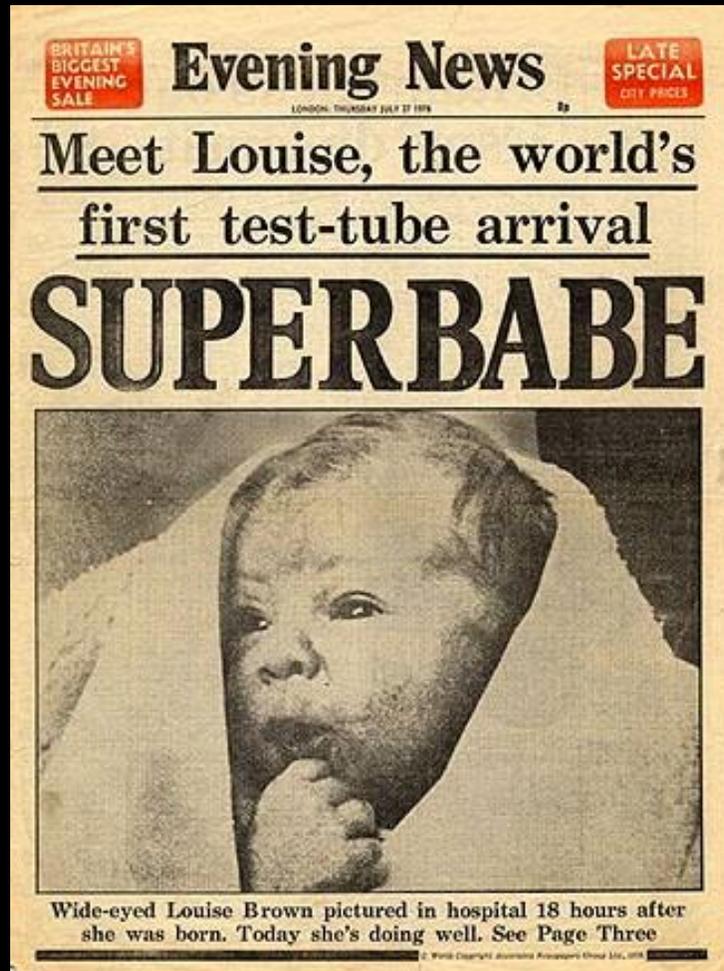


# QUO VADIS? WHERE THE CURRENT REPRODUCTION IS GOING...

**Jan NEVORAL, Olga GARCÍA-ÁLVAREZ, Miriam ŠTIAVNICKÁ**  
Laboratory of Reproductive Medicine

# ASSISTED REPRODUCTIVE TECHNOLOGIES (ART), NOTHING NEW...



Louise Brown,  
1st IVF baby (\*1978)

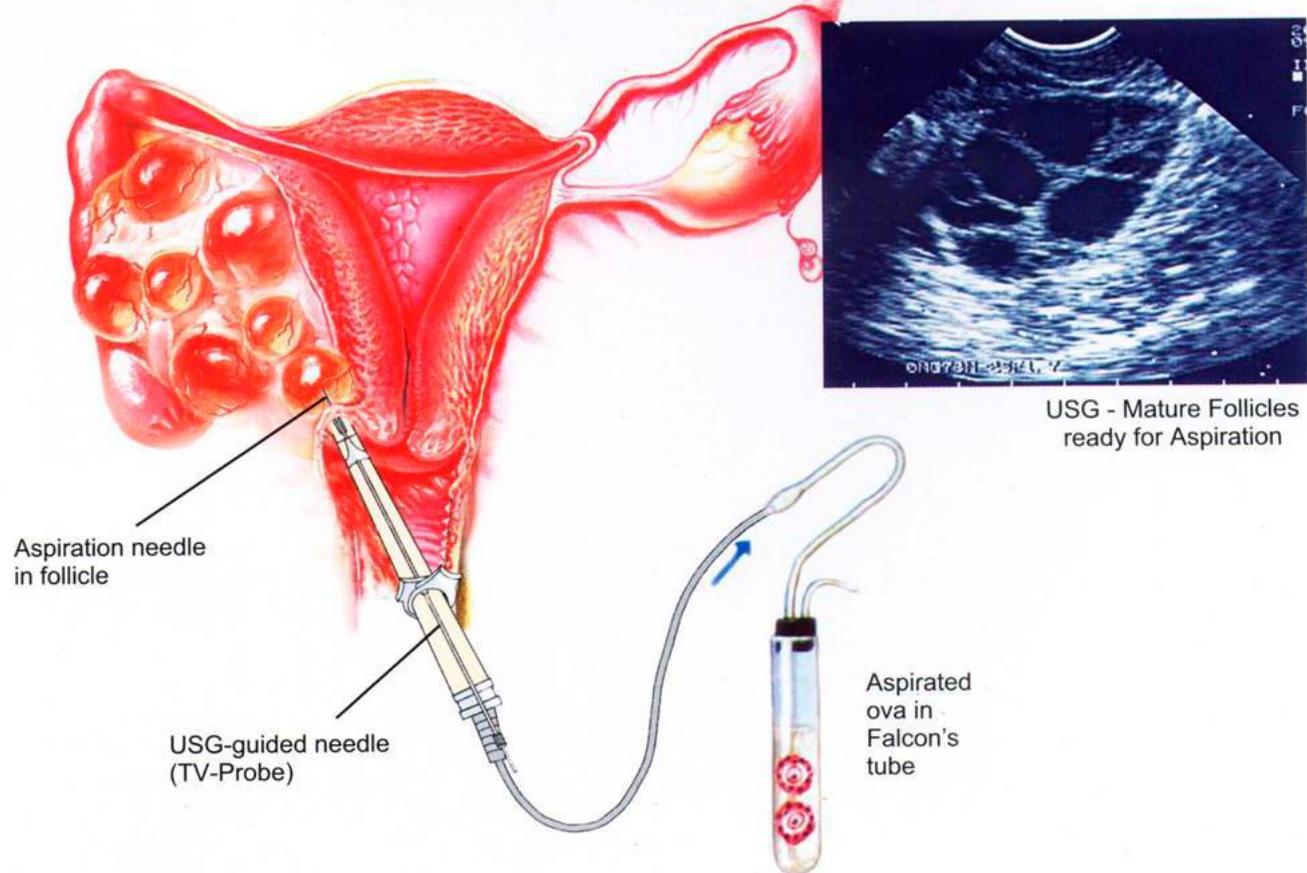
- Assisted reproduction clinics
- **Traditional methods**
  - Ovum pick-up (OPU)
  - *In vitro* fertilization (IVF)
- **Advanced approaches**



