

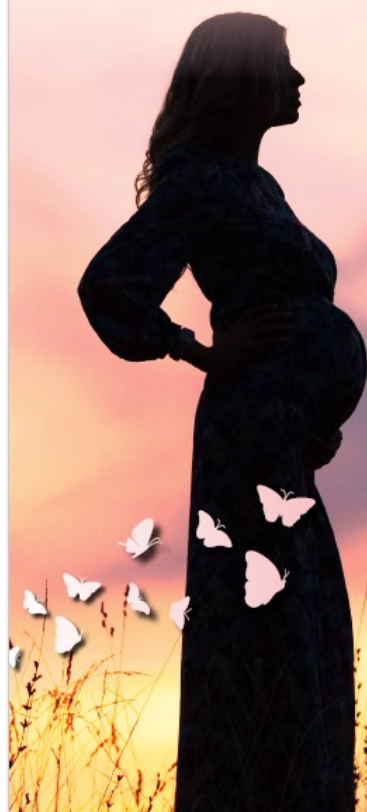


Du jeudi 11 au
vendredi 12 Juin
2026

PALAIS DES CONGRÈS
D'ANTIBES JUAN-LES-PINS
FRANCE

24^{ème}

CONGRÈS INTERNATIONAL
DE GYNÉCOLOGIE
OBSTÉTRIQUE
& REPRODUCTION
DE LA CÔTE D'AZUR



L'Epigénétique dans l'Infertilité



GynAzur
24eme Congres International

11 - 12 Juin 2026

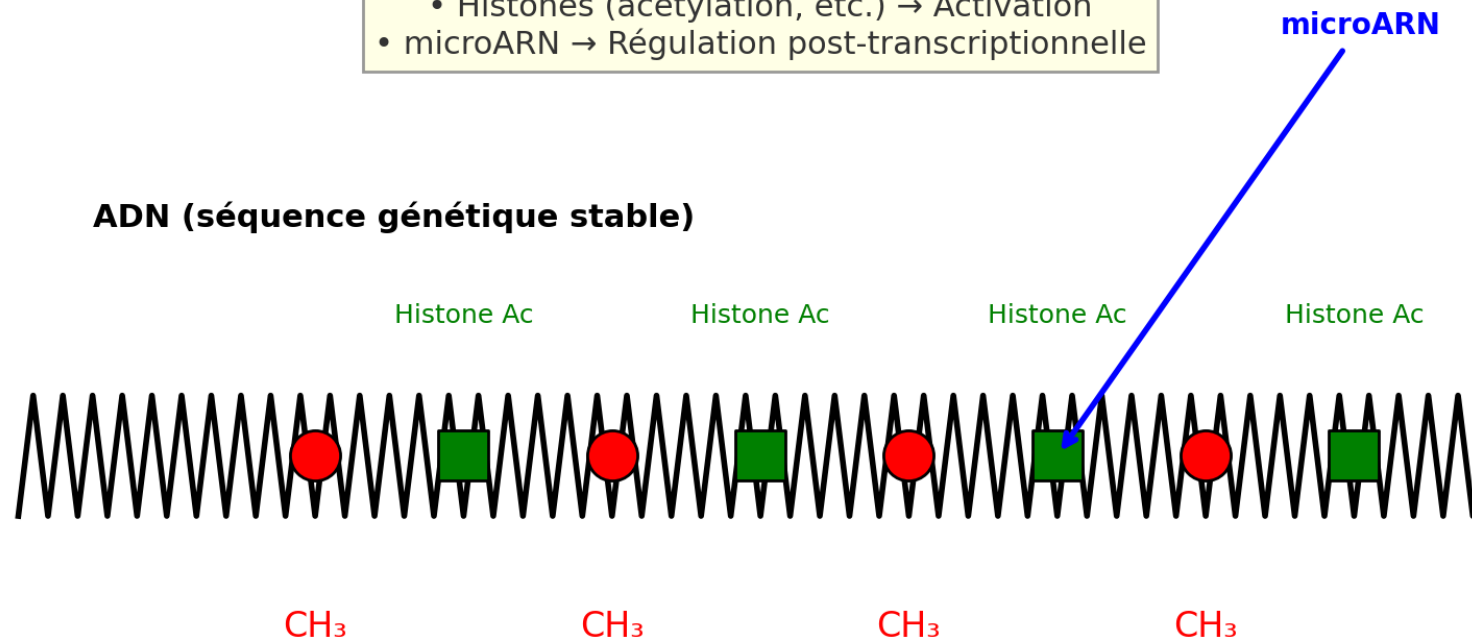
Nino Guy Cassuto ART Unit Drouot Paris



Génétique Stable versus Epigénétique Dynamique

Épigénétique = Régulation dynamique

- Méthylation de l'ADN → Répression
- Histones (acétylation, etc.) → Activation
- microARN → Régulation post-transcriptionnelle



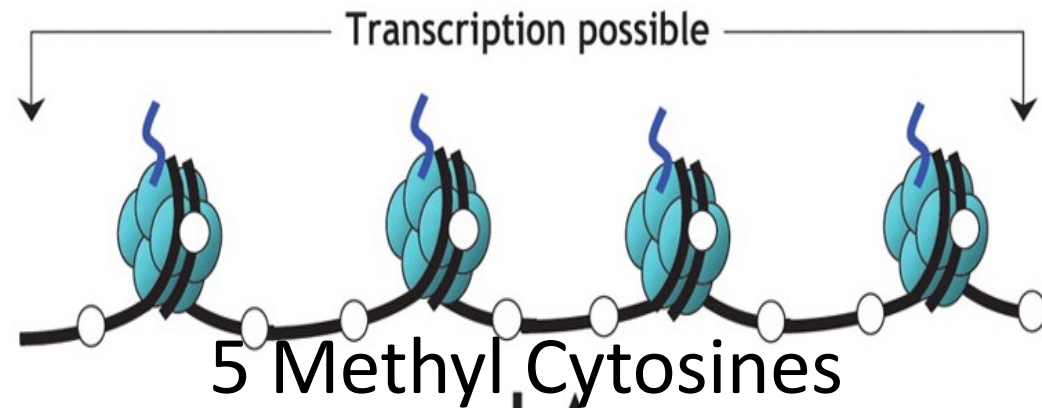
■ Méthylation (répression) ■ Histones (activation) ■ microARN (régulation)



Switched On and Switched Off

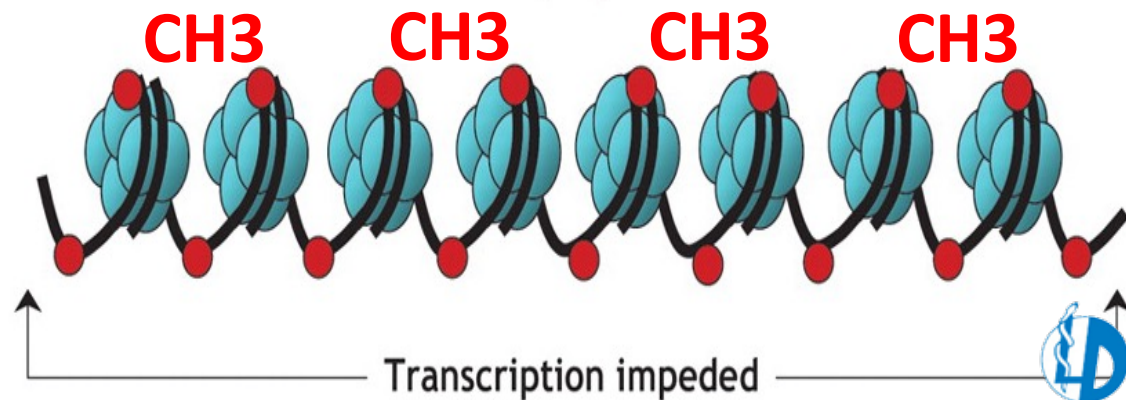
Gene “switched on”

- Active (open) chromatin
- Unmethylated cytosines (white circles)
- Acetylated histones

