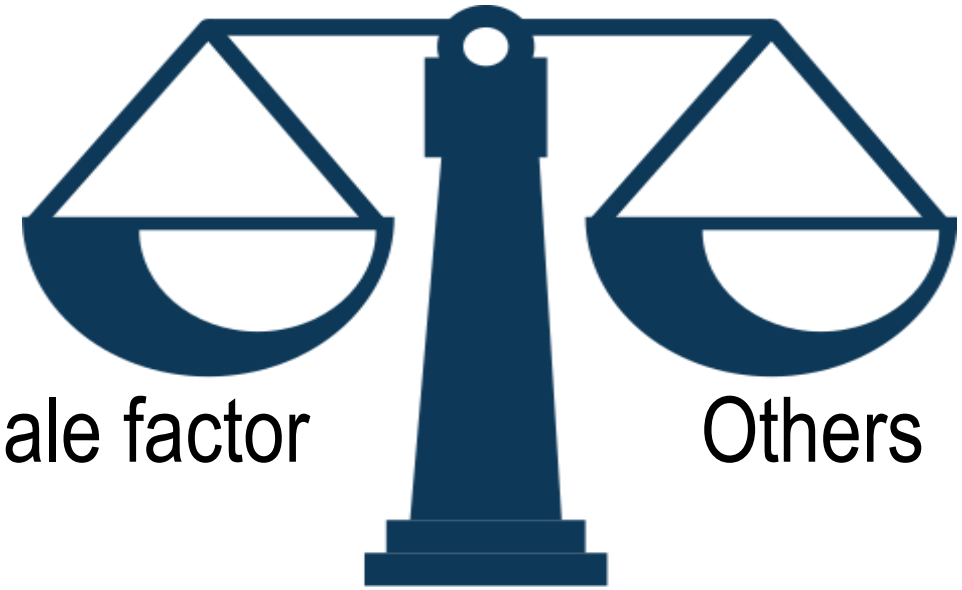
Oocyte ability to repair sperm DNA fragmentation: The effect of maternal age on ICSI outcomes

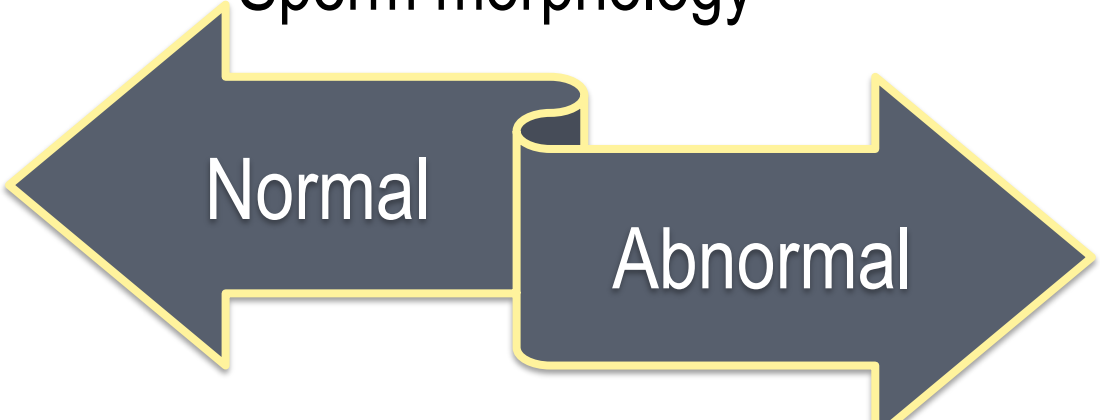
Edson Borges Jr., Daniela Paes de Almeida Ferreira Braga, Amanda Setti, Rodrigo Rosa Provenza, Assumpto Iaconelli Jr.