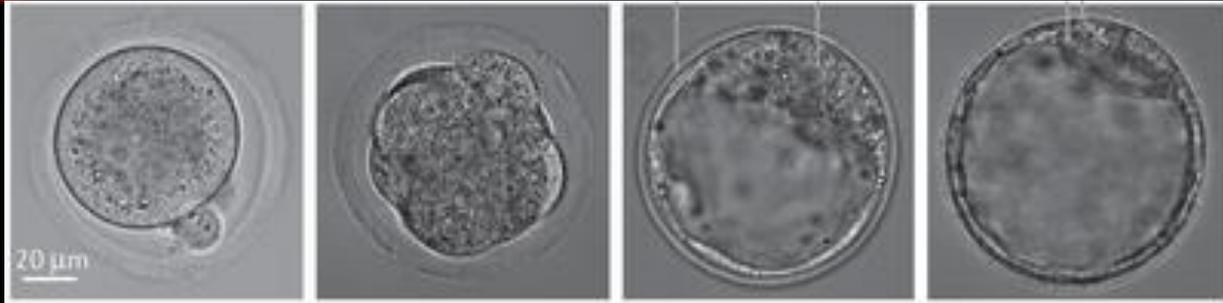
# WHO UTILIZES ART?

- Failure of female reproduction
  - Oviduct obstruction
- Insufficient male reproduction
  - Unsuccessful motility and others

## INVITRO FERTILIZATION

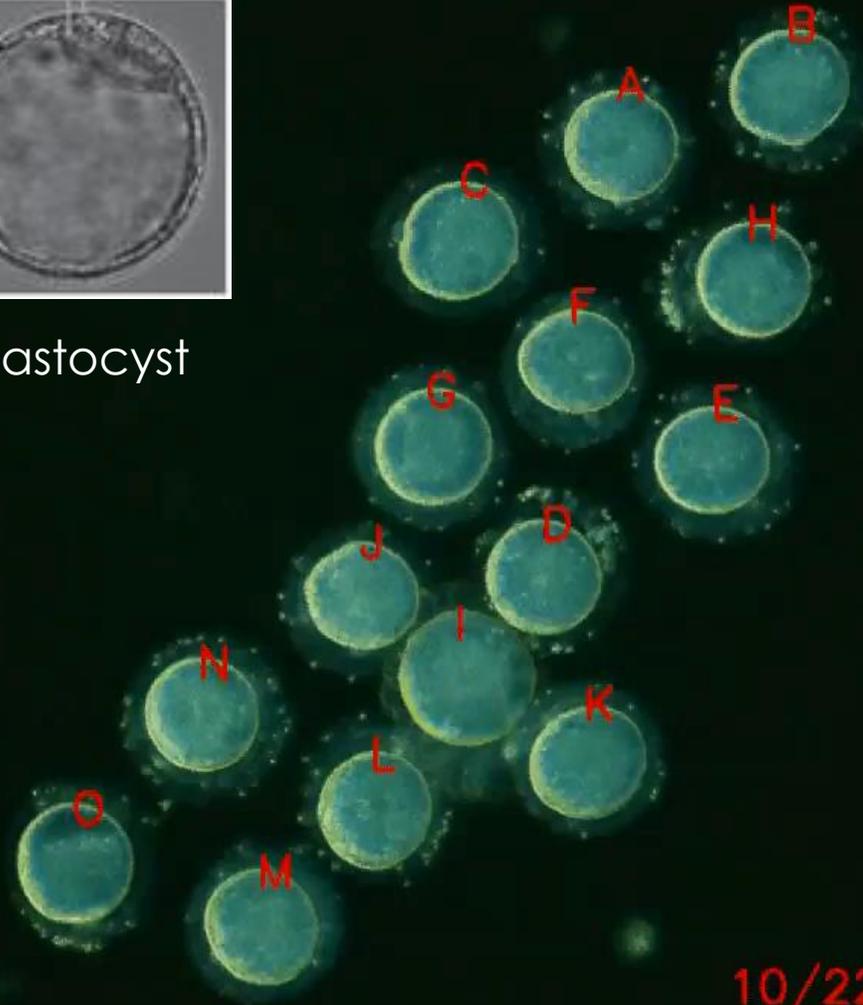
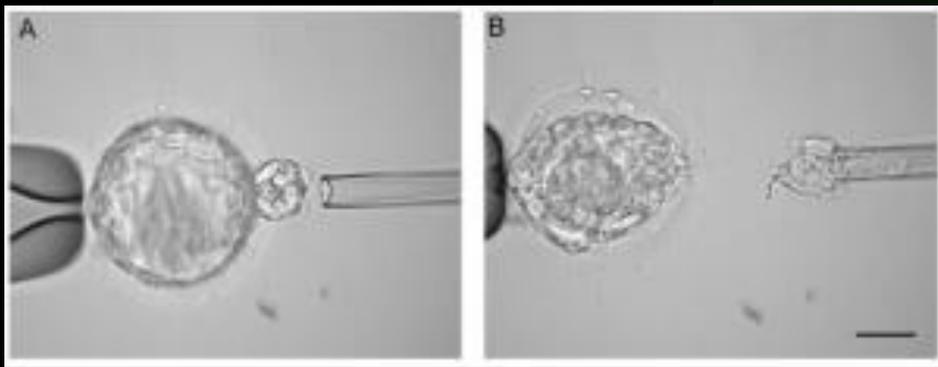