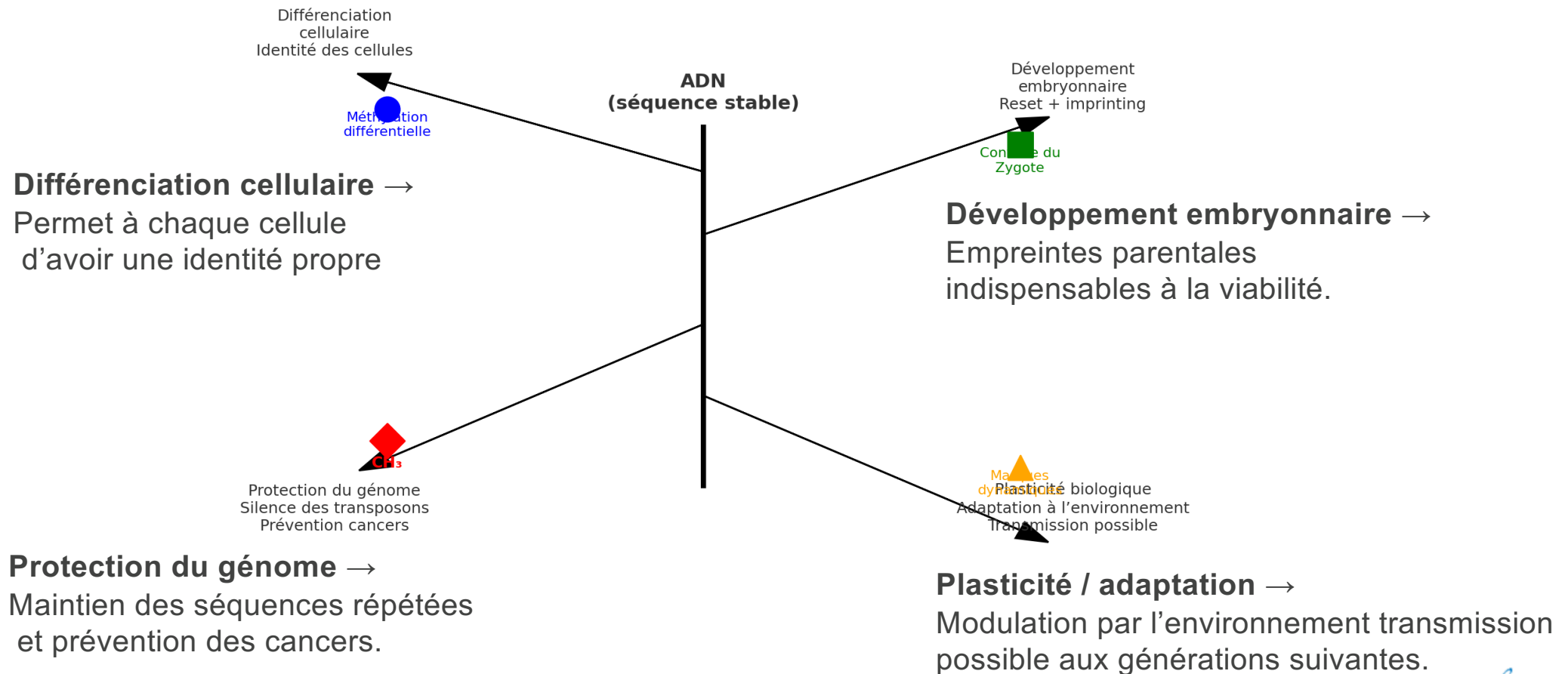


Gene “switched off”

- Silent (condensed) chromatin
- Methylated cytosines (red circles)
- Deacetylated histones



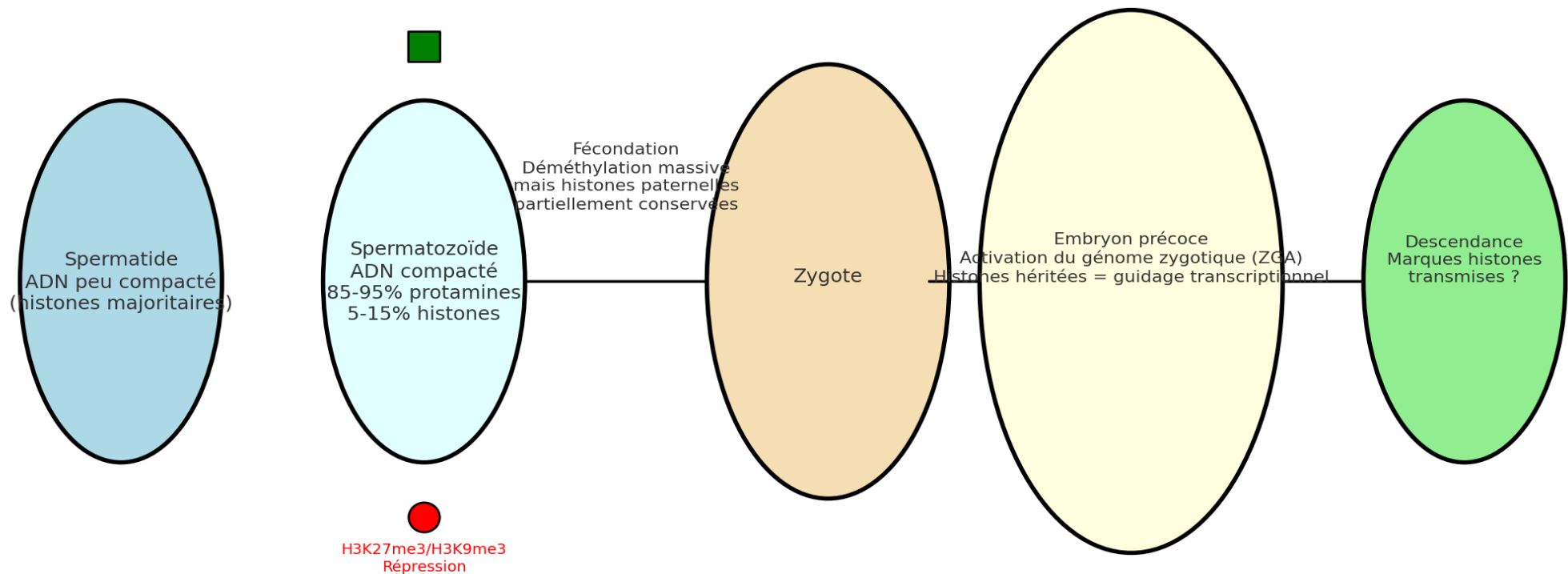
La Méthylation: Une des Clefs de la Vie



Transmission des Histones: de la Spermatogénèse à l'Embryon

Activation: H3K4me3 → gènes actifs **Acétylation H3/H4** → chromatine ouverte, transcription facilitée