INTRODUCTION

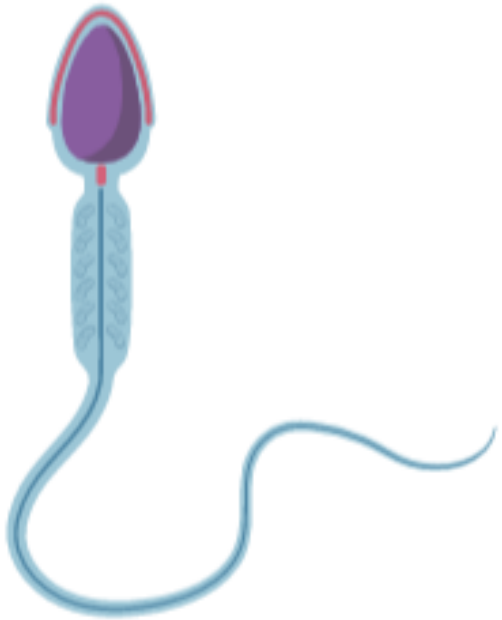
Infertility: 15% of the couples

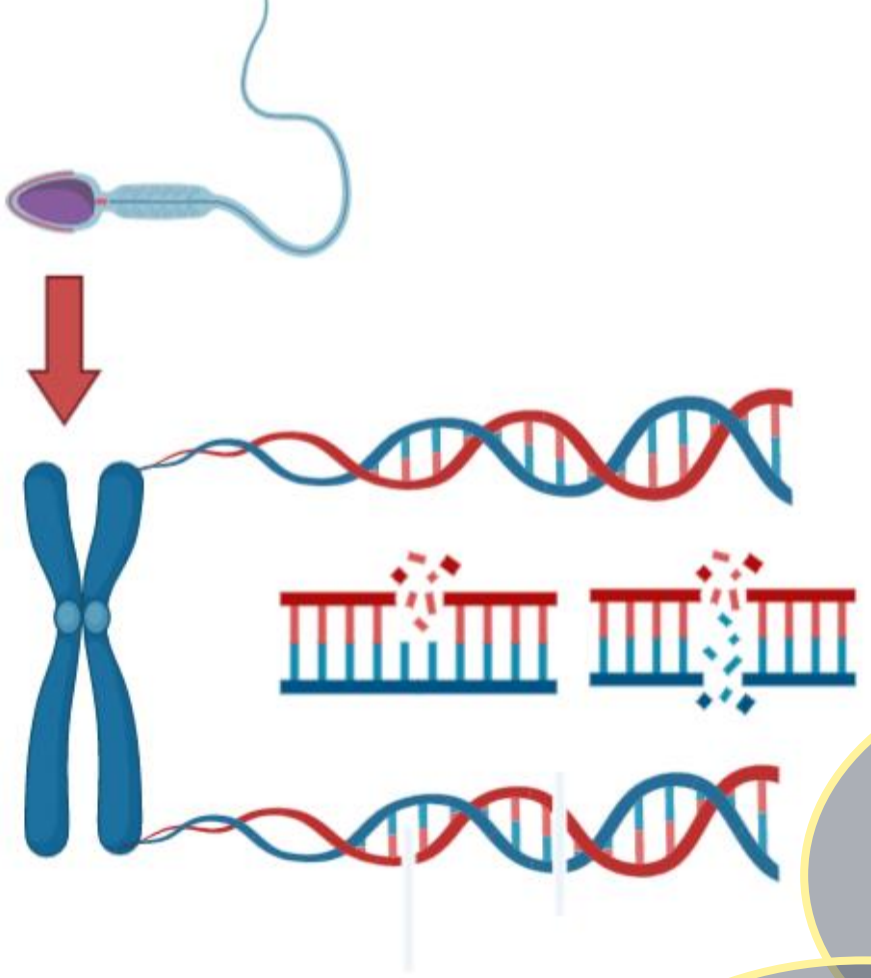


- Sperm Volume
- Sperm count
- Sperm motility
- Sperm morphology



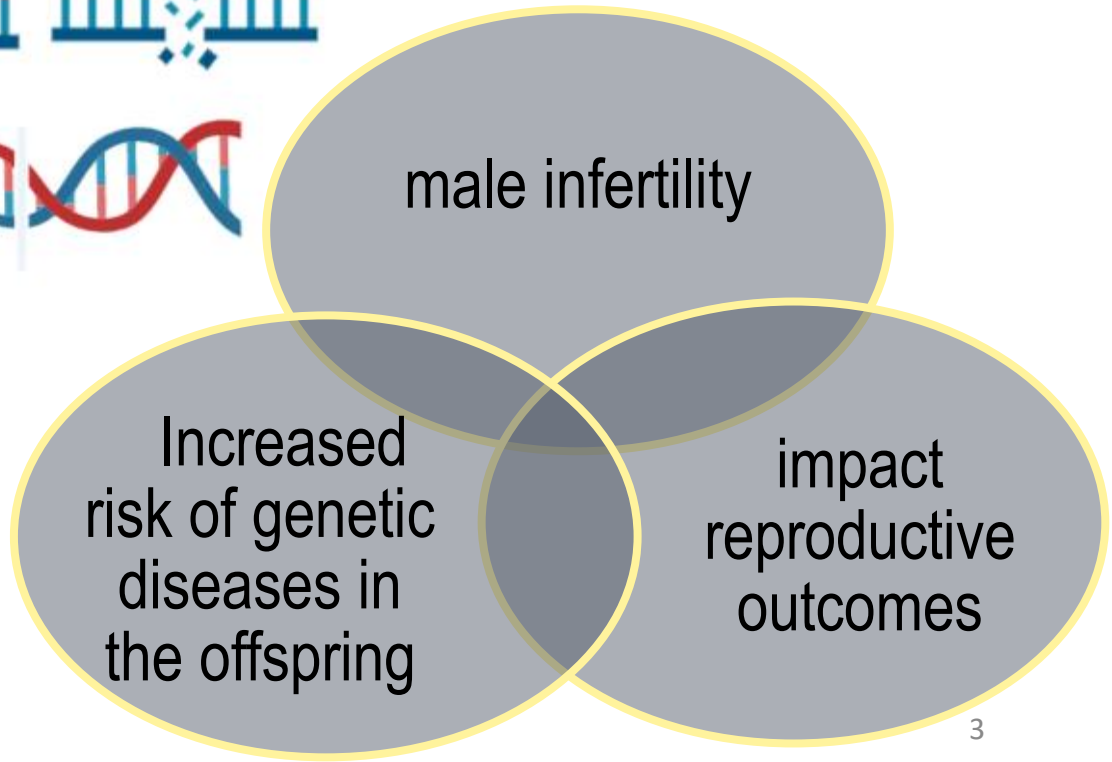
INTRODUCTION





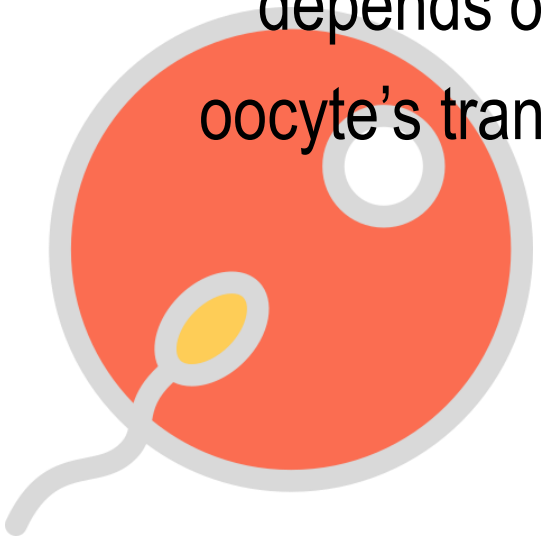
Created with BioRender.com

Novel methods have been introduced to improve semen analysis at a functional level



INTRODUCTION

Spermatozoon: do not possess DRA



Once fertilization takes place, DRA depends on the oocyte's transcripts

Cytoplasmic and genomic qualities

Extent of SDF

INTRODUCTION

Oocyte quality

Oocyte age

?

Effect of sperm DNA fragmentation on pregnancy outcome depends on oocyte quality

Marcos Meseguer, Ph.D.,[a] *Rebeca Santiso, Ph.D.,*[b,c] *Nicolas Garrido, Ph.D.,*[a] *Sandra García-Herrero, Ph.D.,*[a] *Jose Remohí, M.D.,*[a] *and Jose Luis Fernandez, M.D.*[b,c]