# BLASTOCYST: HOLY GRAIL OF ART



Fertilization  $\longrightarrow$  Blastocyst

- **pre-implantation genetic diagnosis (PGD)**



10/22/2008 18:09

# IVF-BABY BOOM



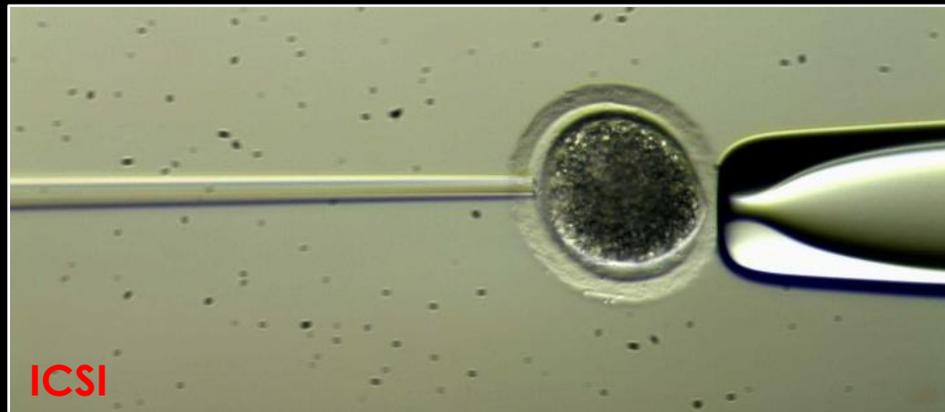
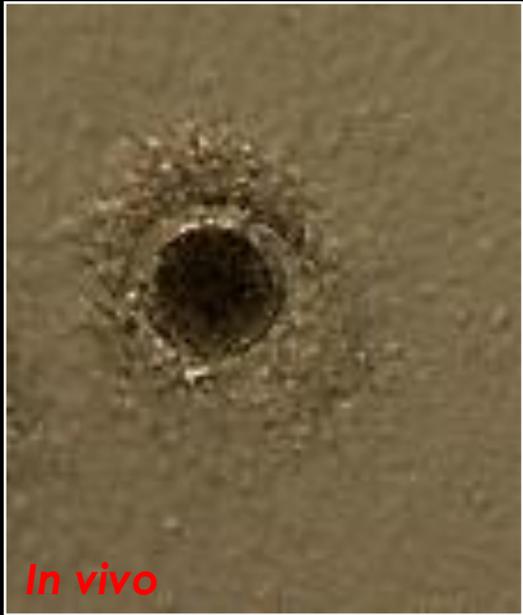
# LOUISE BROWN HAS A BABY!..

- ART seems to be harmless
- Without clinical disorders
- However...