H3K4me3
Activation



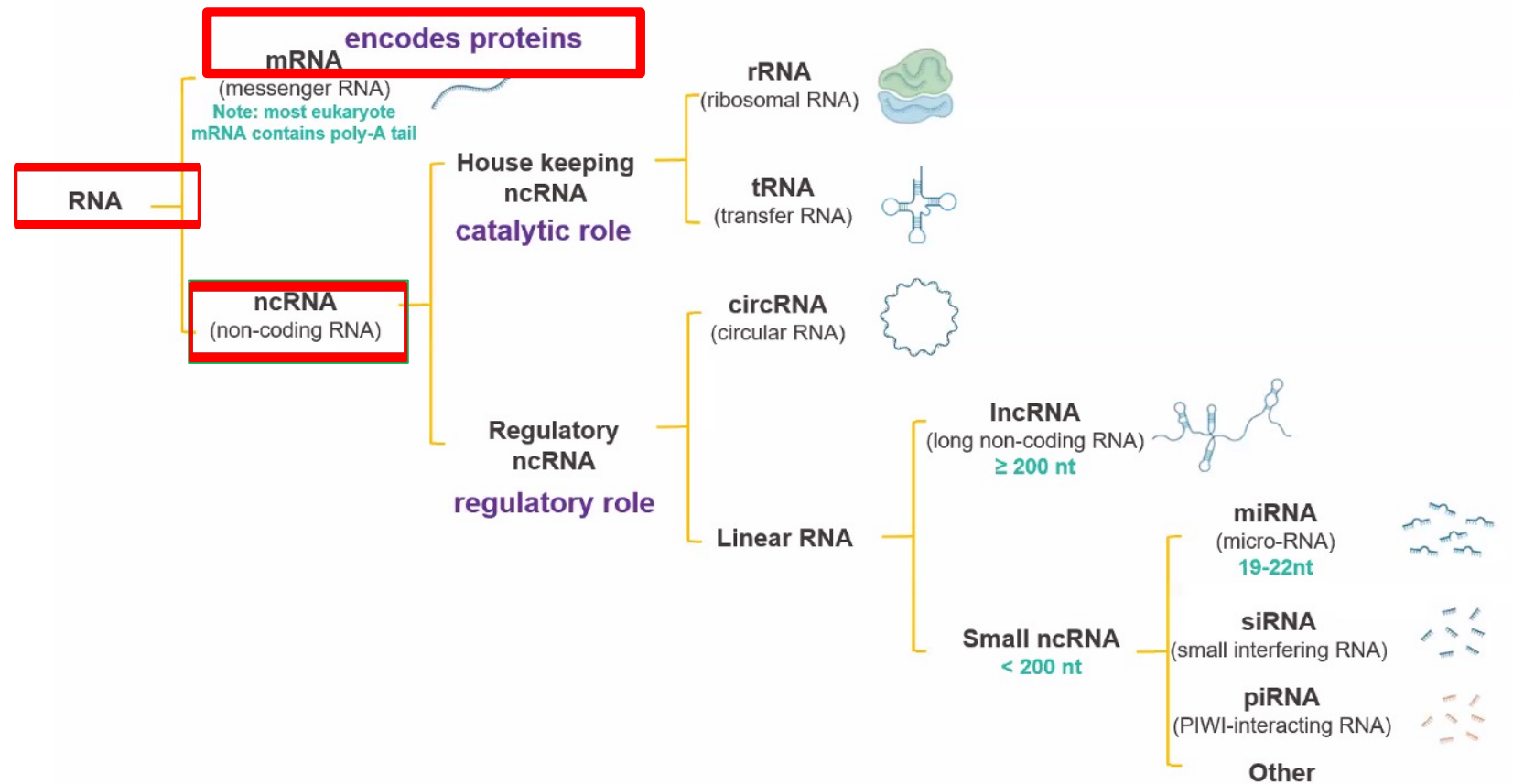
Répression: H3K27me3 → gènes réprimés **H3K9me3** → hétérochromatine silencieuse

Ce système agit comme un **langage chimique**: Décide quels gènes sont accessibles ou silencieux:
Rôle clé dans les spermatozoïdes et l'embryon.

■ Histones d'activation (H3K4me3, H3/H4-Ac) ■ Histones de répression (H3K27me3, H3K9me3)



The transcriptome – Key components



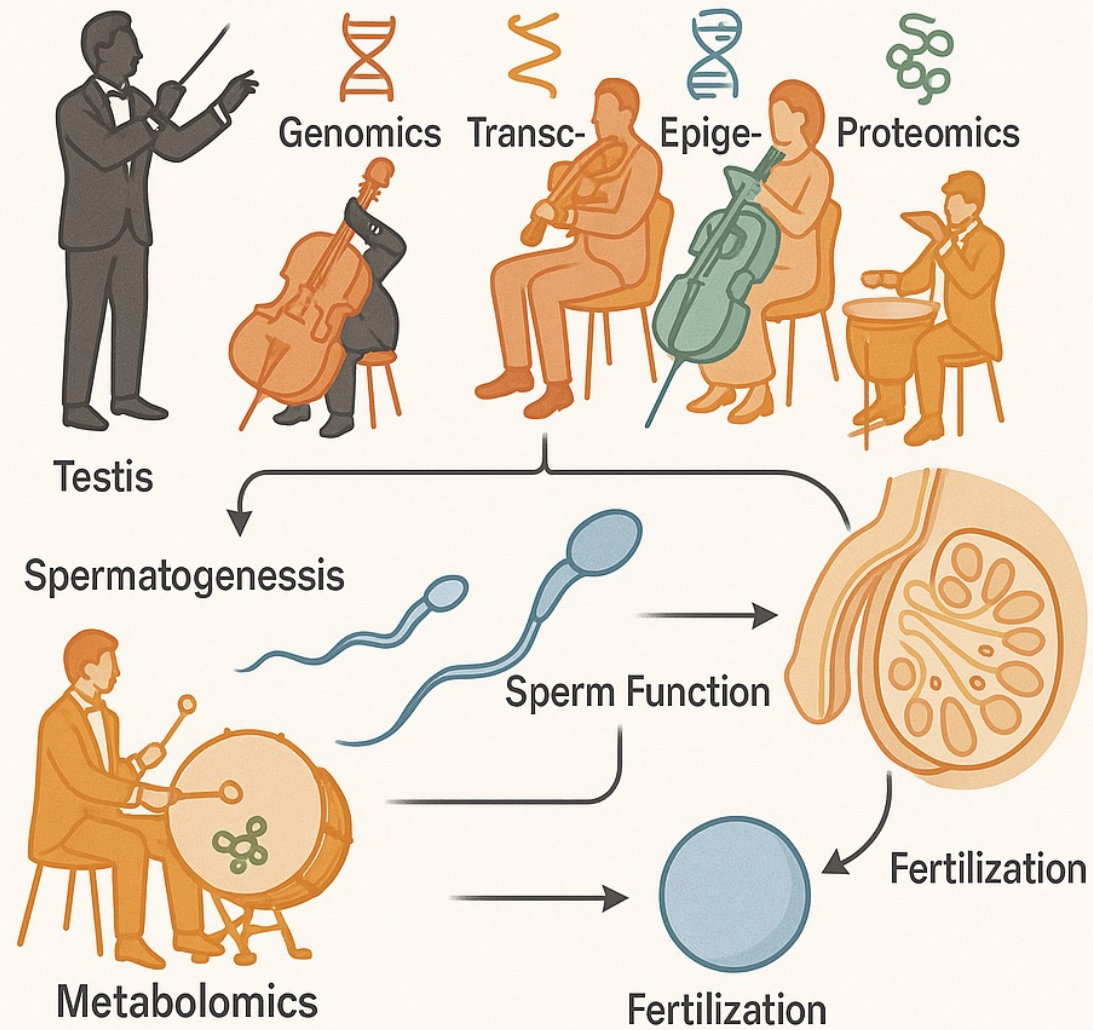


Epigenetic regulation
Orchestrates genes expression

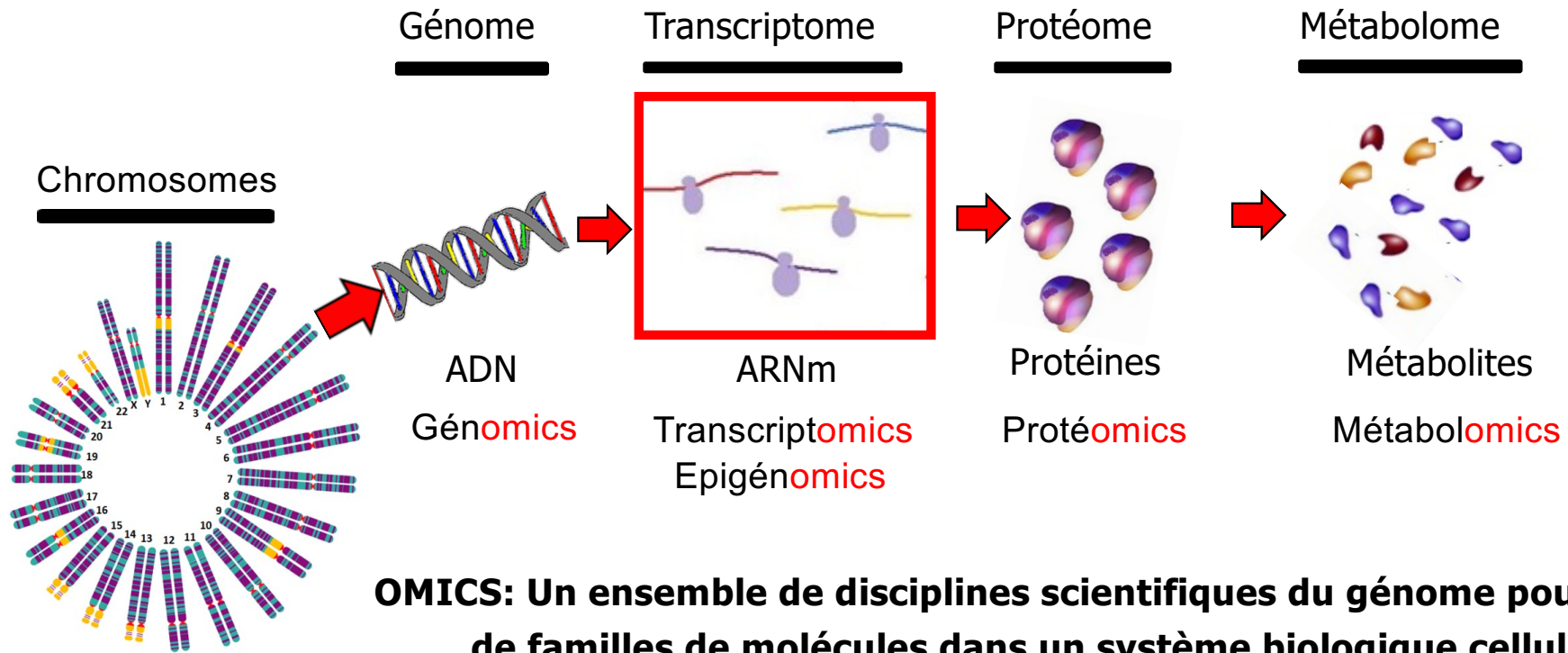
Because epigenetic regulation is not only on a specific-site event
but also spans along stretches of chromosome regions consisting
of clusters of contiguous CpG islands