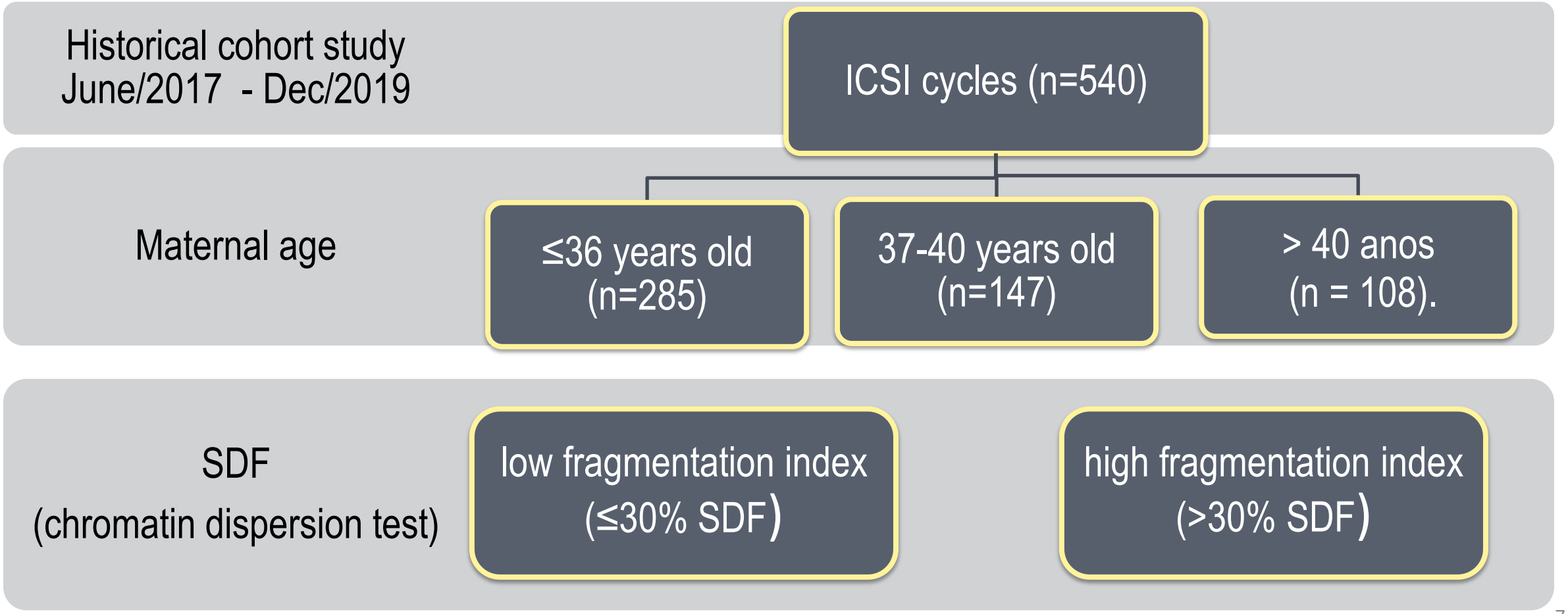
[a] IVI, Universidad de Valencia, Valencia; [b] Sección de Genética y Unidad de Investigación, Hospital "Teresa Herrera," Complejo Hospitalario Universitario A Coruña, A Coruña; and [c] Centro Oncológico de Galicia, A Coruña, Spain

OBJECTIVE

To investigate the impact of nuclear SDF on the outcomes of ICSI in women of different age ranges.

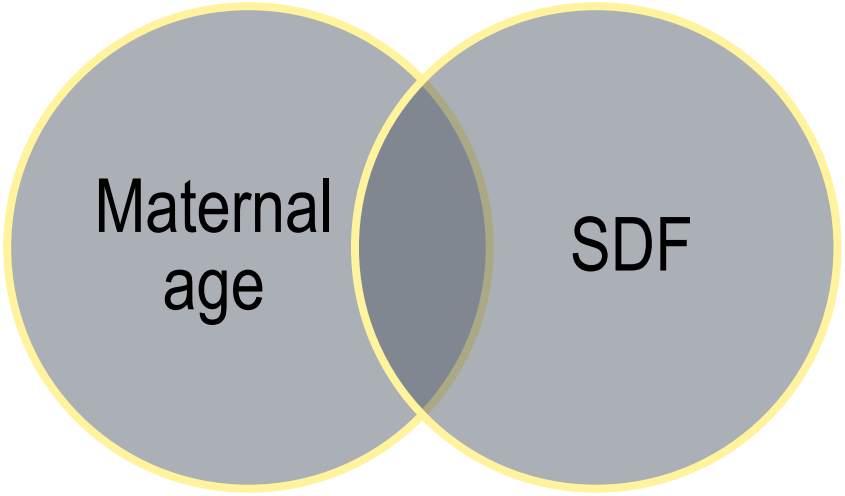
MATERIAL AND METHODS

- ***Patients and Experimental design***



MATERIAL AND METHODS

- ***Patients and Experimental design***



- *Generalized linear models*
- *Bonferroni post hoc test*
- *Adjustment for potential confounders*

RESULTS

GZLM results for the association between SDF and male and female age according to maternal age ranges

Groups	≤36 years old (n=285)			37-40 years old (n=147)			>40 years old (n=108)		
Age	≤30% SDF (n=171)	>30% SDF (n=114)	p	≤30% SDF (n=99)	>30% SDF (n=48)	p	≤30% SDF (n=64)	>30% SDF (n=44)	p
Paternal	35.6 ± 0.2	36.0 ± 0.3	0.720	38.8 ± 0.2	40.7 ± 0.4	0.036	42.1 ± 0.4	43.7 ± 0.5	0.225
Maternal	32.8 ± 0.1	32.7 ± 0.2	0.746	38.5 ± 0.1	38.6 ± 0.1	0.855	42.7 ± 0.1	42.8 ± 0.2	0.879

RESULTS

GZLM results for the association between SDF and response to controlled ovarian stimulation according to maternal age ranges

Groups	≤36 years old (n=285)			37-40 years old (n=147)			>40 years old (n=108)		
Response to COS	≤30% SDF (n=171)	>30% SDF (n=114)	p	≤30% SDF (n=99)	>30% SDF (n=48)	p	≤30% SDF (n=64)	>30% SDF (n=44)	p
Dose of FSH	2439.7 ± 25.9	2408.1 ± 41.5	0.747	2615.9 ± 26.9	2551.8 ± 41.3	0.515	2586.7 ± 39.6	2715.4 ± 59.2	0.367
Retrieved oocytes (n)	13.5 ± 0.3	11.9 ± 0.5	0.194	8.6 ± 0.3	9.0 ± 0.5	0.761	5.8 ± 0.4	7.5 ± 0.6	0.201
Mature oocytes (n)	10.3 ± 0.2	8.5 ± 0.4	0.064	6.2 ± 0.5	6.2 ± 0.8	0.973	4.1 ± 0.3	5.5 ± 0.4	0.200

