



## BIOLOGY OF SPERMATOGENESIS

Paulo Navarro-Costa<sup>1,2</sup>

<sup>1</sup>Institute of Histology and Developmental Biology, Faculty of Medicine – University of Lisbon, Portugal.

<sup>2</sup>CEMEARE – Assisted Reproduction Centre, Lisbon, Portugal.

e-mail: [navarro-costa@fm.ul.pt](mailto:navarro-costa@fm.ul.pt)

---

---

---

---

---

---

---

---

### WHAT IS SPERMATOGENESIS?

Biological program for the the development and differentiation of germ cell precursors into mature sperm

### WHAT DOES IT CONSIST OF?

STAGES OF THE PROGRAM:

- 1- Commitment and proliferation of precursor cells
- 2- Meiosis
- 3- Cellular differentiation into mature sperm

---

---

---

---

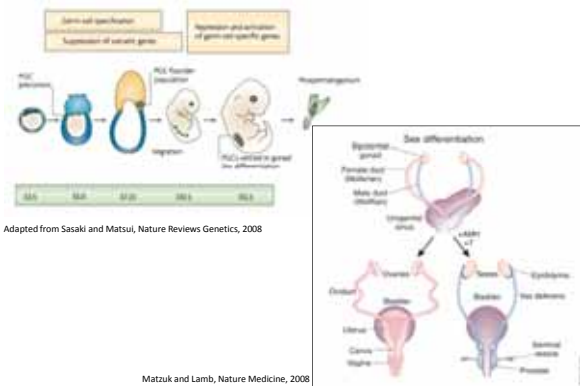
---

---

---

---

### THE MALE GERMLINE AND GONAD DIFFERENTIATE SIMULTANEOUSLY



---

---

---

---

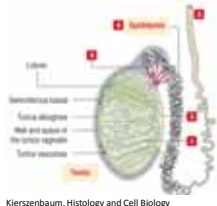
---

---

---

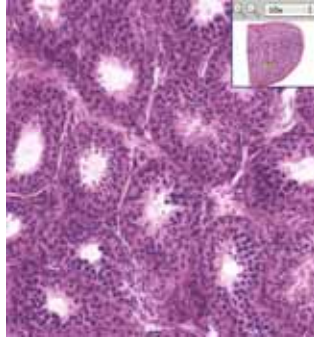
---

**SPERMATOGENESIS STARTS IN A SPECIFIC TESTICULAR NICHE**



Kierszenbaum, Histology and Cell Biology

- Spermatogenesis in the tubular compartment
- Androgen production in the inter-tubular compartment



University of Iowa

---

---

---

---

---

---

---

---

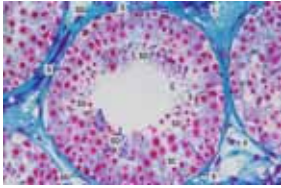
---

---

---

---

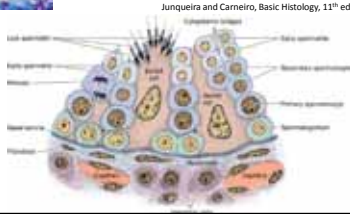
**SEMINIFEROUS TUBULES CONSIST OF GERM-SOMA ASSOCIATIONS**



Jeffrey B. Kerr, Atlas of Functional Histology

Ø = 150 µm  
length = 80 cm

Seminiferous epithelium =  
germline cells + somatic cells  
(Sertoli cells)



Junqueira and Carneiro, Basic Histology, 11th ed

---

---

---

---

---

---

---

---

---

---

---

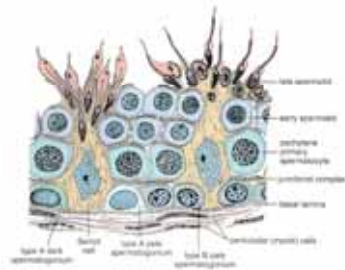
---

**SPERMATOGENESIS IS ALSO A COMPARTMENTALIZED PROCESS**

Ocluding junctions between Sertoli cells form 2 compartments that stage different phases of spermatogenesis

Adluminal

Basal



Ross et al., Histology, 5th Ed.

