DIRECTIONAL ASYMMETRY IN FEMALE AVIAN GONADS

Gala Pujol Infantes, Bachelor in Genetics (2019-2020), Universitat Autònoma de Barcelona (UAB)
Supervised by **Francesc Muñoz Muñoz**, Developmental Biology Department

1. INTRODUCTION

BACKGROUND

- **Vertebrates' left-right body axis**

Involve left-right symmetry breaking mechanisms & asymmetry generation

Three types of left-right asymmetry:
- Fluctuating asymmetry
- Antisymmetry
- **Directional asymmetry**

Birds' directional asymmetry

Asymmetric development of female's reproductive tract with only a left functional ovary and oviduct

Deuterostomia
Hemichordata
Echinocordata
Chordata
Cephalochordata
Tunicat (urochordata)
Vertebrata (craniata)
Agnatha
Gnathostomata
Chondrichthyes
Osteichthyes
Tetrapoda
Non-amniotes: amphibians
Amniotes
Sauropsids: reptiles & birds
Synapsids: mammals

Figure 1. Deuterostomia classification

PROJECT'S OBJECTIVES

1. Identify the embryonic stage when reproductive asymmetry is established.
2. Describe ovarian asymmetry function.
3. Investigate if natural reversals are possible.
4. Determine if secondary characters are related to gonadal asymmetry.
5. Identify genes involved in the gonadal directional asymmetry development.

2. METHODS

RESEARCH SURFACES

- Mendeley
- Science Direct
- "UAB Biblioteques"
- Google Scholar
- PubMed

KEYWORDS

- "Left-right asymmetry"
- "Avian" & "Birds"
- "Gonadal development"
- "Ovary asymmetry"

RESEARCH STRATEGY

- Boolean structures
- Stepwise process

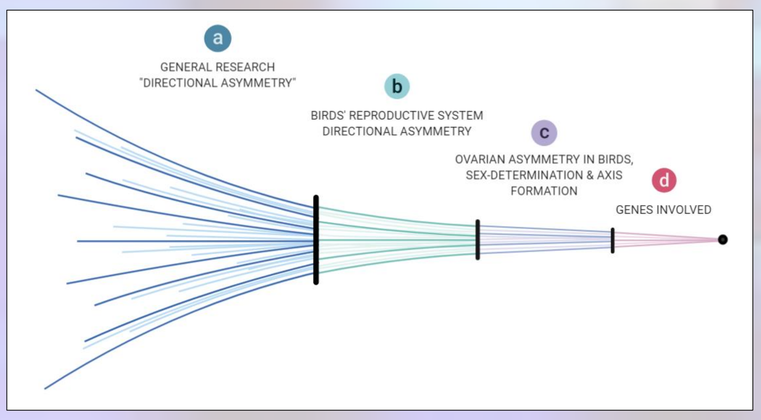


Figure 2. Scheme representing the research stepwise process

3. RESULTS

3.1. Embryonic development and body asymmetries

Germinal crescent
- Non-embryonic
- Containing PGCs

Axis
- Anterior-posterior
- Dorsal-ventral
- Left-right

Left side: *Shh, Nodal & Pitx2*

Right side: *cAct-RIIa & Fgf8*

Midline: *Lefty1*

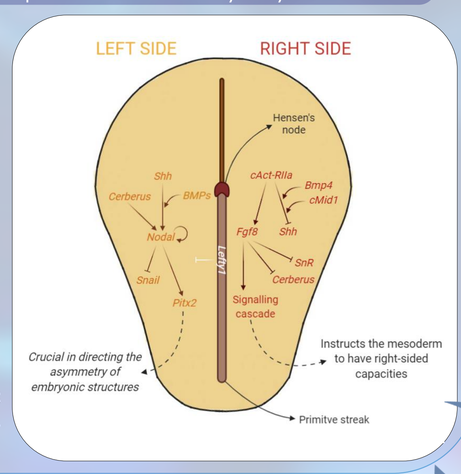
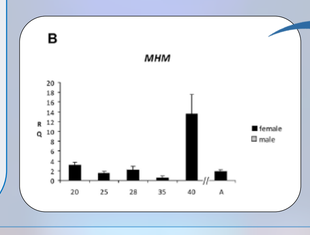


Figure 3. Gene expression during L-R axis establishment. Adapted from A. Raya and J. Izpisua Belmonte, 2004.