RESULTS

GZLM results for the association between SDF and laboratory outcomes according to maternal age ranges

Groups	≤36 years old (n=285)			37-40 years old (n=147)			>40 years old (n=108)		
Lab results	≤30% SDF (n=171)	>30% SDF (n=114)	p	≤30% SDF (n=99)	>30% SDF (n=48)	p	≤30% SDF (n=64)	>30% SDF (n=44)	p
Fertilization	89.1	89.5	0.645	79.4	83.4	0.356	78.3	76.5	0.745
High-quality embryos	42.6	42.5	0.977	38.1	36.0	0.676	54.4	33.1	**0.005**
Blastocyst development	85.3	84.2	0.645	42.6	51.6	0.224	49.6	30.2	**0.035**
Embryos transferred	1.2 ± 0.2	1.2 ± 0.3	0.843	1.1 ± 0.1	1.1 ± 0.2	0.473	1.1 ± 0.1	1.2 ± 0.1	0.789

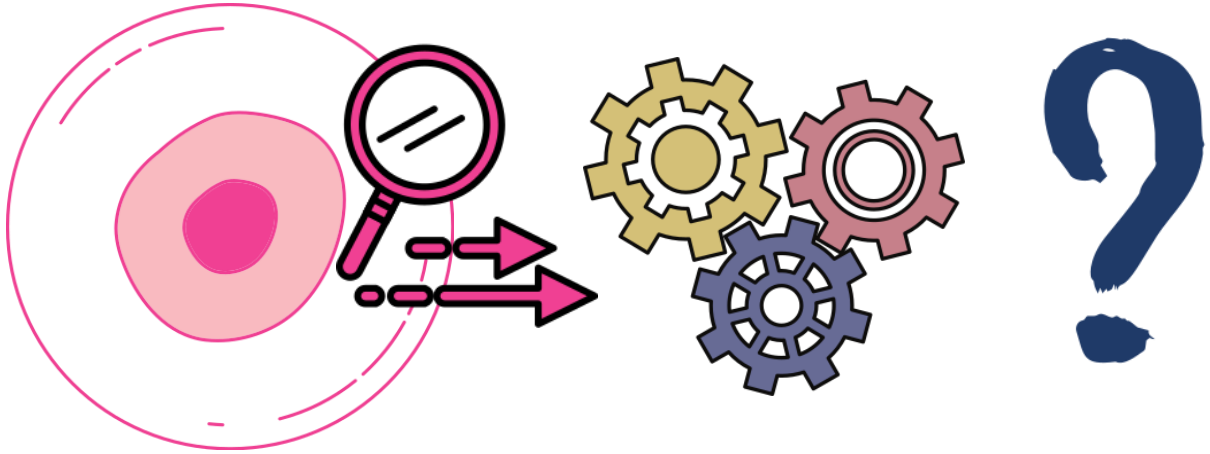
RESULTS

GZLM results for the association between SDF and clinical outcomes according to maternal age ranges

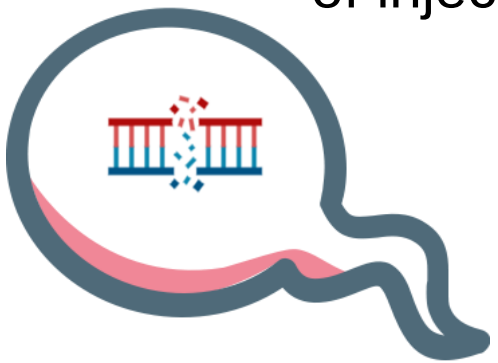
Groups	≤36 years old (n=285)			37-40 years old (n=147)			>40 years old (n=108)		
Clinical results	≤30% SDF (n=171)	>30% SDF (n=114)	p	≤30% SDF (n=99)	>30% SDF (n=48)	p	≤30% SDF (n=64)	>30% SDF (n=44)	p
Implantation rate (%)	42.3	41.5	0.880	28.9	30.6	0.757	19.7	11.9	**<0.001**
Pregnancy rate (%)	40.0	39.1	0.840	27.7	28.6	0.781	20.0	7.7	**0.040**
Miscarriage rate (%)	9.3	11.1	0.665	31.2	22.2	0.875	12.5	100	**<0.001**

DISCUSSION

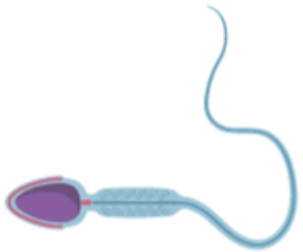
Ageing compromises the oocyte’s DNA repair activity



Oocytes from the study were in fact provided with DNA repair activity or to what extent the DNA of injected spermatozoa was damaged ?