---

---

---

---

---

---

---

---

---

---

---

---

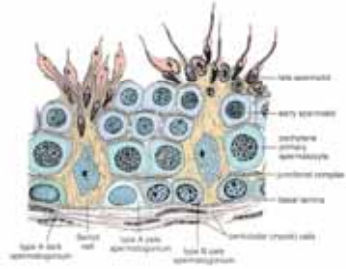
**SPERMATOGENESIS IS ALSO A COMPARTMENTALIZED PROCESS**

Occluding junctions between Sertoli cells form 2 compartments that stage different phases of spermatogenesis

3 - spermiogenesis

2 - meiosis

1 - spermatocytogenesis



Ross et al., Histology, 5<sup>th</sup> Ed.

---

---

---

---

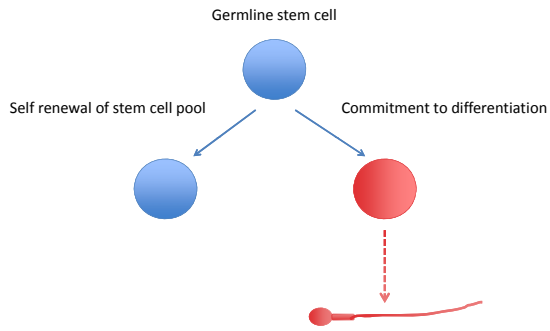
---

---

---

---

**SPERMATOCYTOGENESIS IS A LINEAGE EXPANSION EVENT**



---

---

---

---

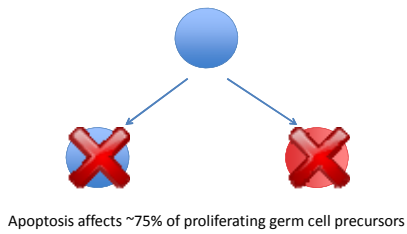
---

---

---

---

**SPERMATOCYTOGENESIS IS A LINEAGE EXPANSION EVENT**



---

---

---

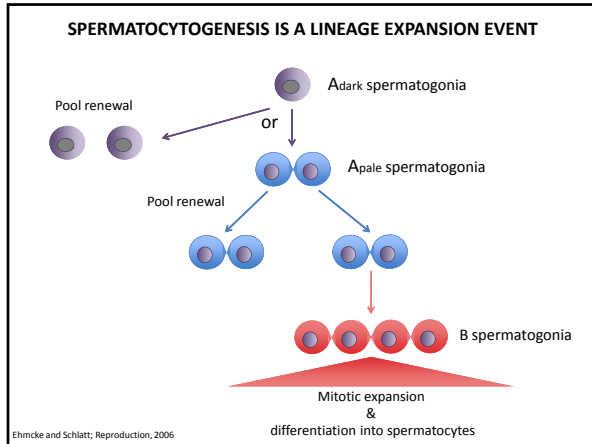
---

---

---

---

---




---

---

---

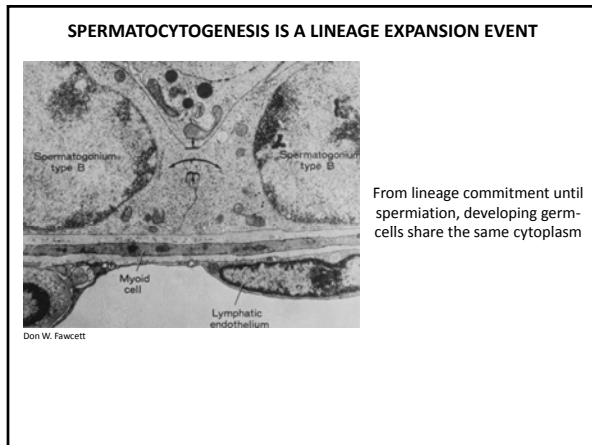
---

---

---

---

---




---

---

---

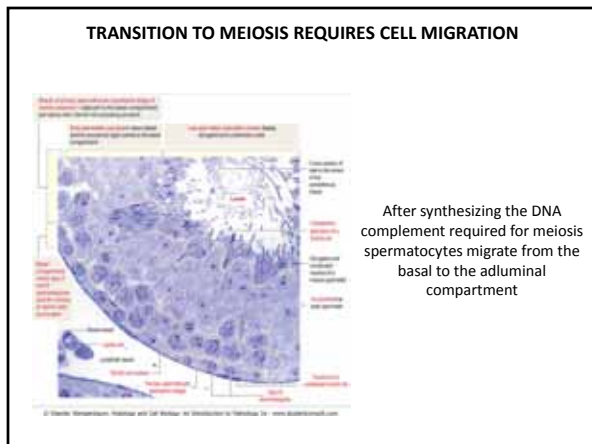
---

---

---

---

---




---

---

---

---

---

---


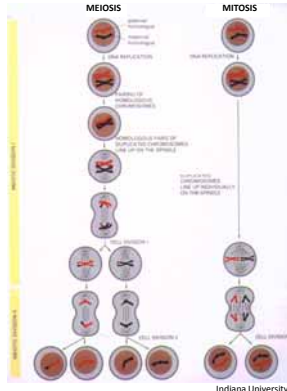
---

---

**MEIOSIS = HAPLOIDIZATION + GENETIC DIVERSITY**

Prophase I:

- pairing of homologues
- synapsis via synaptonemal complex
- crossing over between non sister chromatids

Kierszenbaum, Histology and Cell Biology

Indiana University

---

---

---

---

---

---

---

---

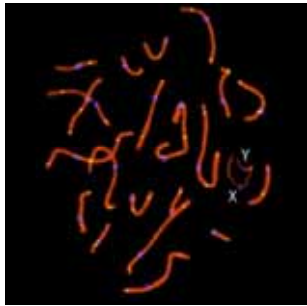
---

---

---

---

**MEIOSIS = HAPLOIDIZATION + GENETIC DIVERSITY**



The X and Y chromosomes due to their imperfect pairing are condensed into the sex vesicle

R. Martin

---

---

---

---

---

---

---

---

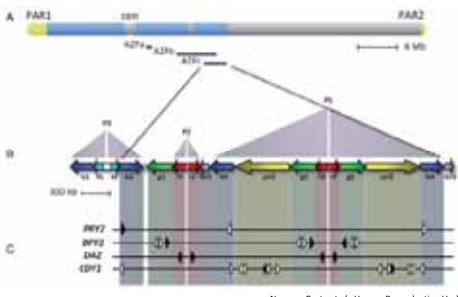
---

---

---

---

**MEIOSIS = HAPLOIDIZATION + GENETIC DIVERSITY**



Navarro-Costa et al., Human Reproduction Update, 2010

---

---

---

---

---

---

---

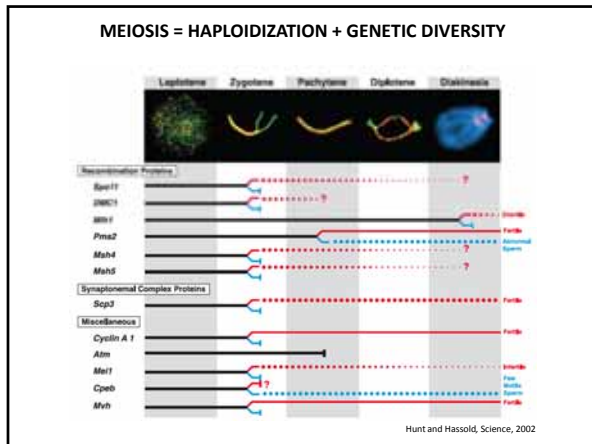
---

---

---

---

---




---

---

---

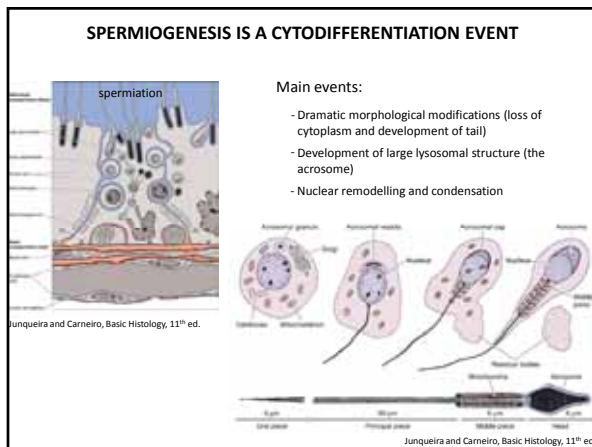
---

---

---

---

---



- Main events:
- Dramatic morphological modifications (loss of cytoplasm and development of tail)
  - Development of large lysosomal structure (the acrosome)
  - Nuclear remodelling and condensation