3.2. Birds' sex determination

♂ ZZ *Sex-chromosomes*	♀ ZW *Sex-chromosomes*
MHM → Methylated	*MHM* → Hypomethylated
Genes: *DMRT1, HINTZ, SOX9*	Genes: *HINTW, FOLX2, FET1*
No *SRY* gene identified	

Two hypotheses:
- W-linked genes dominance
- Z dosage



Dosage compensation

Figure 4. MHM expression. Retrieved from L. Caetano et al., 2014.

3.3. Gonadal asymmetry

3.3.1. Gonadal development and asymmetric structure

Symmetric development until stage HH28

Ovaries layers
- Cortex
  - Asymmetric
- Medulla
  - Symmetric

PGCs
- Blood vessels by diapedesis
- Migrate via bloodstream
- Chemoattractant influence

Higher levels and proliferation of PGCs in the left gonad

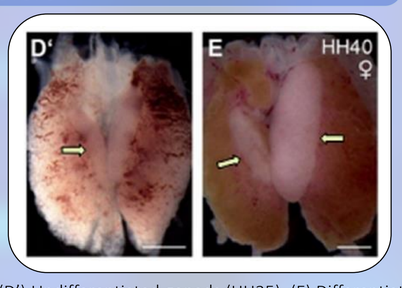


Figure 5. (D') Undifferentiated gonads (HH35). (E) Differentiated female gonads (HH40). Retrieved from L. Caetano et al., 2014.

3.3.2. Related genes

Asymmetric gene expression
- Most in autosome chromosomes

Estrogens' important role in ovarian development

Expressed in both gonads but its receptor (ER-a) is left-specific

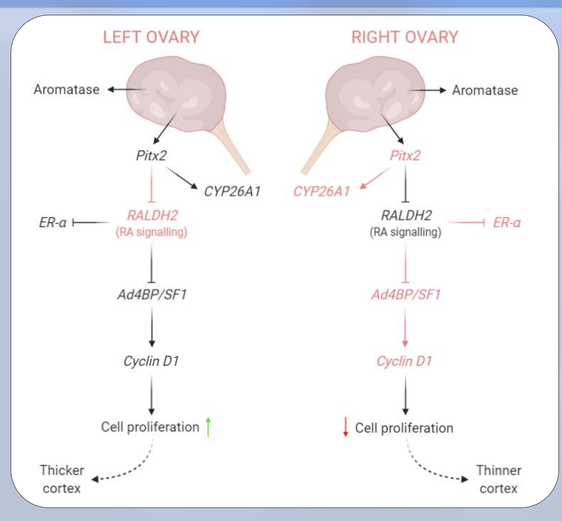


Figure 6. Asymmetrical gonad genes expression. Adapted from Y. Ishimaru et al., 2008.

MORE IMPORTANT REGULATORS
- Apoptotic & cell proliferation genes
- ***Ovex1:*** endogenous retrovirus highly expressed in the left gonad
- MicroRNAs
- Long non-coding RNAs

3.3.3. Function

SPACE RESTRICTIONS
- Reduced body cavity
- Asymmetric positioning of other organs

WEIGHT REDUCTION
- Better ability to fly
- Related to 1 oviduct/1 ovary

SURVIVAL RATE
- Related to egg fragility
- Higher survival rate avoiding proximal eggs

Most accepted hypothesis, also seen in other egg-laying mammals like the platypus

3.3.4. Possible reversal & secondary sexual traits induction

- **Right ovary compensation of left misfunction**
  - Seen in males
  - Right gonad would act as a "back-up"
  - Important in seasonal breeding species

Secondary sexual traits

Determined by hormonal expression

4. DISCUSSION & CONCLUSION

Birds left-right axis establishment

Nodal & Pitx2 → Internal organs asymmetric organization → Directional asymmetry **Why?**

Birds' ovarian directional asymmetric development
- First observation at stage HH28
- Differential gene expression

LEFT-SPECIFIC
Cell proliferation & pluripotency

RIGHT-SPECIFIC
Meiosis arrest & apoptosis

FUNCTION HYPOTHESES
1. Space constraints
2. Weight reduction (fly)
3. **Higher survival rate**

REVERSAL & SECONDARY SEXUAL TRAITS
- "Back-up" right ovary function
- Hormonal regulation of secondary sexual traits

DEVELOPMENT HYPOTHESES
1) Other vertebrates avoid reproductive asymmetry
2) Female birds potentiate reproductive tract asymmetries

CONLUSIONS
- **Ovarian asymmetric growth**
  - Related to sex-determination
  - Mediated by coding & non-coding genes

Functional left ovary & right gonad regression

Further studies are needed to fully understand the process

5. RELEVANT BIBLIOGRAPHY

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