OMICS ORCHESTRATE MALE FERTILITY



OMICS : Nouveau Temps....Nouvelles Opportunités



OMICS: Un ensemble de disciplines scientifiques du génome pour l'analyse de familles de molécules dans un système biologique cellulaires.

Relient les différentes couches de régulation biologique: **Du Gène à la Fonction**

Qualitative, Quantitative et Fonctionnelle

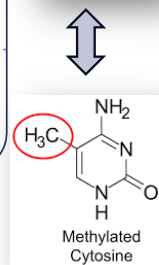
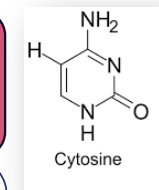
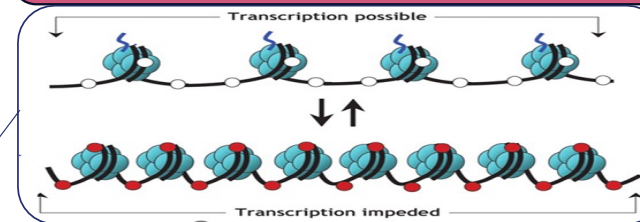


Different Sperm Head Morphology

Same Genetic Information
Same DNA sequences



Different Epigenetic
Profiles Methylation

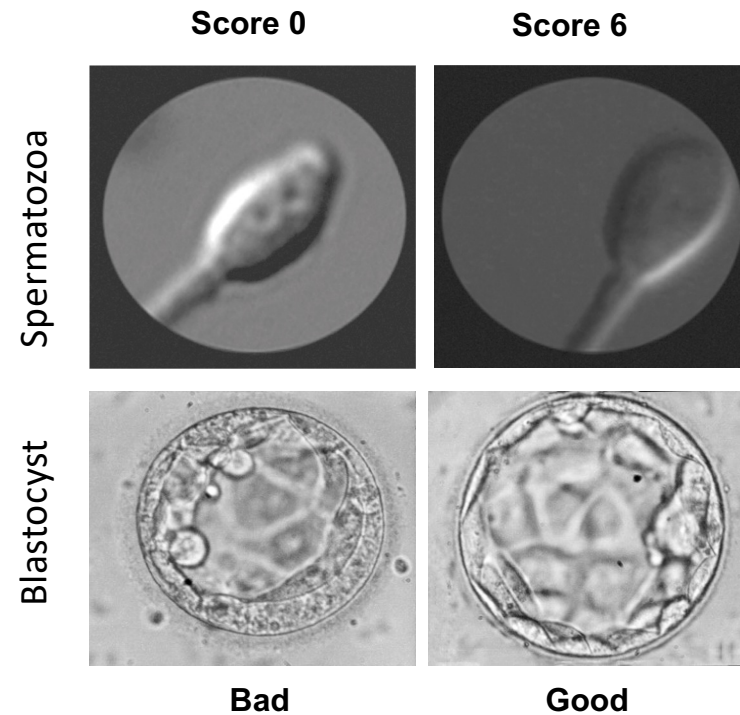


Different Outcome:

- Fertilization
- Blastocysts
- Pregnancies rate and Birth Defect



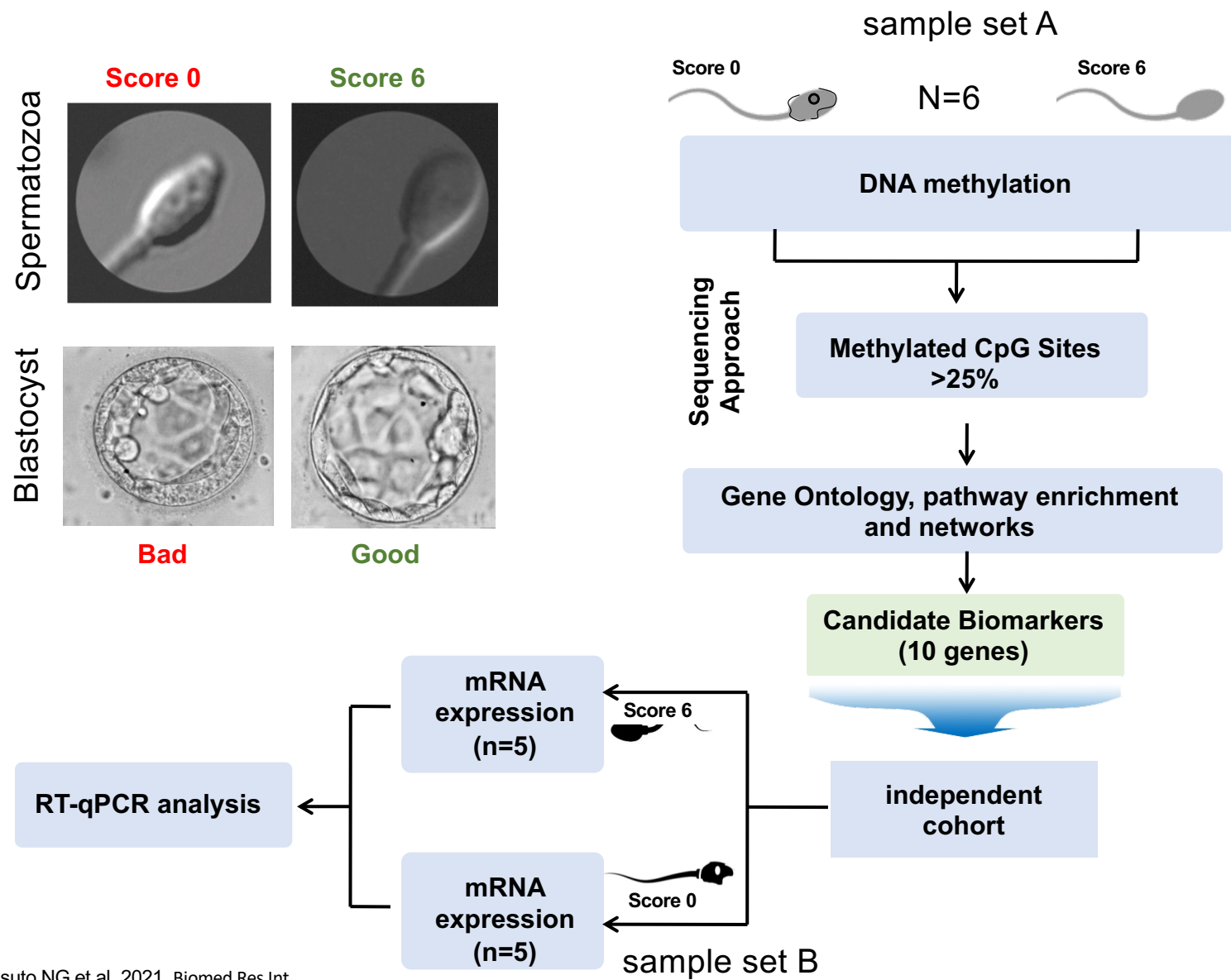
Strict morphological criteria for sperm head