---

---

---

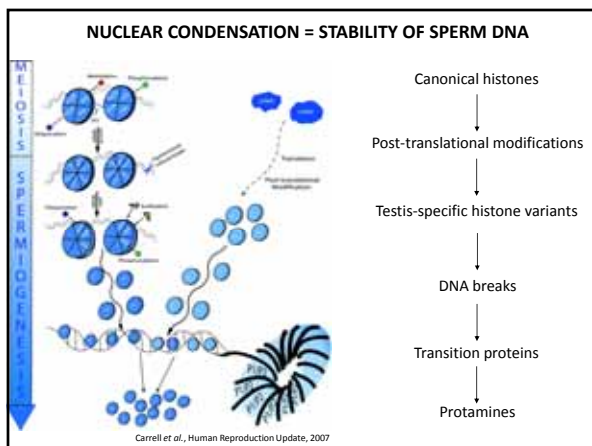
---

---

---

---

---



- Canonical histones
- ↓
- Post-translational modifications
- ↓
- Testis-specific histone variants
- ↓
- DNA breaks
- ↓
- Transition proteins
- ↓
- Protamines

---

---

---

---

---

---

---

---

**NUCLEAR CONDENSATION = GENE EXPRESSION REGULATION IN THE EARLY EMBRYO?**



Sperm retains ~15% of histone-bound DNA, and such regions are enriched in genes involved in developmental pathways

↓  
 Is this selective packaging functionally related to early embryo development?

---

---

---

---

---

---

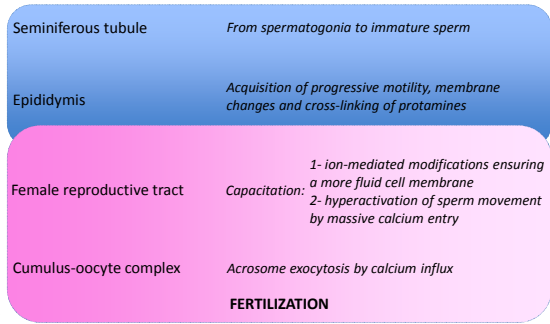
---

---

---

---

**THE ACQUISITION OF FULL FUNCTIONAL SPERM COMPETENCE IN VIVO OCCURS IN FEMALES**




---

---

---

---

---

---

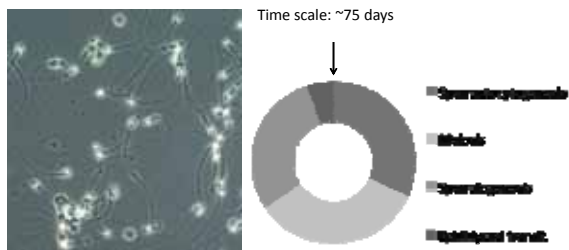
---

---

---

---

**HUMAN SPERMATOGENESIS AT A GLANCE**




---

---

---

---

---

---


---

---

---

---

### HUMAN SPERMATOGENESIS AT A GLANCE



Time scale: ~75 days

Average daily production:  $150 \times 10^6$  spz

---

---

---

---

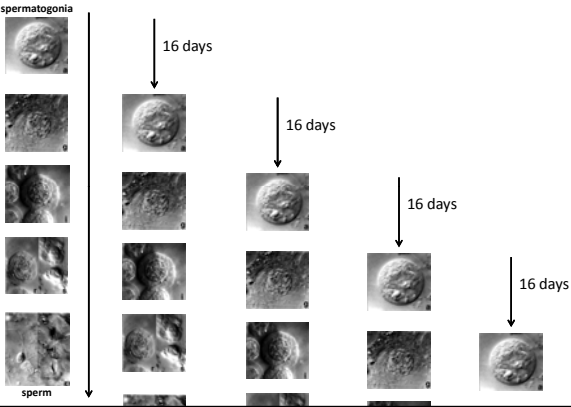
---

---

---

---

### SPERMATOGENIC CYCLE AND WAVE



The diagram illustrates the spermatogenic cycle and wave. On the left, a vertical column of cells is labeled 'spermatogonia' at the top and 'sperm' at the bottom. To the right, a series of stages are shown, with arrows indicating a 16-day interval between each stage. The stages are labeled I, II, III, IV, V, and VI.

---

---

---

---

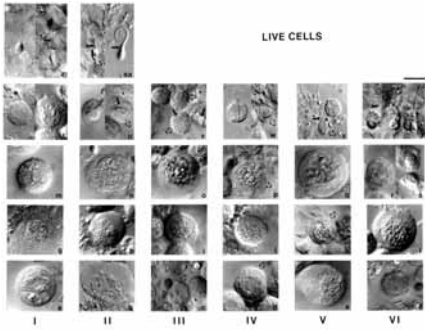
---

---

---

---

### SPERMATOGENIC CYCLE AND WAVE



LIVE CELLS

SPERMATOGENIC STAGES IN THE HUMAN

Johnson et al., Human Reproduction, 2001

---

---

---

---

---

---

---

---



### SPERMATOGENIC CYCLE AND WAVE

Silber, Seminars in Reproductive Endocrinology, 1991

Zhang et al., Asian Journal of Andrology, 2004

The spatial distribution of the spermatogenic cycle along the tubules ensures a constant sperm output

