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## **EVOLUTION OF THE NUCLEAR RECEPTOR DAF-12 IN PARASITIC NEMATODES**

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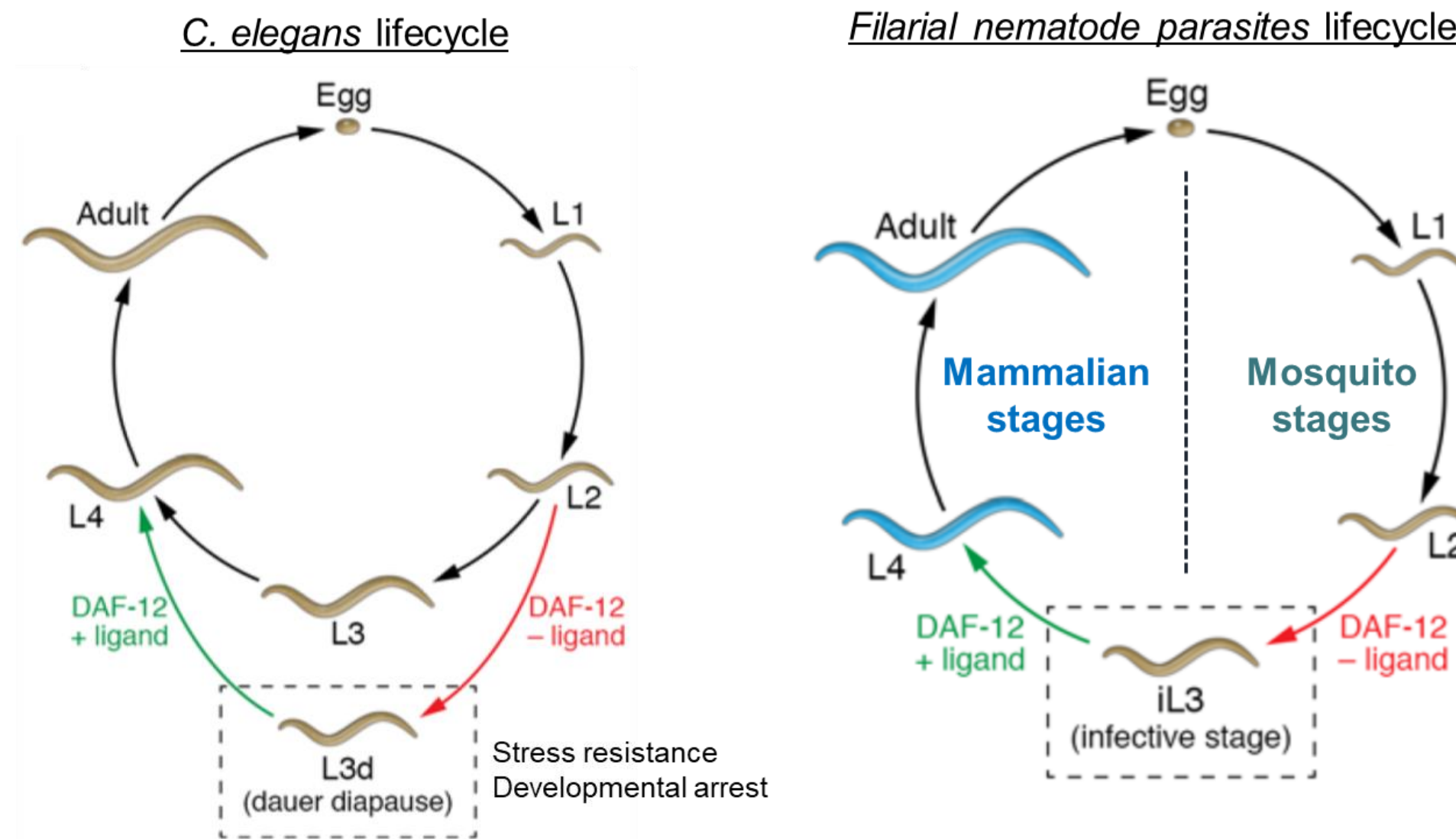