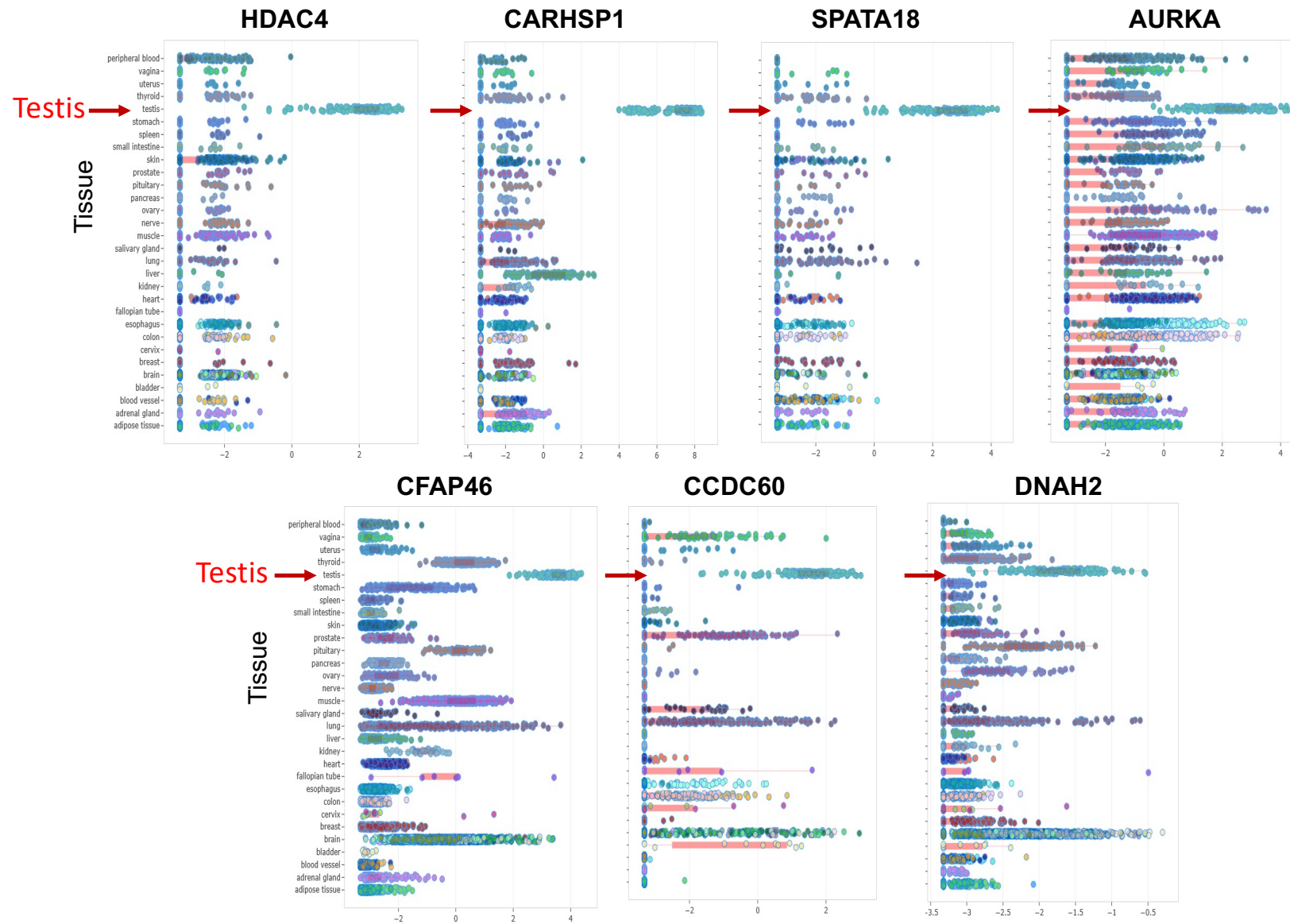


Morphological criteria are used to score spermatozoa at high magnification (6100x) and to assess expanded good blastocyst quality

Cassuto et al., 2021







Cassuto NG et al. 2021, Biomed Res Int

Research Article

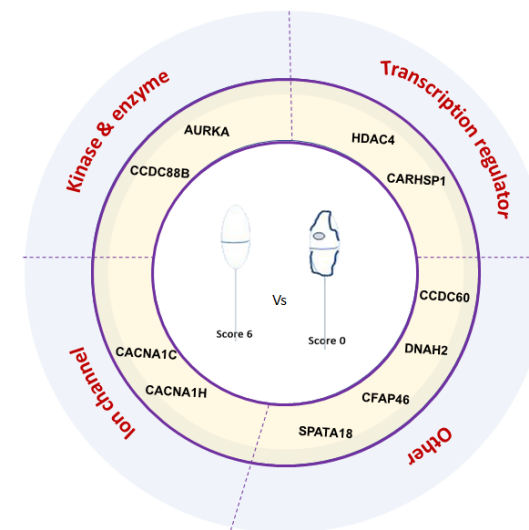
Molecular Profiling of Spermatozoa Reveals Correlations between Morphology and Gene Expression: A Novel Biomarker Panel for Male Infertility

Nino Guy Cassuto ¹, David Piquemal ², Florence Boitrelle ^{3,4}, Lionel Larue ⁵,
Nathalie Lédée ⁶, Ghada Hatem ⁷, Léa Ruoso ¹, Dominique Bouret ¹,
Jean-Pierre Siffroi ⁸, Alexandre Rouen ⁸, and Said Assou ⁹

September 2021

Genes selected by differential methylation level and sperm morphology
with Gene Ontology

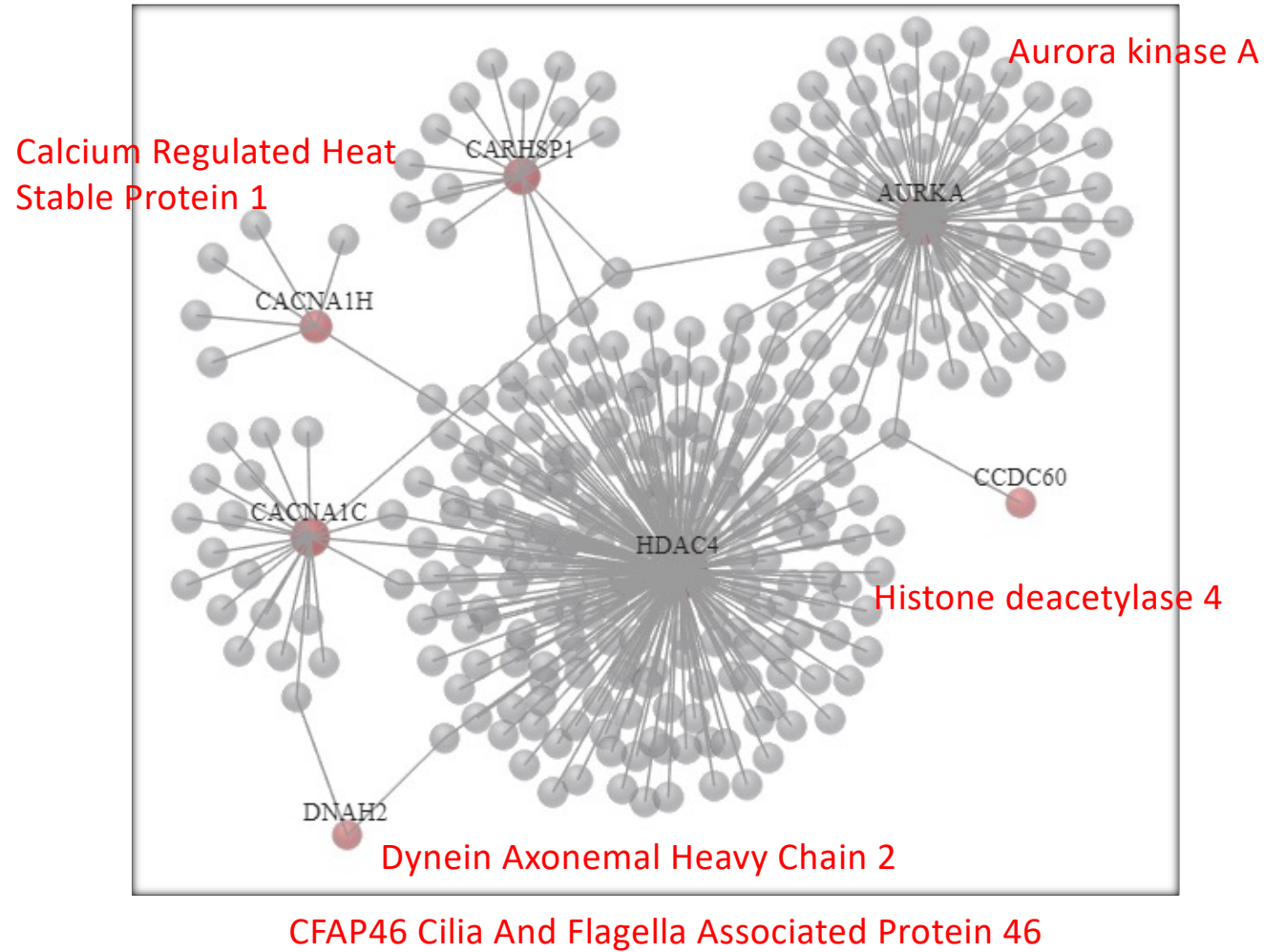
AURKA, HDAC4, CFAP46, SPATA18,
CACNA1C, CACNA1H, CARHSP1,
CCDC60, DNAH2, and CDC88B