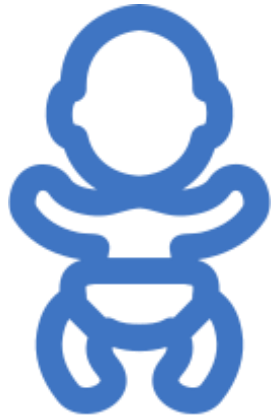


DISCUSSION

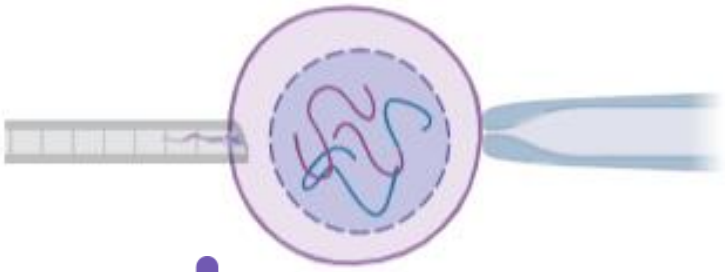


> 30% de SDF

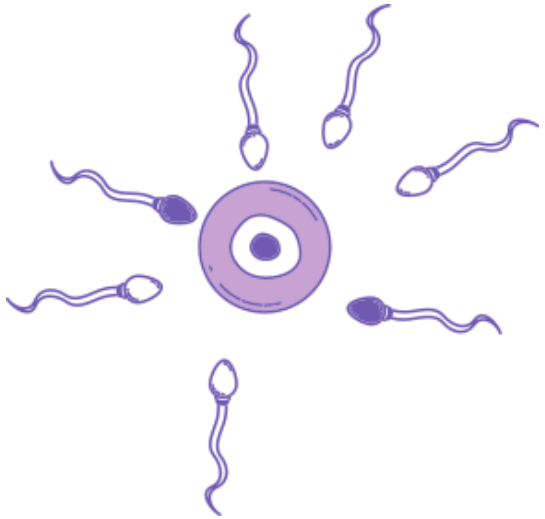
> 40 y-old



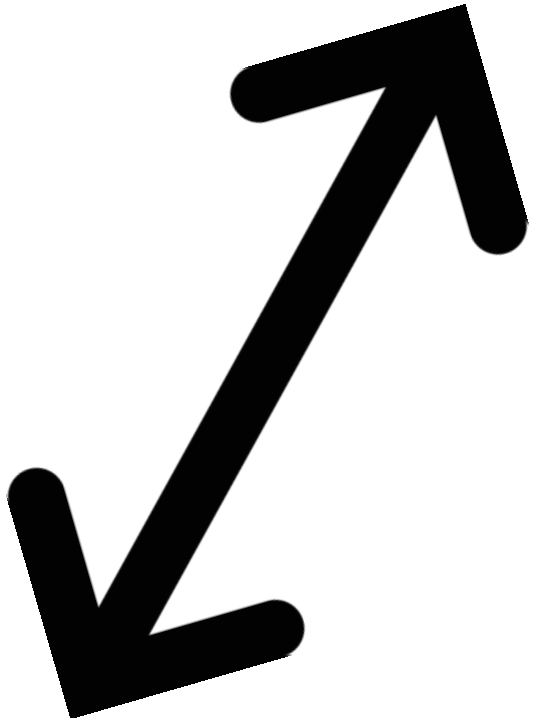
DISCUSSION



VS



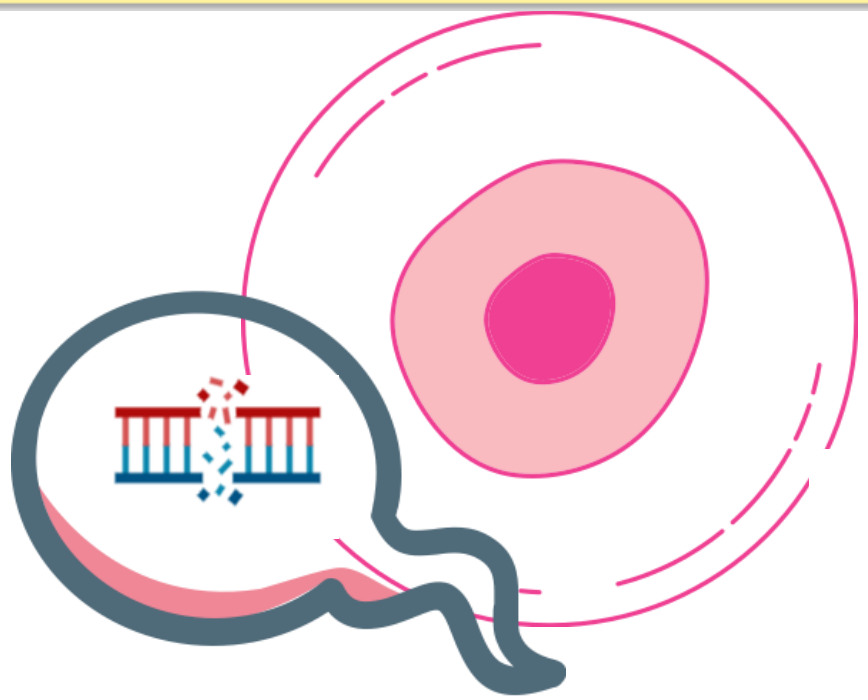
The higher the chance of selecting one with fragmented DNA