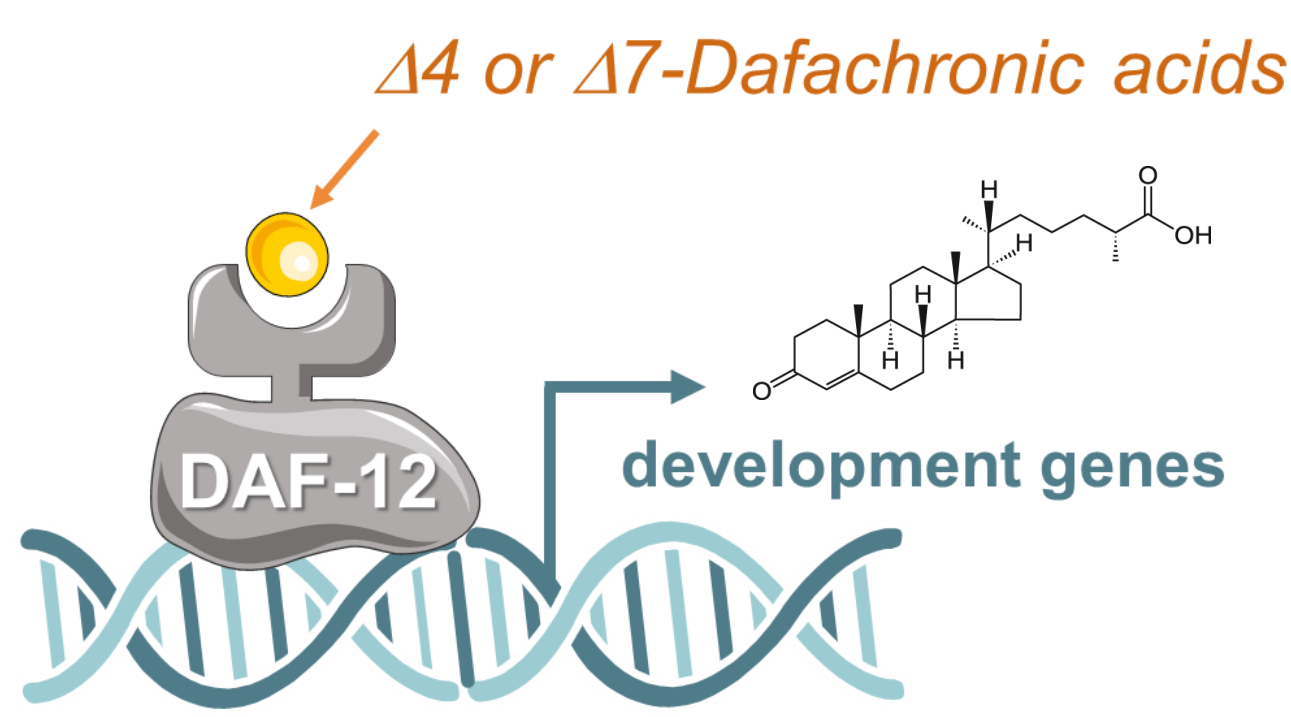
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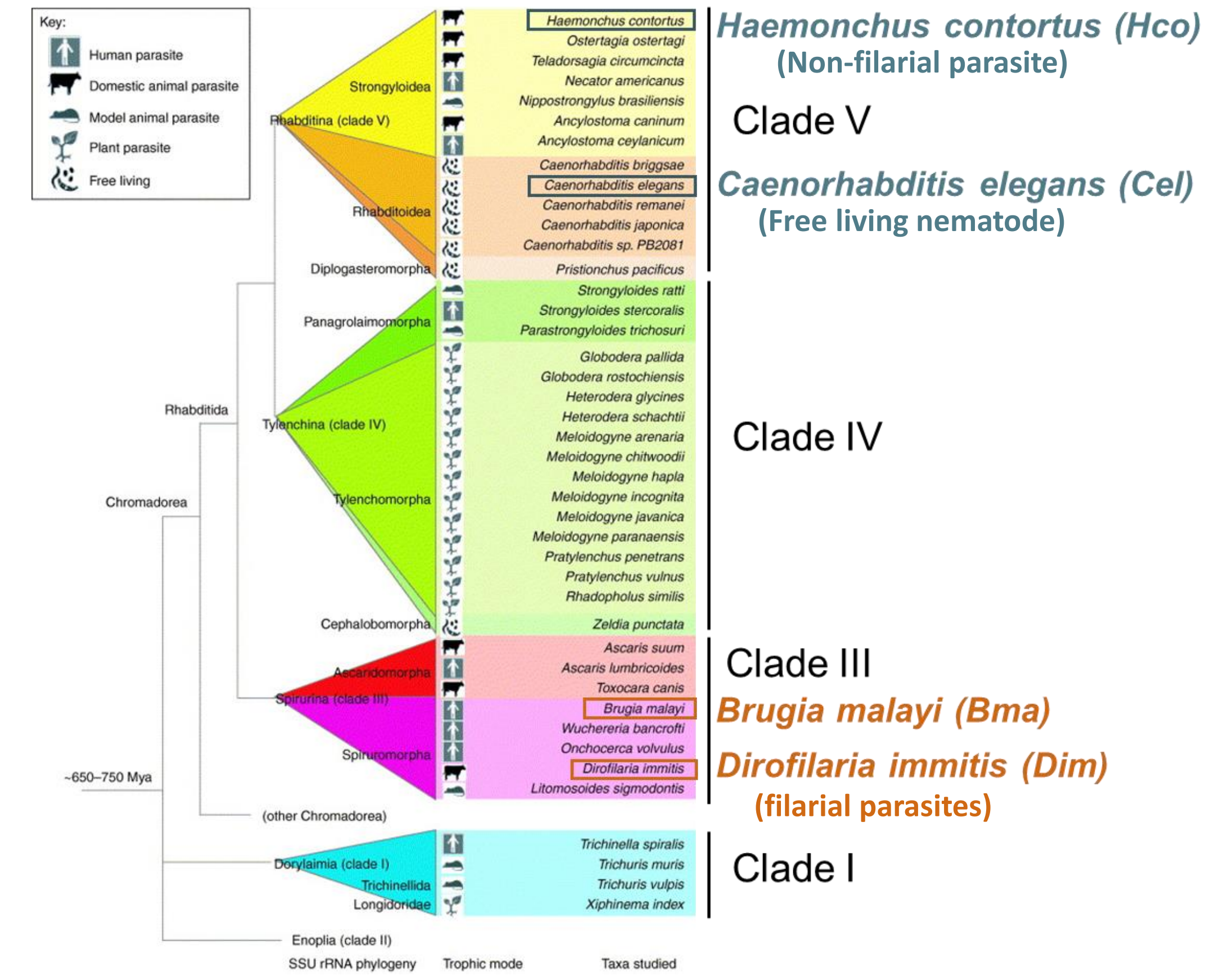


## INTRODUCTION

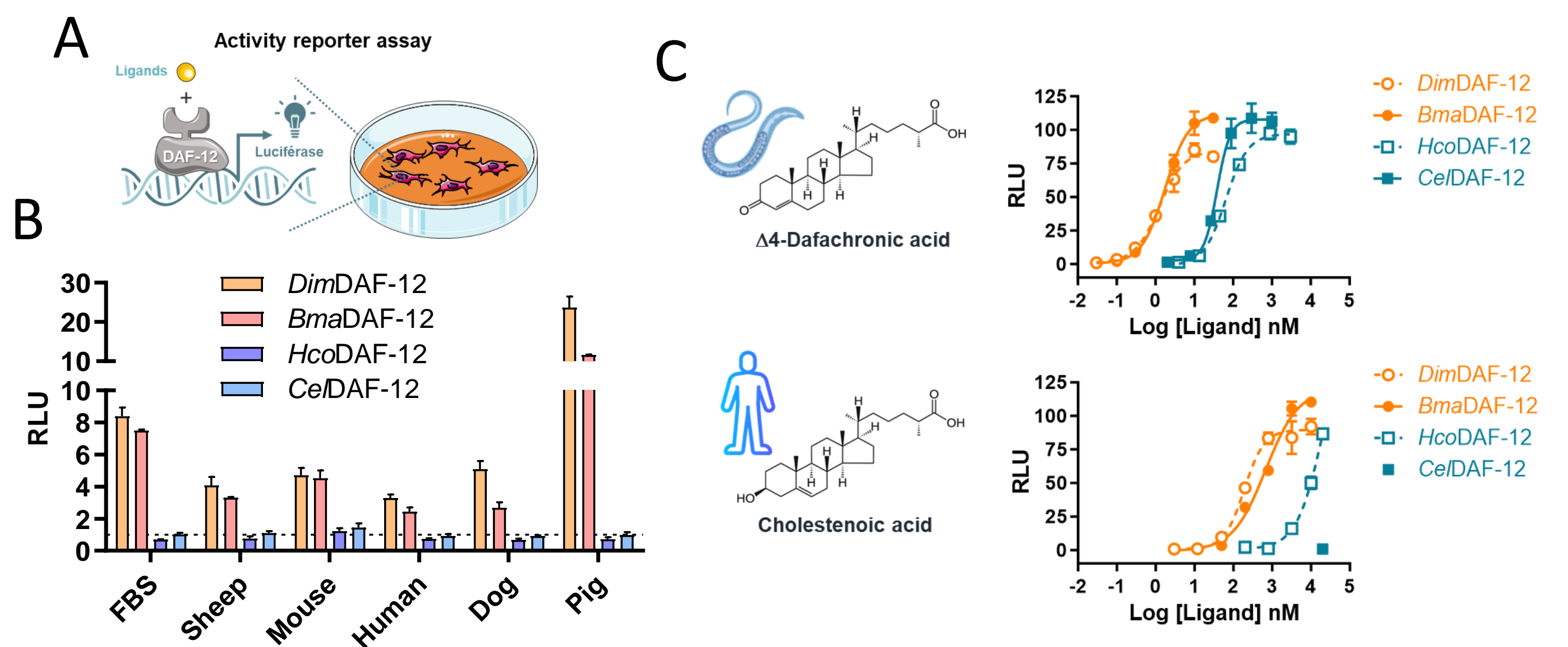
- The nematode model *Caenorhabditis elegans* harbours **284 Nuclear Receptor**
- DAF-12 is the only *C. elegans* NR with known **ligands, the dafachronic acids**.