Graphical representation of the 10 genes differentially expressed
in score 0 and score 6 spermatozoa.



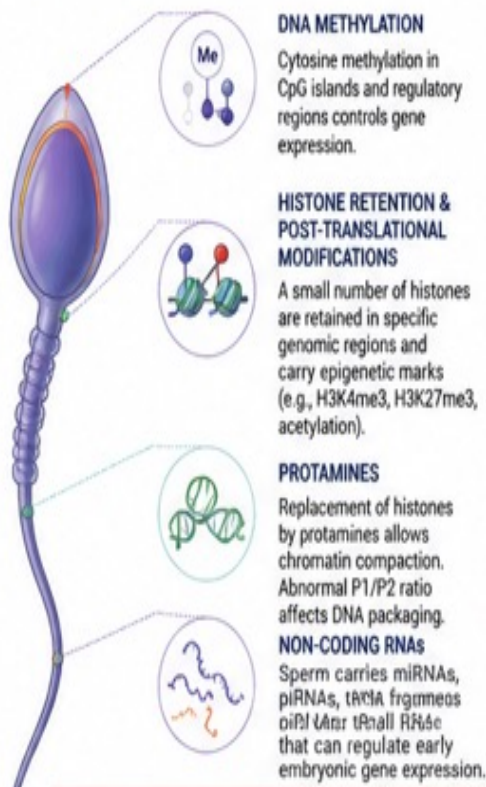
Top-ranked functional protein interaction network



SPERM EPIGENETICS AND IMPLANTATION FAILURE

Paternal epigenetic alterations can compromise embryo competence and reduce the chances of successful implantation

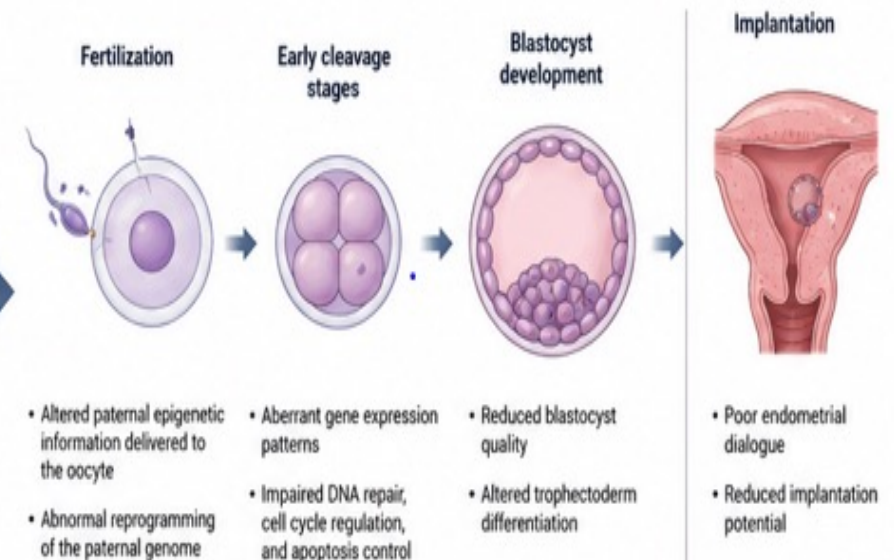
1. SPERM EPIGENETIC LANDSCAPE



2. FACTORS ALTERING SPERM EPIGENETICS



3. CONSEQUENCES FOR THE EMBRYO



4. HOW SPERM EPIGENETIC ALTERATIONS CAN LEAD TO IMPLANTATION FAILURE



GENOME-WIDE DNA METHYLATION CHANGES

Affect key developmental genes and imprinting control regions.



ABNORMAL HISTONE MARKS & RETENTION

Disturb chromatin organization and transcription of genes critical for development.



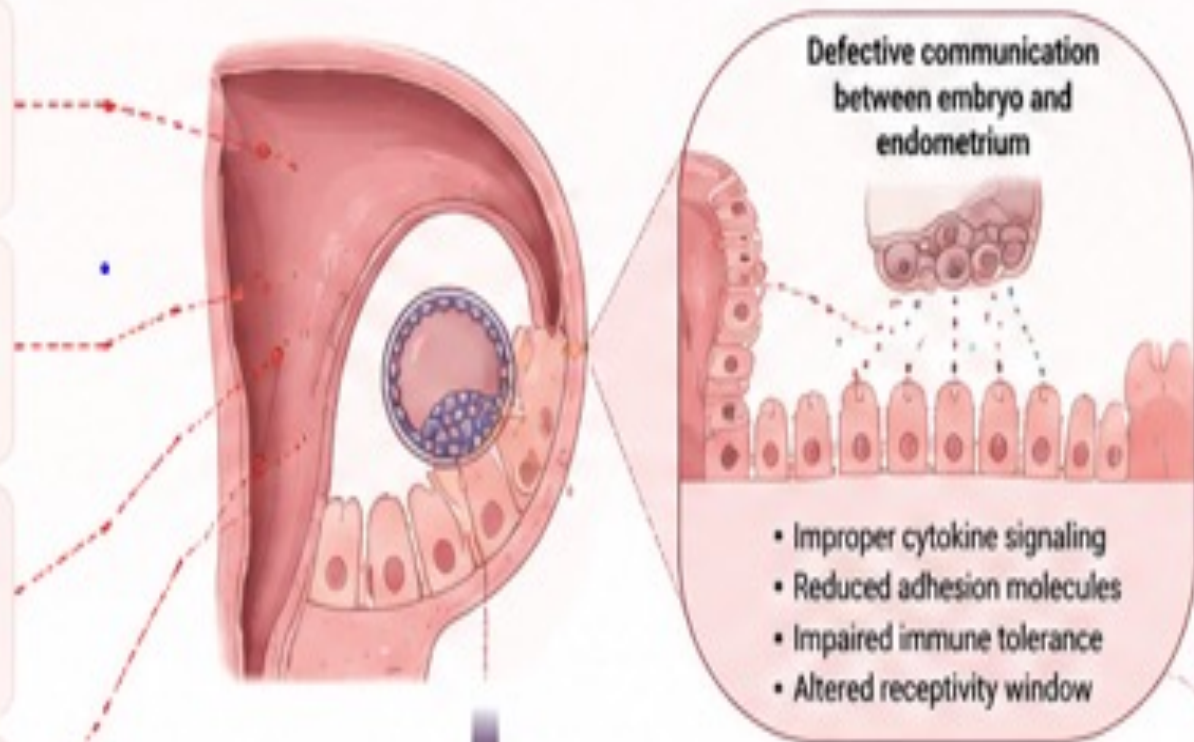
PROTAMINE DEFICIENCY & DNA DAMAGE

Increase DNA fragmentation, impaired chromatin integrity, and reduced embryo viability.