---

---

---

---

---

---

---

---

---

---

### SPERMATOGENIC CYCLE AND WAVE

Higher primates

$4 \times 10^6$  sperm / g

Other species

$25 \times 10^6$  sperm / g

---

---

---

---

---

---

---

---

---

---

### SPERMATOGENIC CYCLE AND WAVE

WHO laboratory manual for the examination and processing of human semen - 5<sup>th</sup> Ed.

Considerable intra-individual variability in spermatogenic output, as well as geographical differences are characteristic of human spermatogenesis

---

---

---

---

---

---


---

---

---

---

**HUMAN SPERMATOGENESIS AT A GLANCE**



Time scale: ~75 days  
 Average daily production:  $150 \times 10^6$  spz  
 ~50% of the sperm are progressively motile following ejaculation

---

---

---

---

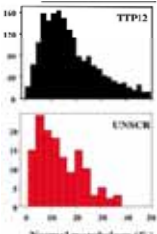
---

---

---

---

**HUMAN SPERMATOGENESIS AT A GLANCE**



Time scale: ~75 days  
 Average daily production:  $150 \times 10^6$  spz  
 ~50% of the sperm are progressively motile following ejaculation  
 Significant morphological variability is tolerated (>85% sperm forms are abnormal)

Cooper et al., Human Reproduction Update, 2010

---

---

---

---

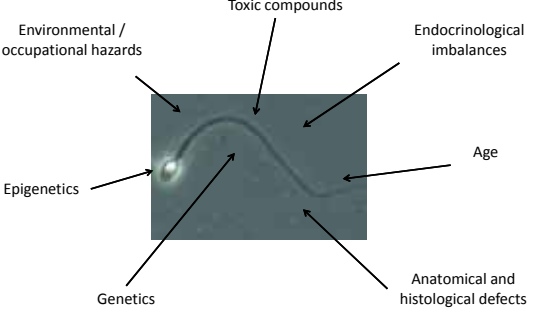
---

---

---

---

**DISRUPTORS OF SPERMATOGENESIS**



Environmental / occupational hazards  
 Toxic compounds  
 Endocrinological imbalances  
 Age  
 Anatomical and histological defects  
 Genetics  
 Epigenetics

---

---

---

---

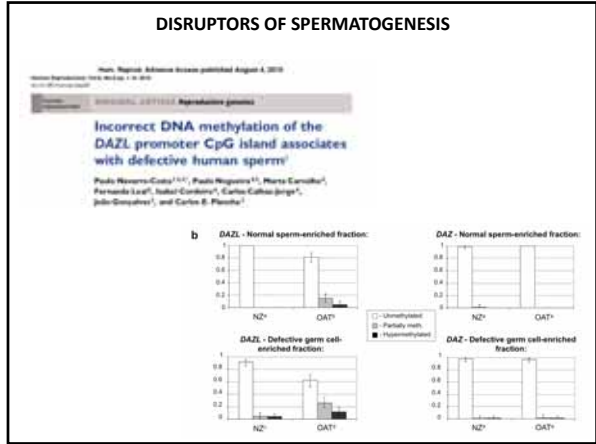
---

---

---

---

**DISRUPTORS OF SPERMATOGENESIS**




---

---

---

---

---

---

---

---

---

---

**TAKE-HOME MESSAGES**

- 1- Spermatogenesis is a tightly regulated process that starts in the seminiferous tubule and ends, in functional terms, in the female reproductive tract
- 2- The program is under somatic cell control and is influenced by environmental and (epi)genetic cues
- 3- Spermatogenic output is extremely variable, even in the fertile population

---

---

---

---

---

---

---

---

---

---

**ACKNOWLEDGEMENTS**

C.E. Plancha  
 L. Parreira  
 A.J. Cidadão

M.J. Carvalho  
 P. Sá e Melo  
 M. Rato  
 S. Pimentel

J. Gonçalves  
 J. Lavinha

C. Calhaz-Jorge  
 I. Cordeiro  
 F. Leal  
 M. Carvalho

J. Becker  
 P. Borges

All anonymous men that contributed with samples for our studies

**FCT** Fundação para a Ciência e a Tecnologia

---

---

---

---

---

---

---

---

---

---