Sperm with hidden abnormalities may be selected for injection

The higher the SDF index

DISCUSSION

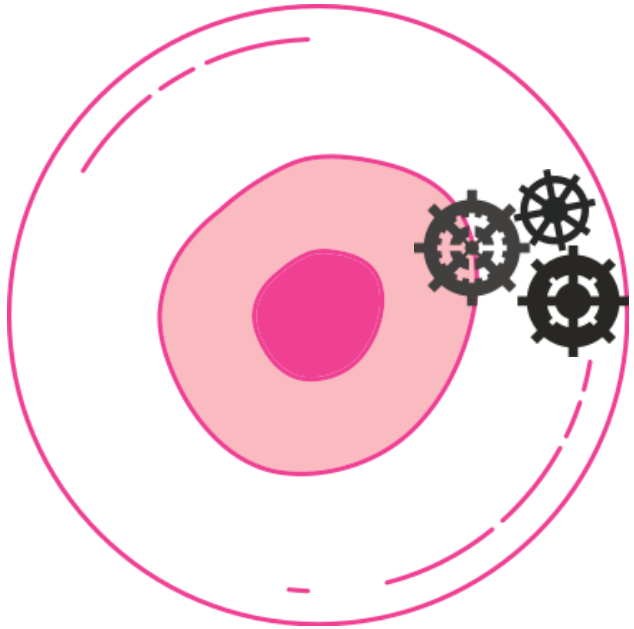


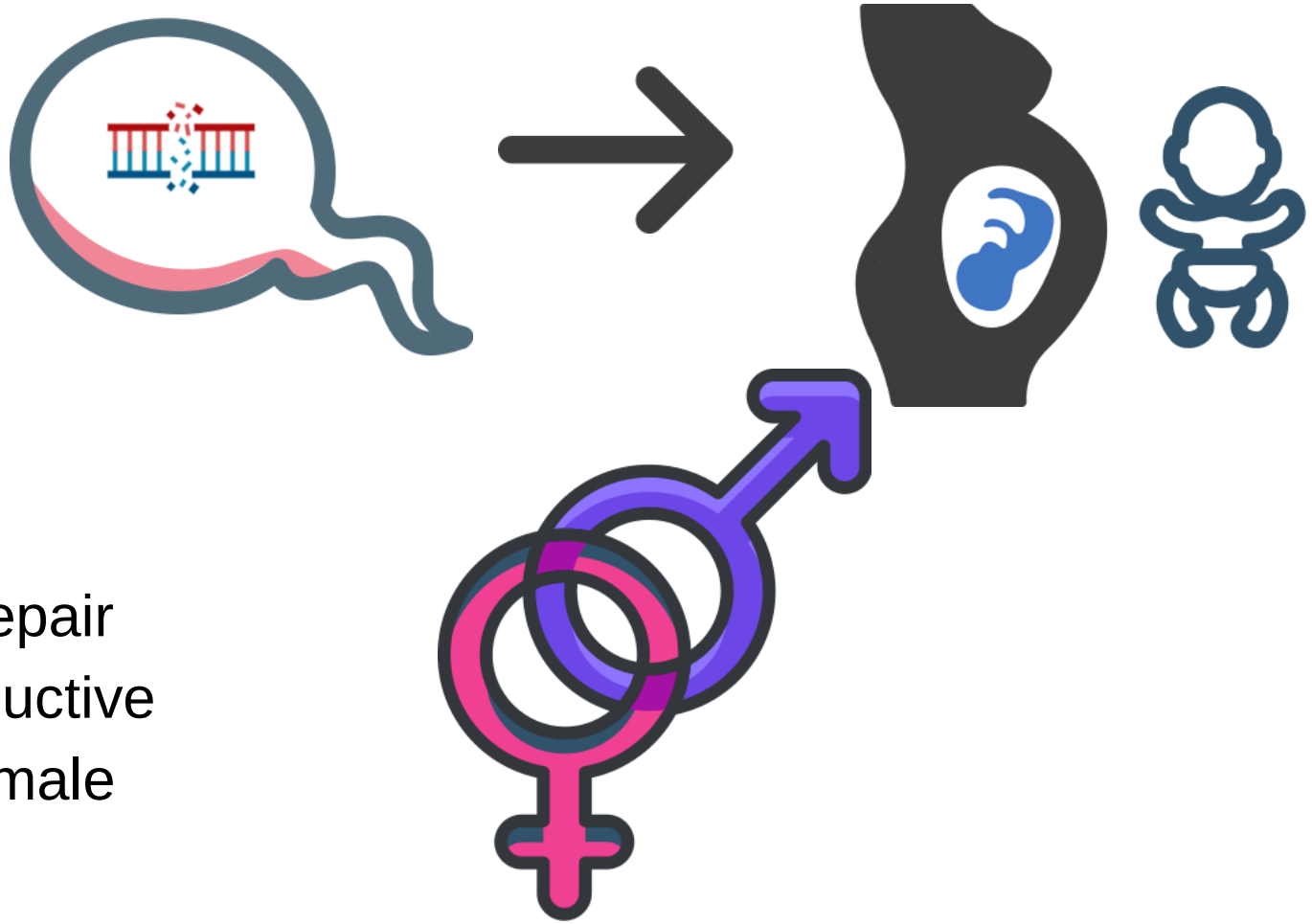
Apoptosis, which will destroy one or more blastomeres, reducing embryo viability

Tolerate the lesion, which may lead to mutation and eventual carcinogenesis in the offspring

Repair the lesionng

DISCUSSION





Once the oocyte is provided with repair activity, the impact of SDF on reproductive outcomes is a combination of both male and female factors

DISCUSSION

Ability to cope with SDF

Advanced maternal age is associated with reduced oocytes' mRNA stores and DRA

Human Molecular Genetics, 2004, Vol. 13, No. 19 **2263–2278**
doi:10.1093/hmg/ddh241
Advance Access published on August 18, 2004

Age-associated alteration of gene expression patterns in mouse oocytes

Toshio Hamatani†, Geppino Falco†, Mark G. Carter, Hidenori Akutsu, Carole A. Stagg, Alexei A. Sharov, Dawood B. Dudekula, Vincent VanBuren and Minoru S.H. Ko*

Developmental Genomics and Aging Section, Laboratory of Genetics, National Institute on Aging, National Institutes of Health, 333 Cassell Drive, Suite 3000, Baltimore, MD 21224, USA

Received May 9, 2004; Revised and Accepted July 20, 2004

CONCLUSIONS

- ✓ High SDF index leads to lower implantation and pregnancy rates, and higher miscarriage rate, in ICSI cycles of women with advanced maternal age
- ✓ The same is not observed when maternal age is < 40 years old
- ✓ Ageing may affect the oocyte DRA, leading to the development of an embryo with poor development and implantation potential, when the oocyte is injected with a DNA-damaged spermatozoon

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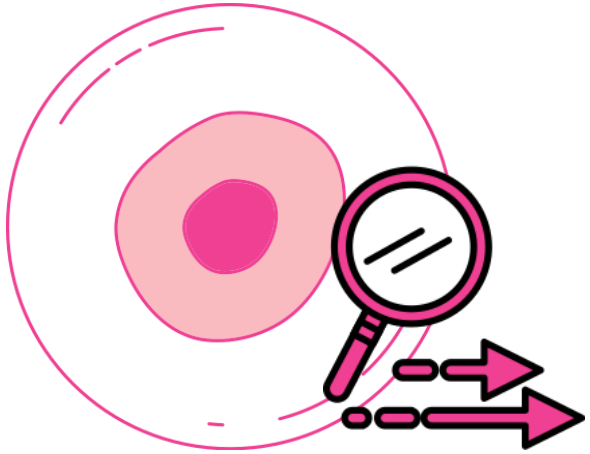
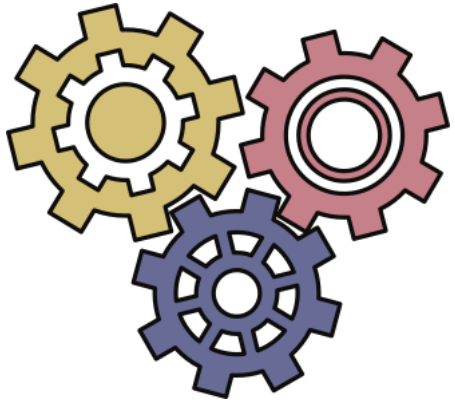
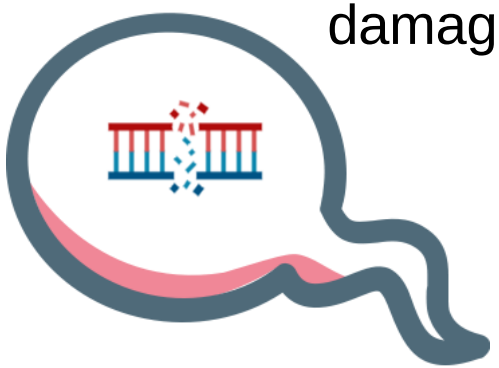
DISCUSSION