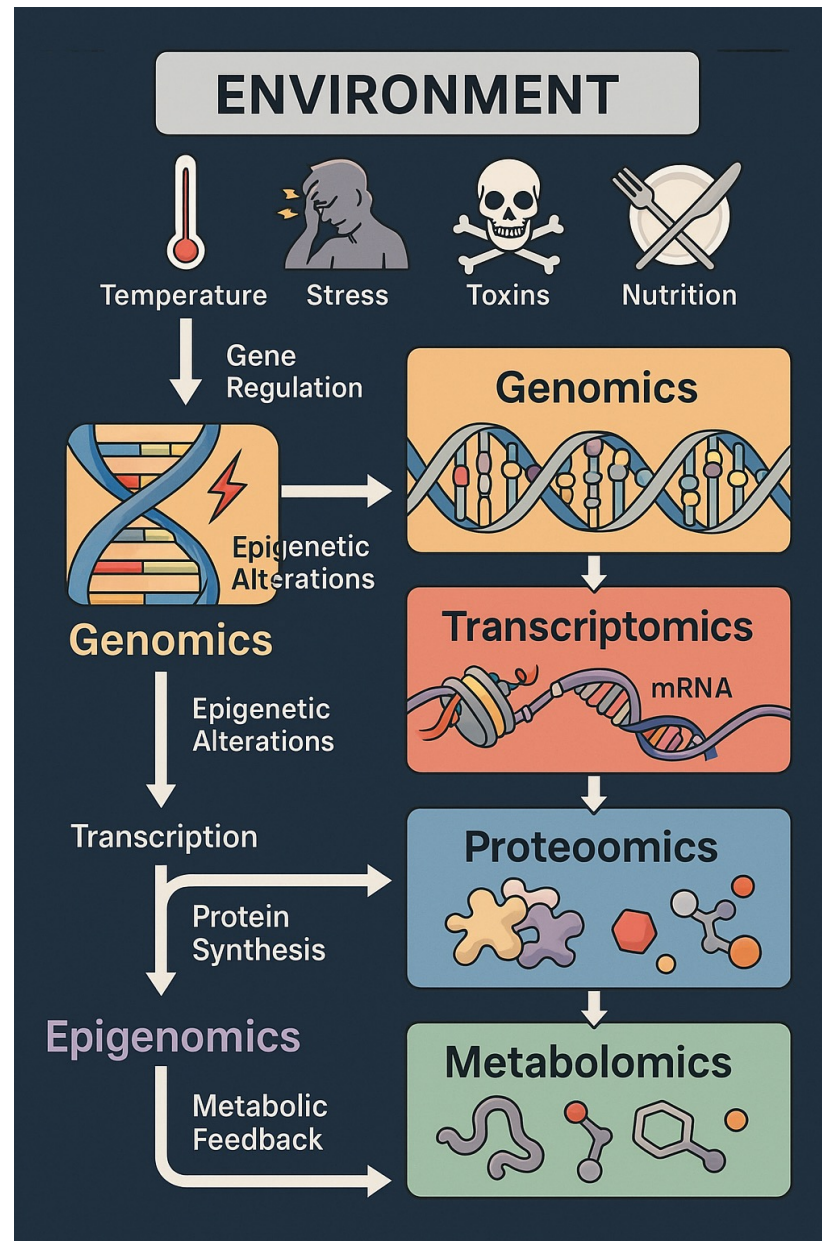
ALTERED SMALL RNA PROFILES

Dysregulation of miRNAs/piRNAs involved in gene regulation, cell proliferation and apoptosis.



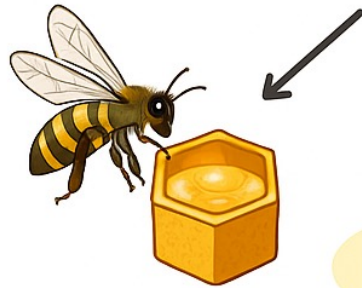
IMPLANTATION FAILURE
(Biochemical pregnancy loss or no implantation)



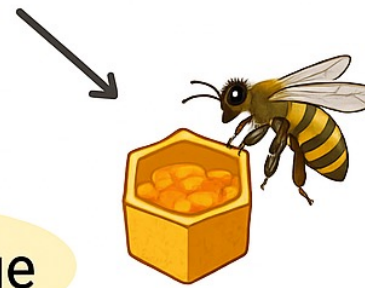


GENOME IDENTIQUE

↓
environnement et alimentation



gelée royale



pollen, miel

Épigenétique



2 à 5 ans
Ovaires: 2 000 œufs/jour

REINE



4 à 6 semaines
Ovaires: Atrophiés-Stériles

OUVRIÈRE



GENOMICS



TRANSCRIPTOMICS



EPIGENOMICS



PROTEOMICS



METABOLOMICS



AI



**SPERM
SELECTION**



Intelligence artificielle en routine au laboratoire : choix des gamètes **AI in a routine laboratory work: Gametes' selection**

l'IA permet d'établir des liens avec des profils épigénétiques d'expression génique.
Cette technologie s'intègre de manière efficace et éthique dans les pratiques de routine de biologie de la reproduction

Nino Guy Cassuto
Laboratoire Drouot, Paris, France

Médecine de la Reproduction, vol. 27, n° 2, avril-mai-juin 2025



AI needs huge data! It's a hungry giant!!!



Data: 800 hours of videos:
More than 3 months in continued vision

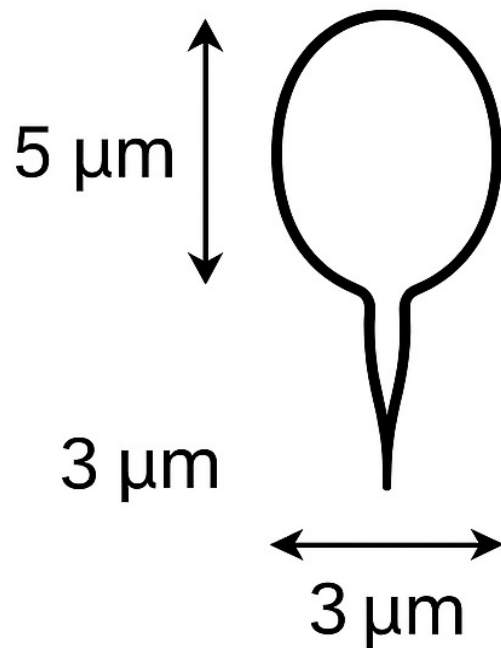
Sorted: 15 000 frames were randomly
captured

Arranged: by embryologist experts
labeling and classified

Presented visually on the screen
Machine learning / Deep learning
Teach the machine to do the job

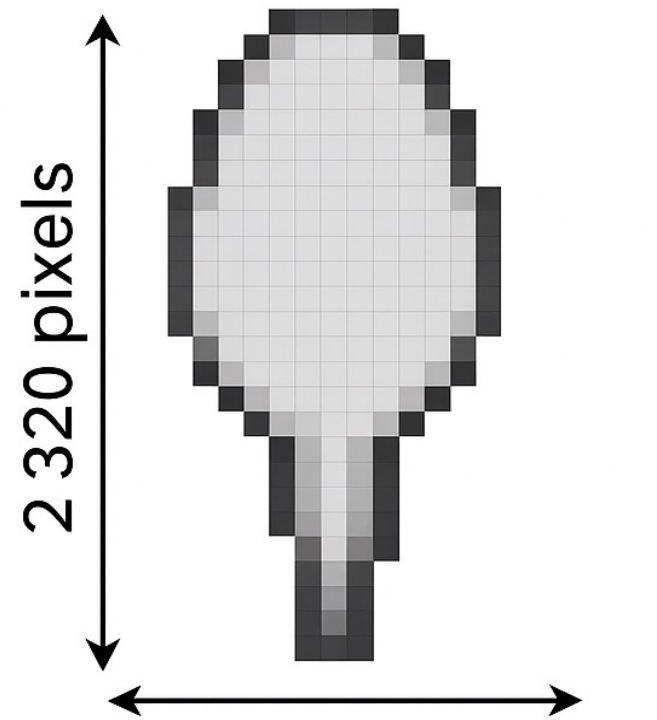


Grossissement optique projette l'image
du SPZ sur le capteur de la caméra
 $3,45 \mu\text{m} \times 1600 = 0,00215625$