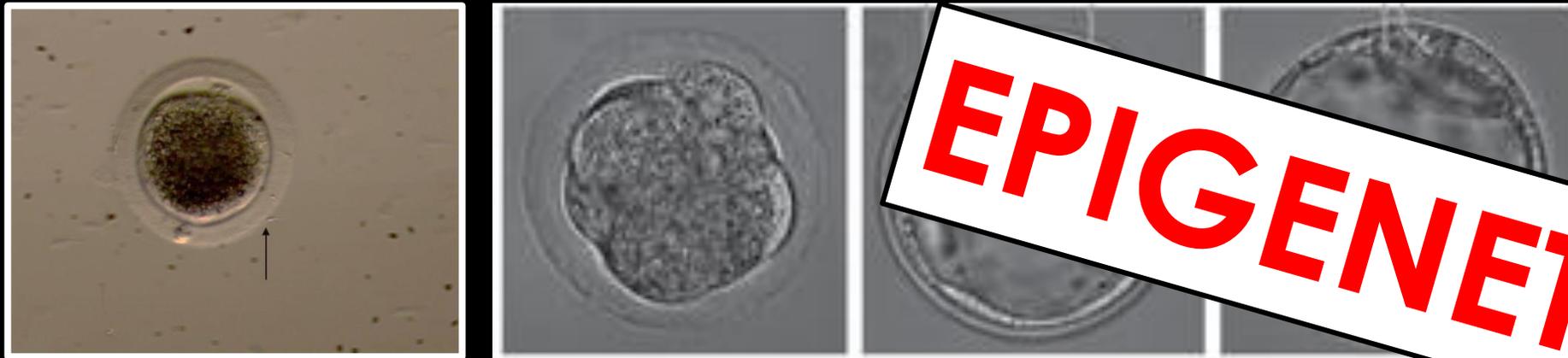
# HOWEVER...

- Why doubt?
  - *In vitro* conditions only simulate optimal *in vivo* environment
  - *In vitro* fertilization artificially remove physiological barrier for sperm selection
  - Genetic sperm defects are not excluded



# WHERE COULD BE A PROBLEM?

- Fertilization = fusion of sperm and oocyte
  - Sperm and oocyte are terminally differentiated cells
  - Furious de-differentiation - totipotent zygote
  - Progressive re-differentiation – embryonic stem cells

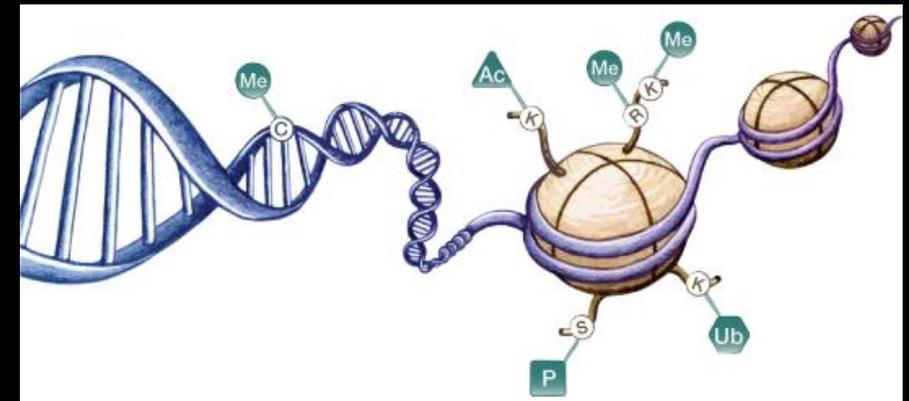
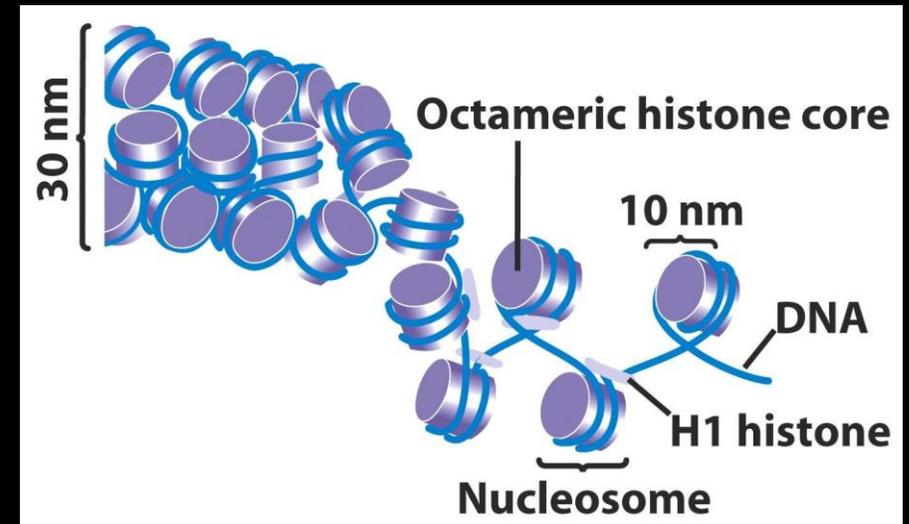