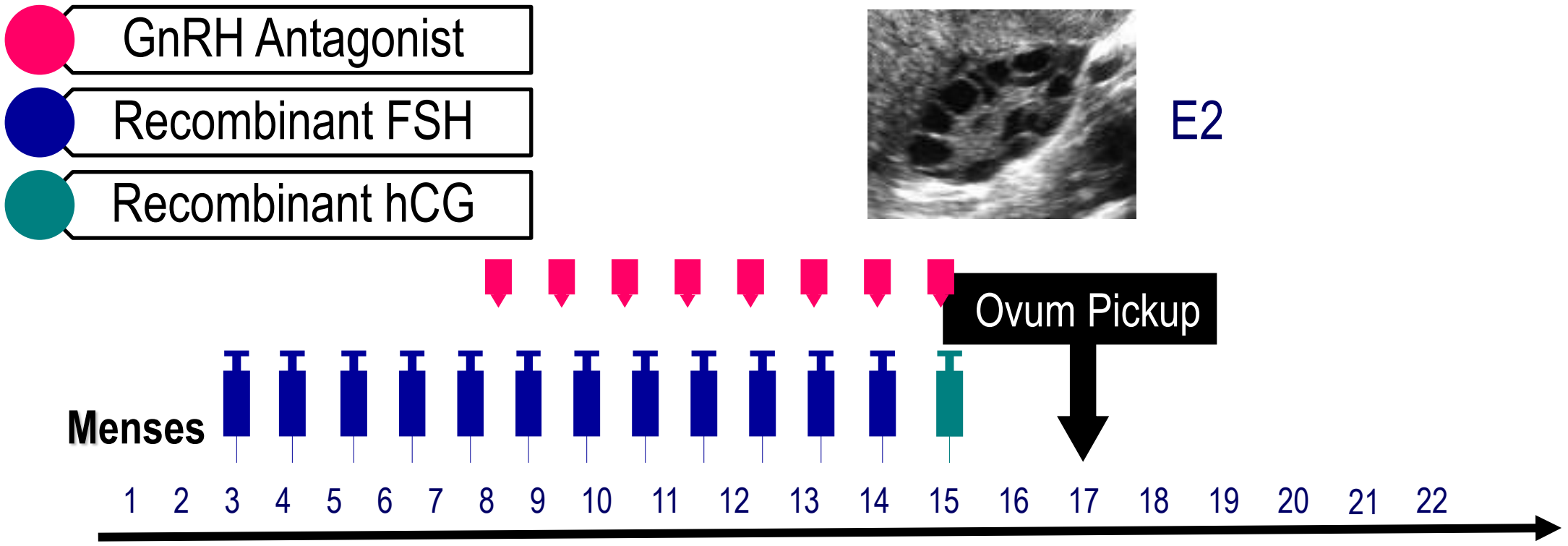


Oocytes from the study were in fact provided with DNA repair activity or to what extent the DNA of injected spermatozoa was damaged ?

oocytes from women with advanced maternal age were less likely to repair SDF, thus resulting in lower pregnancy outcomes.

MATERIAL AND METHODS

- ***Controlled ovarian stimulation***



INTRODUCTION

Asian Journal of Andrology (2017) 19, 80–90

www.asiaandro.com; www.ajandrology.com

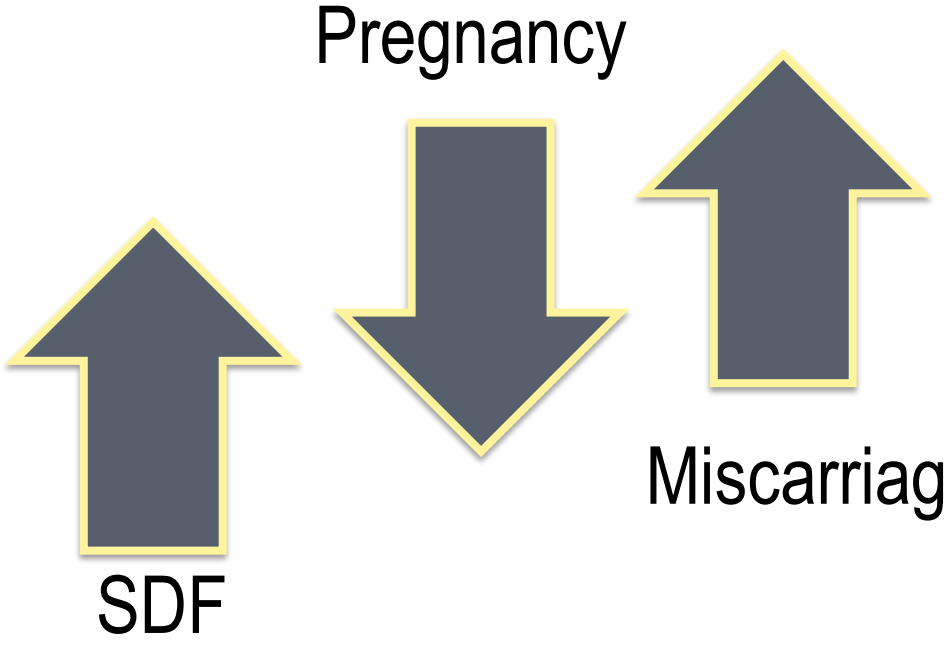
Open Access

ORIGINAL ARTICLE

Sperm Biology

A systematic review and meta-analysis to determine the effect of sperm DNA damage on *in vitro* fertilization and intracytoplasmic sperm injection outcome

Luke Simon[1,*], Armand Zini[2,*], Alina Dyachenko[2], Antonio Ciampi[2], Douglas T Carrell[1,3,4]



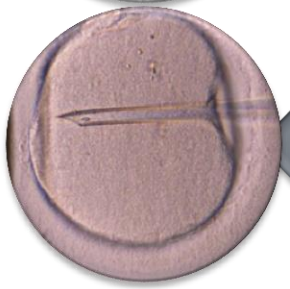
Sperm DNA fragmentation and recurrent pregnancy loss: a systematic review and meta-analysis

Dana B. McQueen, M.D., M.A.S., John Zhang, Ph.D., and Jared C. Robins, M.D.