Surface réelle: $15 \mu\text{m}^2$

Grossissement : $1600\times$
Surface projetée : $38,4 \text{ mm}^2$



$\approx 3\ 224\ 800$ pixels

Caméra numérique Haute Résolution ayant des pixels de $3,45 \mu\text{m}$



HOW IT'S WORK



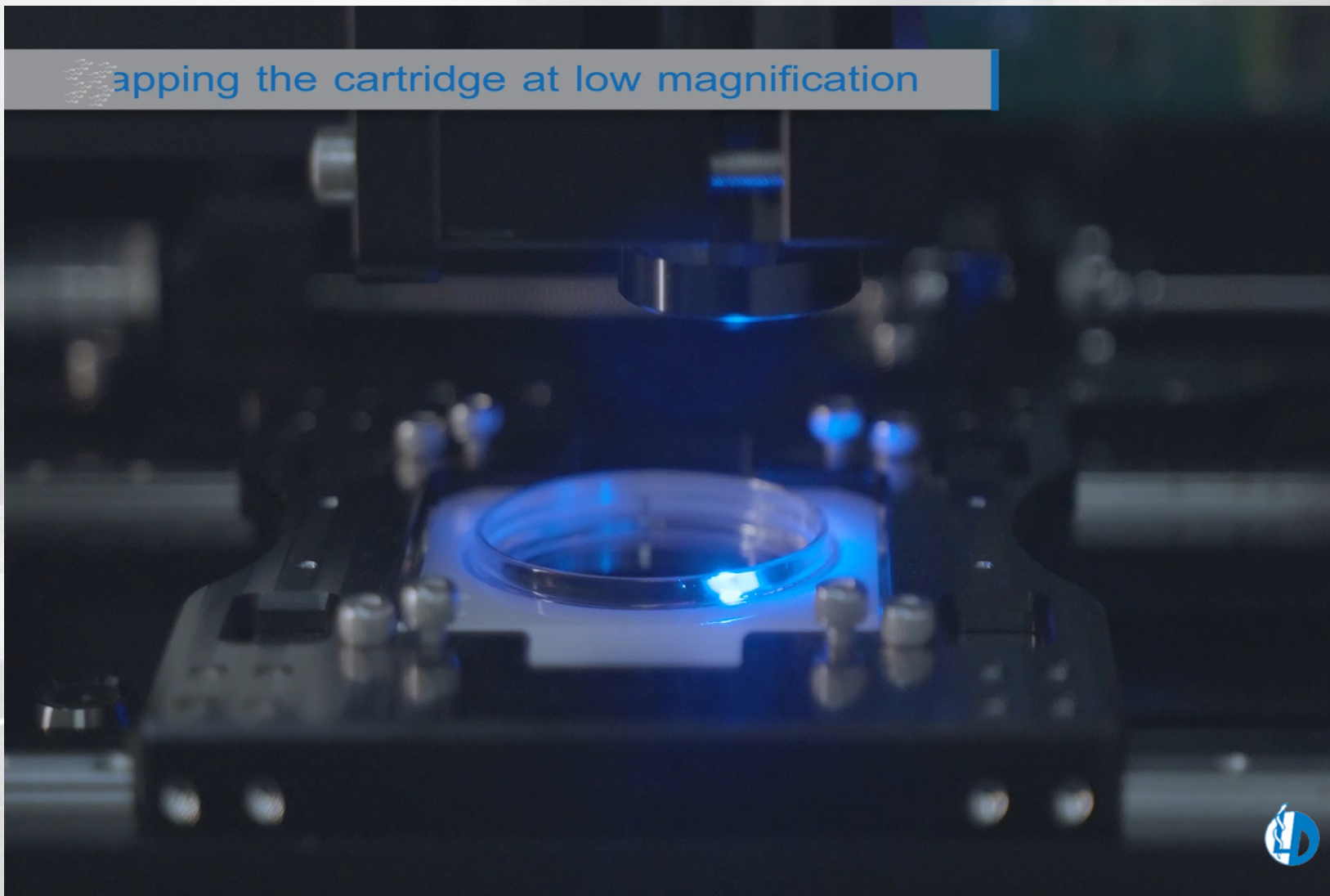
30 frames /Seconds

Control Panel of the system and Codes for all the system generated by AI





Mapping the cartridge at low magnification



AN AUTONOMOUS AI-ASSISTED ROBOTIC SYSTEM FOR SPERM SELECTION RESULTING IN CLINICAL PREGNANCY

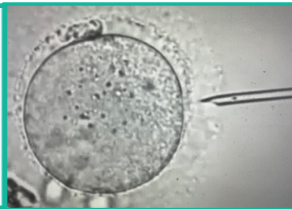
L. RUOSO¹, B. Meiri Ferber², A. Shulman², N.G. Cassuto¹

¹ Laboratory DROUOT, IVF, Paris, France – ² Assuta MC, In Vitro Fertilization, Tel Aviv, Israël

BACKGROUND

In ICSI, sperm selection is still driven largely by subjective human judgment, introducing variability that may impair early embryo development, reduce the number of high-quality blastocysts, decrease pregnancy rates, and, in rare cases, contribute to congenital anomalies

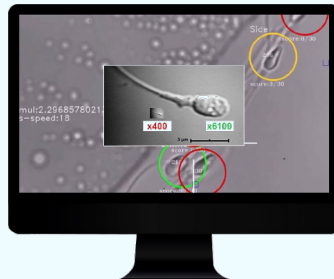
A fully automated approach offers the potential to replace inconsistency with precision, reproducibility, and improved clinical performance



METHOD

AI algorithm classifies sperm cells morphology at high magnification

- Deep learning models, trained on over 20,000 high-magnification frames independently annotated by at least 2 senior embryologists, process a video stream of motile spermatozoa in real time
- The system analyzes 30 high-magnification frames per second to select sperm cells, evaluating them from different angles using its algorithm based on their morphology, size, and motility according to all WHO manual (6th ed.) criteria
- A motorized submicron X-Y stage maintains selected sperm cells in the center of the field of view
- Selected sperm is then aspirated by a micropipette connected to a patented pump and moved to a separate collection droplet from which it is used for ICSI



SAIBYS
Select with care

RESULTS

Preliminary report in **3 couples** with recurrent implantation failure:

- Female ages: 32, 37, 41 years old
- Ovarian stimulation with an antagonist

The operator confirmed the required number of spermatozoa, after which the system autonomously performed sperm tracking, selection, aspiration, and transfer to a clean droplet without manual manipulation.

The selected spermatozoa were then re-evaluated under high magnification to confirm strict morphology criteria and progressive motility before immobilization and ICSI

Outcomes

- All injected oocytes were successfully fertilized
- Two patients underwent fresh embryo transfer, and one patient produced two high-quality blastocysts that were vitrified
- A clinical pregnancy was achieved in the 37-year-old patient, whereas the 41-year-old patient did not conceive

CONCLUSIONS

- An AI-driven autonomous robotic system may enable standardized, operator-independent sperm selection and automated physical pickup of selected sperm cells
- By integrating morphological, motility, and epigenetic criteria, this approach may improve reproducibility and clinical outcomes in routine ICSI.
- A multinational randomized controlled trial is currently underway to evaluate its impact on fertilization, blastocyst development, and pregnancy rates.

Conclusions

Morphology is correlated with the DNA quality;

- ☑ Sperm selection before ICSI is a crucial step;
because we are at the beginning of the process.

Autonomous sperm selection system;

- ☑ based on DNA quality and epigenetic profiles.

Using AI combined with Micro Robotic.

- ☑ **Sperm epigenetics opens new opportunities for future research and clinical innovation in reproductive medicine**





MERCI