**EPIGENETICS**

- Extremely sensitive period for damage of regulatory mechanism



# EPIGENETICS

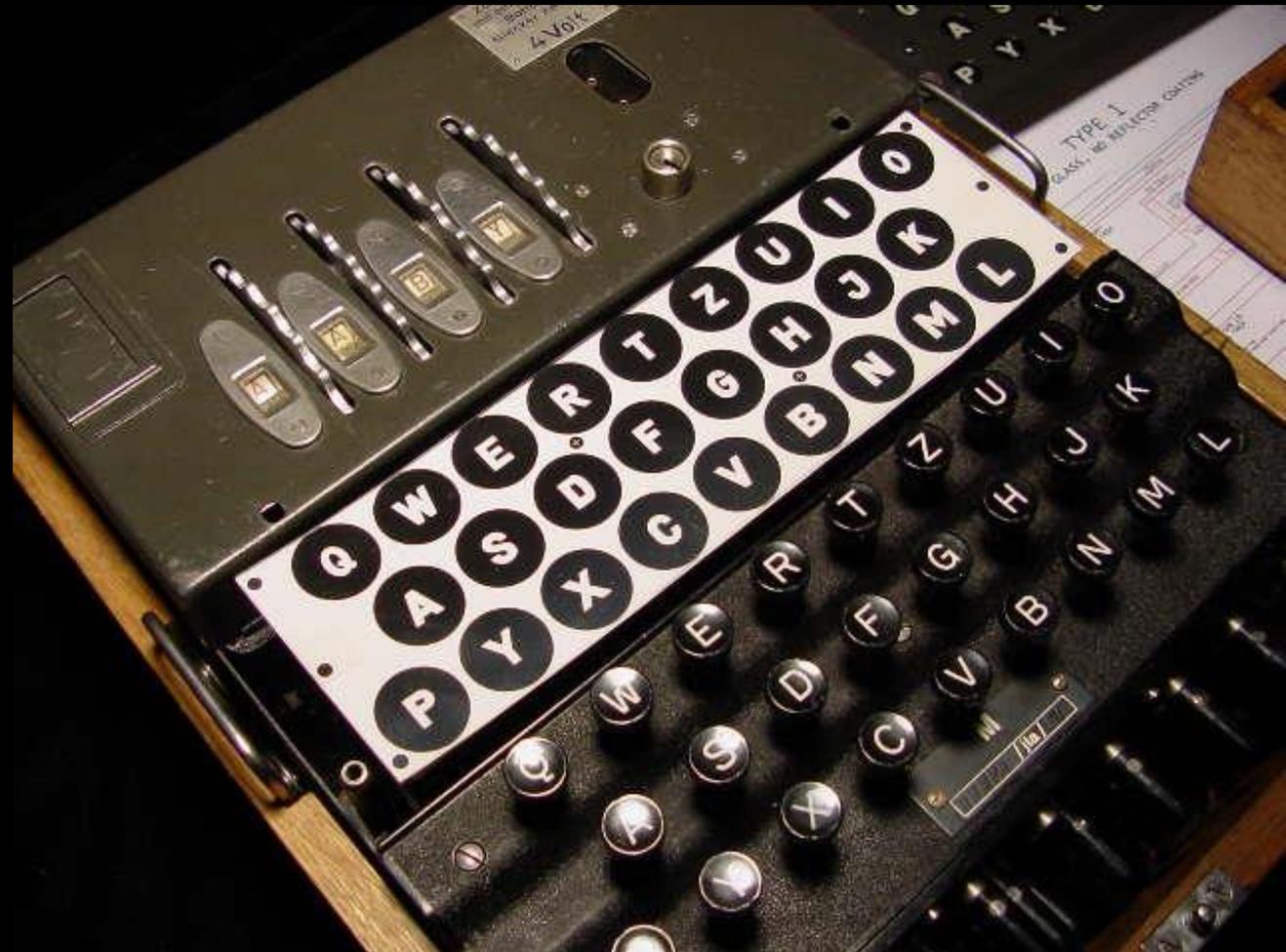


# EPIGENETIC CHANGES DURING EMBRYOGENESIS

- 1) DNA and histone demethylation after fertilization
  - De-differentiation
  - EUCHROMATIN
- 2) DNA re-methylation and **histone code** establishment
  - Stem cell differentiation and further tissue creation
  - X-chromosome inactivation
  - HETEROCHROMATIN