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Northwestern University, Chicago, Illinois

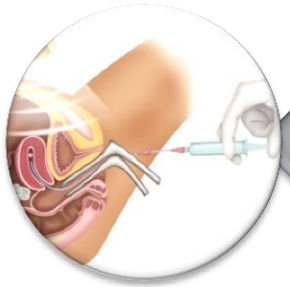
MATERIAL AND METHODS

Incubation, denudation and nuclear maturation evaluation



ICSI - (Palermo et al., 1992)

Embryo culture until day 5

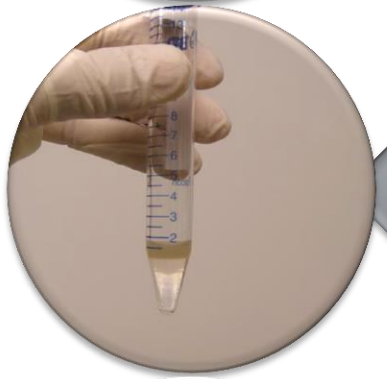


One or two blastocysts transferred

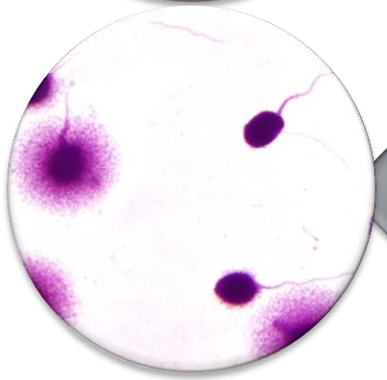
FERTILITY MEDICAL GROUP

MATERIAL AND METHODS

Semen samples were evaluated according to the threshold values established by the WHO in 2010



Sperm preparation: 2-layered density gradient centrifugation technique

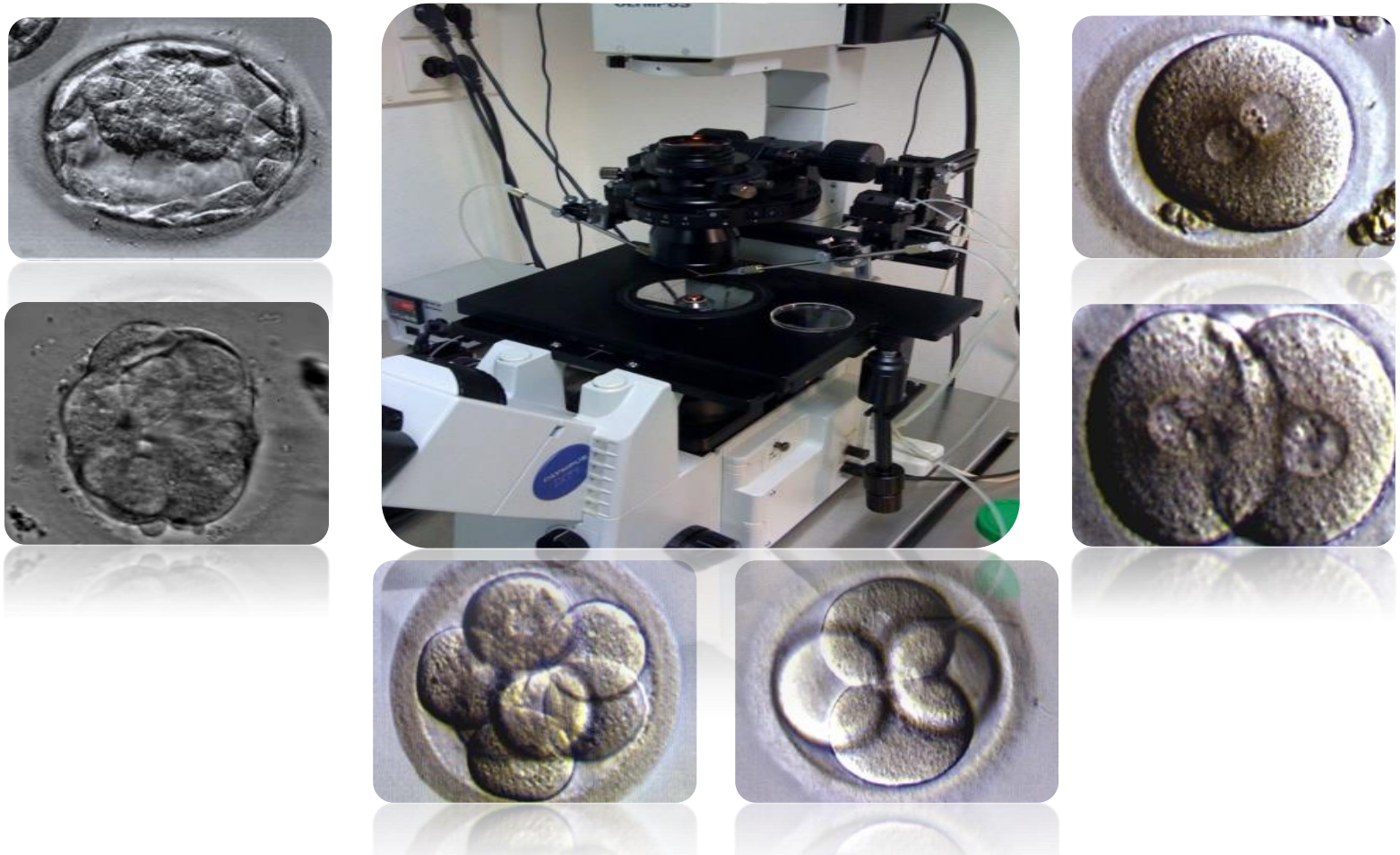


The sperm DNA fragmentation: Sperm chromatin dispersion test

FERTILITY MEDICAL GROUP

MATERIAL AND METHODS

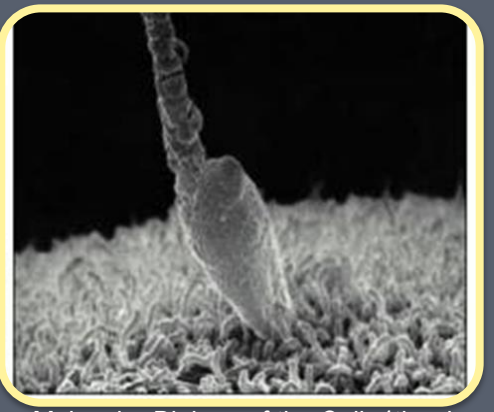
- ***Embryo morphology and transfer***



INTRODUCTION

Studies showing a correlation between semen quality and reproductive outcomes

So far, there is no predictive threshold for success for conventional semen parameters



Molecular Biology of the Cell, 4th ed.

Spermatozoa

- subcellular or nuclear factors that are not recognized during conventional semen analysis,
- May contribute to male factor infertility