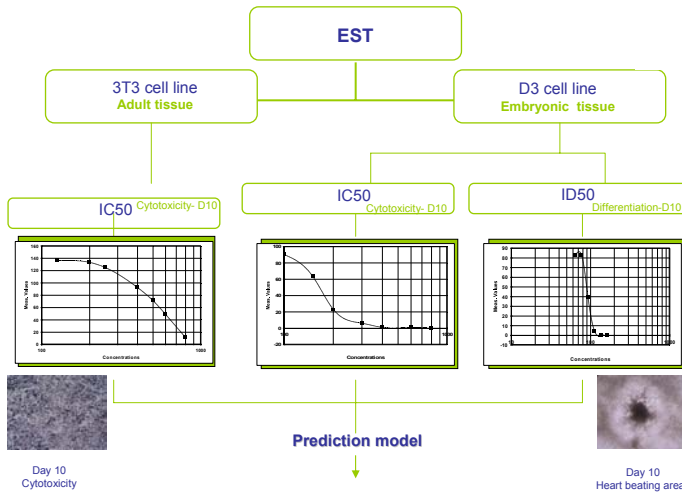
Models the pre-implantation and early post implantation embryo development



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EST = Mouse Embryonic Stem cell Test

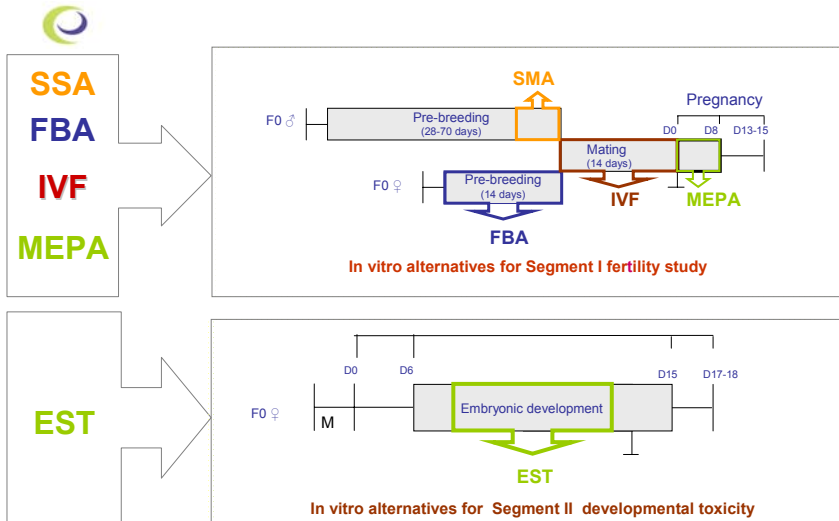


Non, Weak or Strong Embryo Toxic Compound

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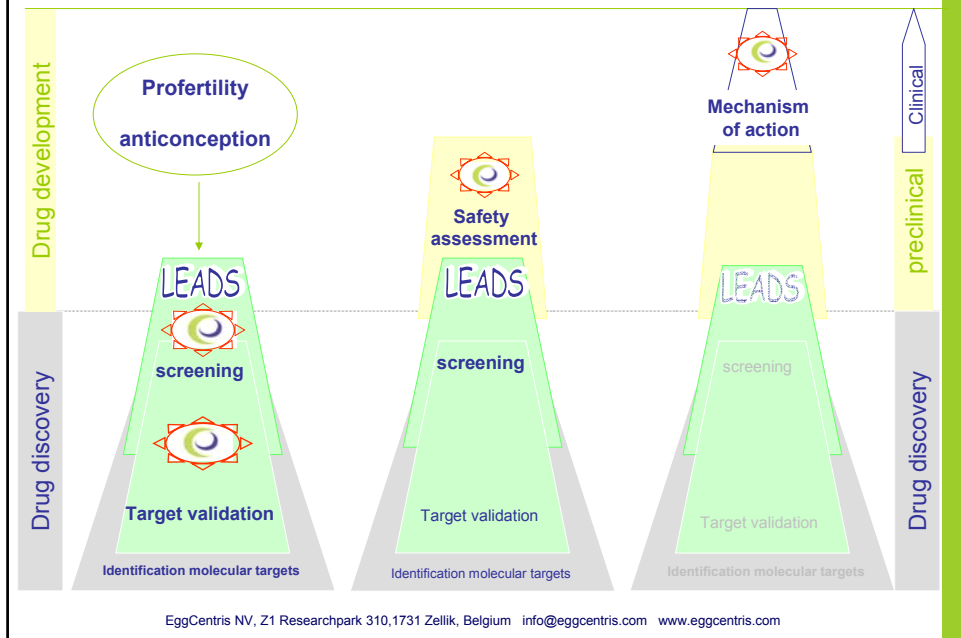


REACH Available in vitro tools



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Innovation Gap - Pharma tools



Advantages of our *in vitro* bioassays

- fast
- reliable quantitative and qualitative results
- cost saving

small amount of product – early screening

animal saving – fitting the 3Rs principle

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Quality Control



Assisted Reproduction supplies

- Labware
- Medical devices
- Culture media

Tools:

- MEA (Oil / oil-free system available)
- IVF (gamete toxicity)
- LAL
- SMA



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EggCentris

Center of Excellence
for Reproductive Function Testing

EggCentris a Contract Research laboratory specialised in the assessment of the reproductive function

Screening

*pharmaceutical compounds for toxicity or proactive effects
chemical molecules for hazard identification
materials for fertility treatments (QC)*



In depth research

Elucidation of the mechanism of action compounds

Model development on demand



R&D

to fill the gaps

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In Vitro Veritas

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