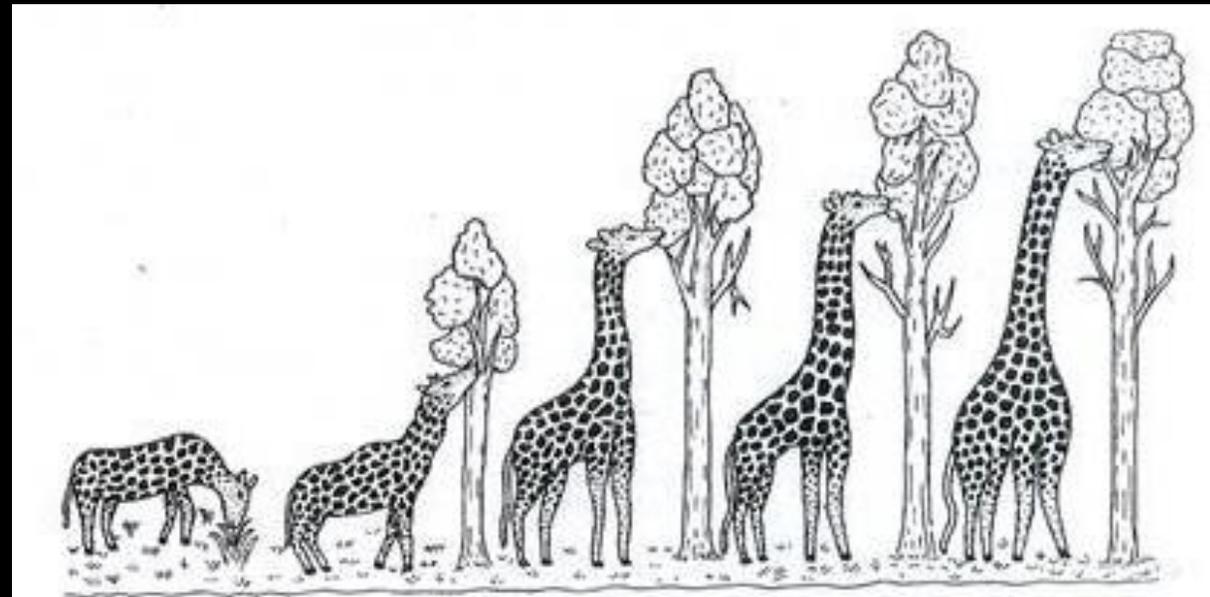
# EPIGENETIC REGULATORS

- DNA methyl transferases
- Histone code
  - Histone methyltransferases
  - Histone acetyltransferases
  - Histone demethylases
  - Histone deacetylases

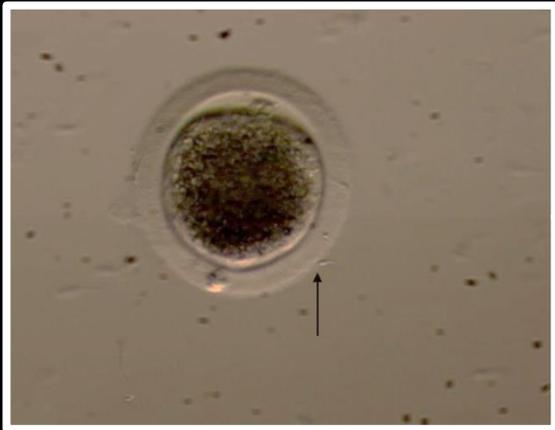


# EPIGENETICS IN SPERM AND TRANSEGENERATIONAL INHERITANCE

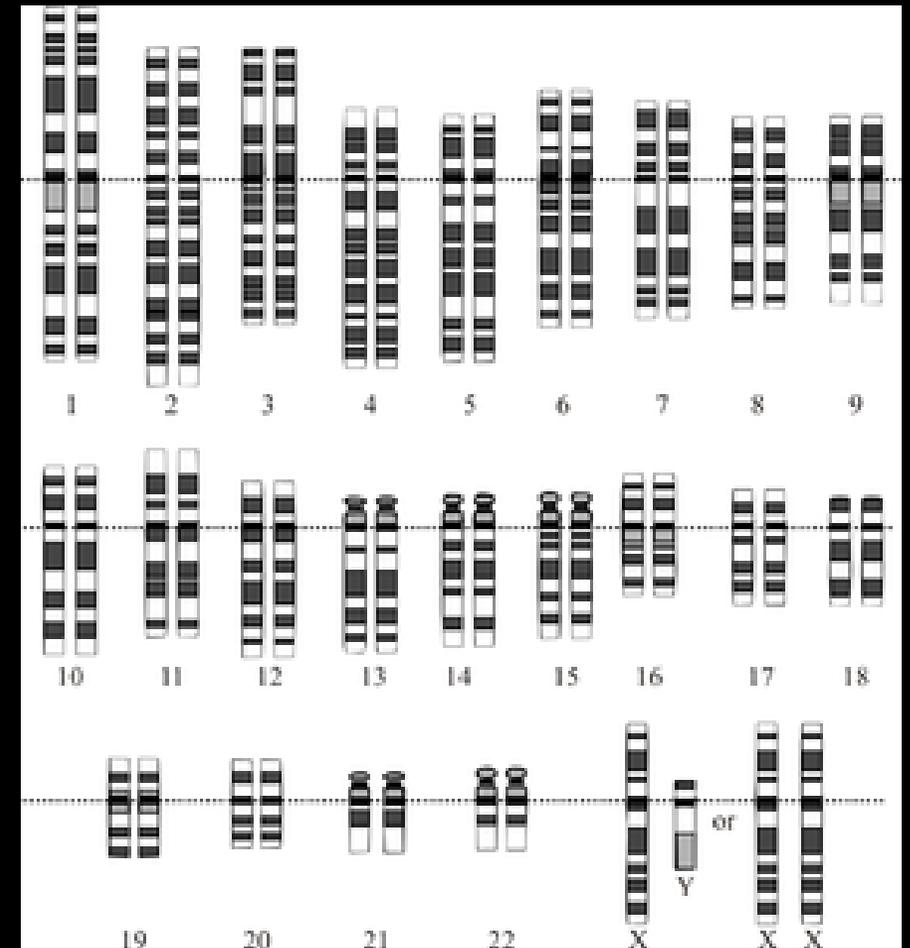
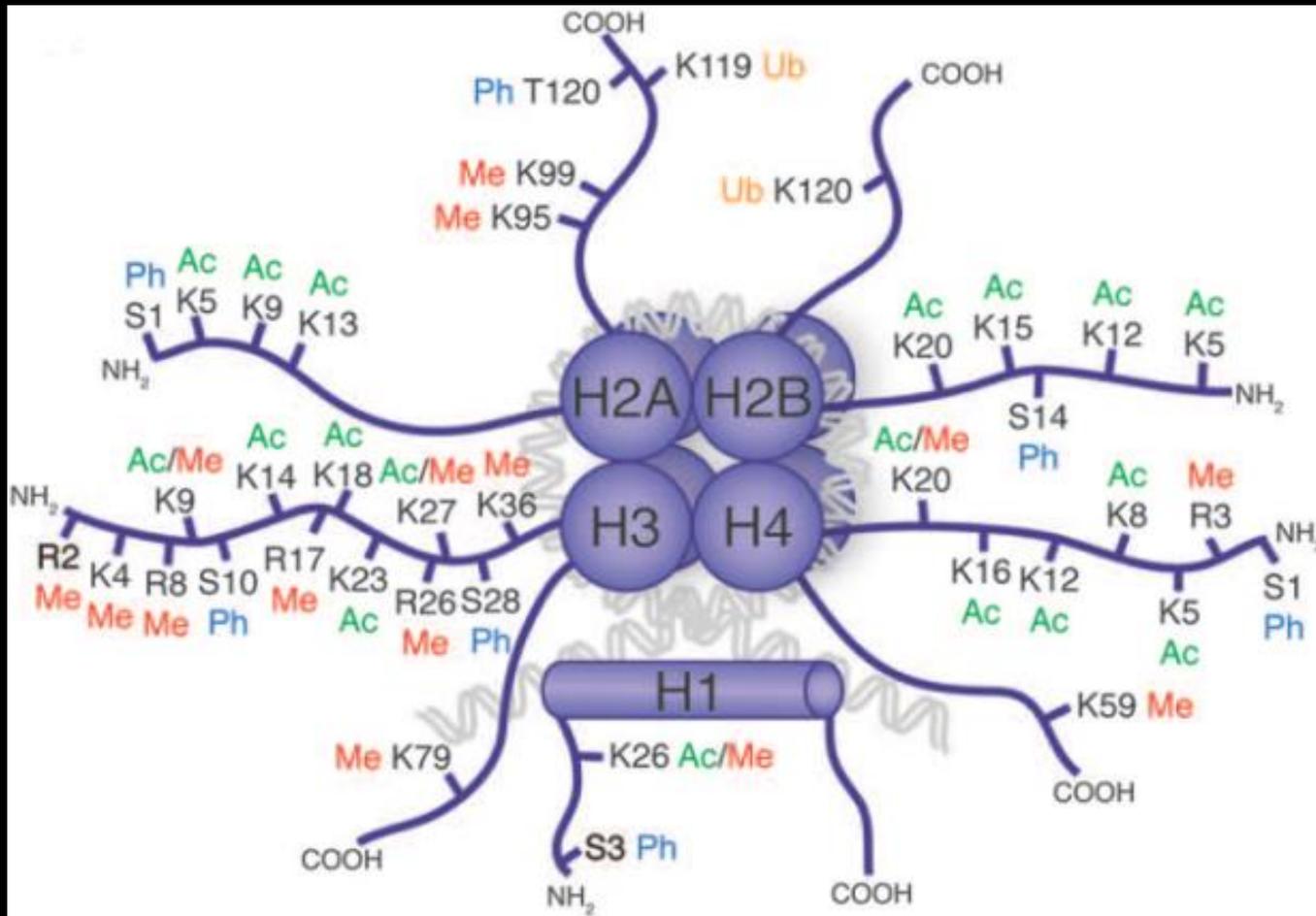
- Sperm-brought small non-coding RNA
- Modifications of residual sperm histone
- Transgenerational inheritance as influence of
  - high-fat diet
  - others
- It doesn't mean resurrection of Lamarckism



# EMBRYO EPIGENETICS AS A RESULT OF OOCYTE AND SPERM CONTRIBUTION

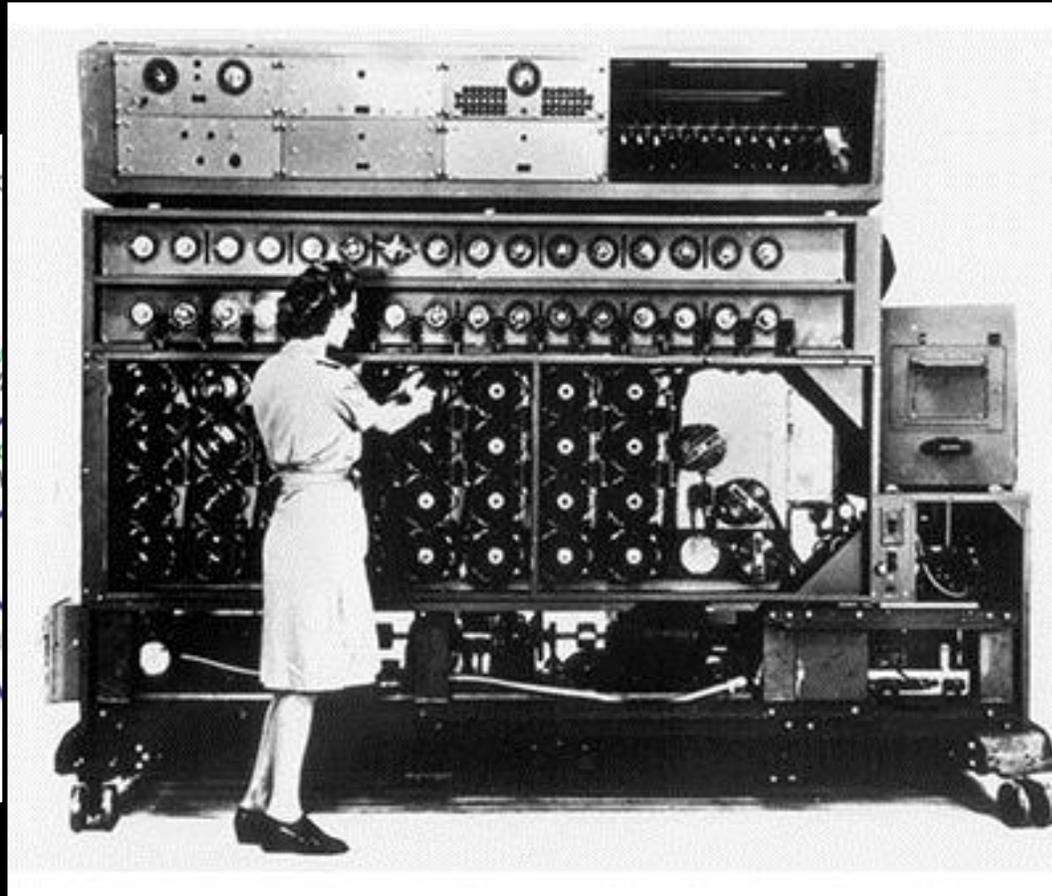
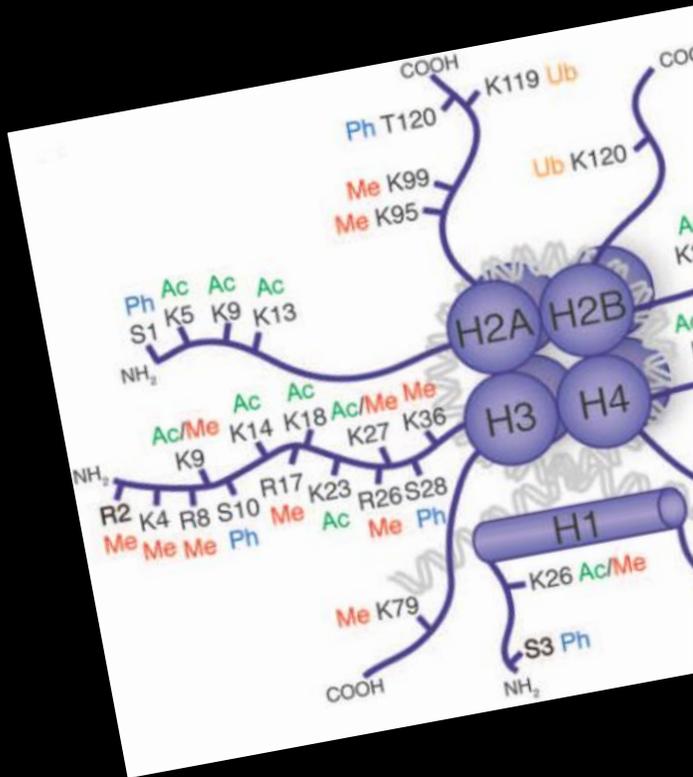


# HISTONE CODE IS SHARED BY BOTH GAMETES



# HISTONE CODE IN EMBRYO

## HAVE WE A DECIPHER MACHINE FOR ITS DECODING?



# AIMS OF THE LAB

- Basic study of gametogenesis, fertilization and embryogenesis, emphasizing epigenetics
  - Mouse model
- Transfer of knowledge to human reproduction
  - Human material
- Development of assessment methods for sperm selection and embryo evaluation
  - Both mice and human

# LABORATORY OF REPRODUCTIVE MEDICINE

Jan NEVORAL, researcher

Olga GARCÍA-ÁLVAREZ, researcher

Miriam ŠTIAVNICKÁ, Ph.D. student

Katka FLEISIGOVÁ, Mgr. student

& Assoc. Prof. Milena KRÁLÍČKOVÁ, senior leader

## ACKNOWLEDGEMENTS

Prof. Jaroslav PETR

Tereza ŽALMANOVÁ, Ph.D.

Kristýna HOŠKOVÁ, Ph.D.

Prof. Peter ŠUTOVSKÝ

Prof. Jean-Francois BODART

Assoc. Prof. Adriana KOLESÁROVÁ