- DAF-12 is structurally and functionally related to the mammalian FXR
- DAF-12 controls:
  - The expression of reproducible development genes
  - Entry to and exit from the dauer stage (*C. elegans*), an alternative quiescent stage more resistant to degraded environments and the infective larval stage (parasitic nematodes)



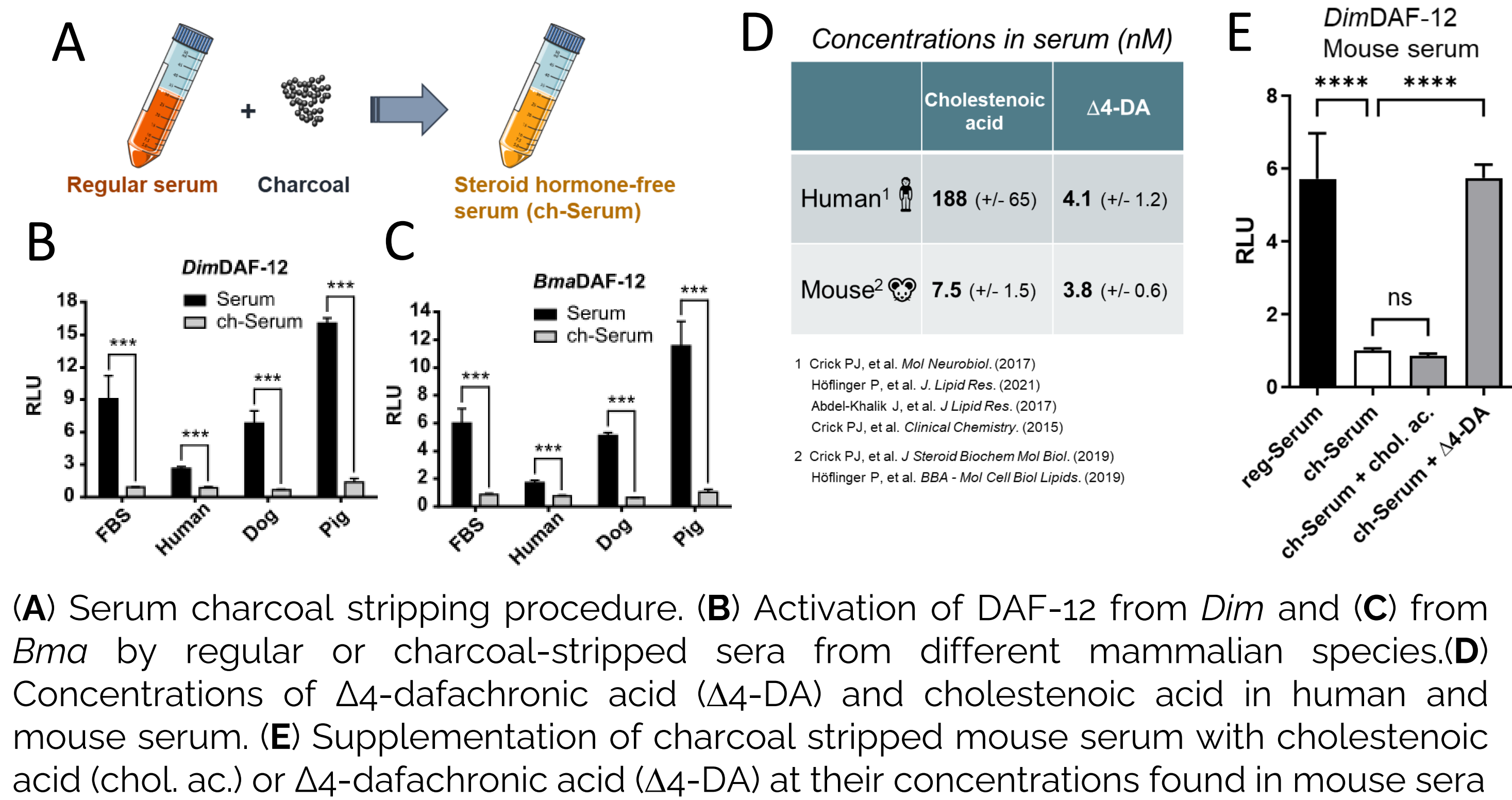
## OBJECTIVE: Compare DAF-12 activity and function in filarial and non-filarial nematodes



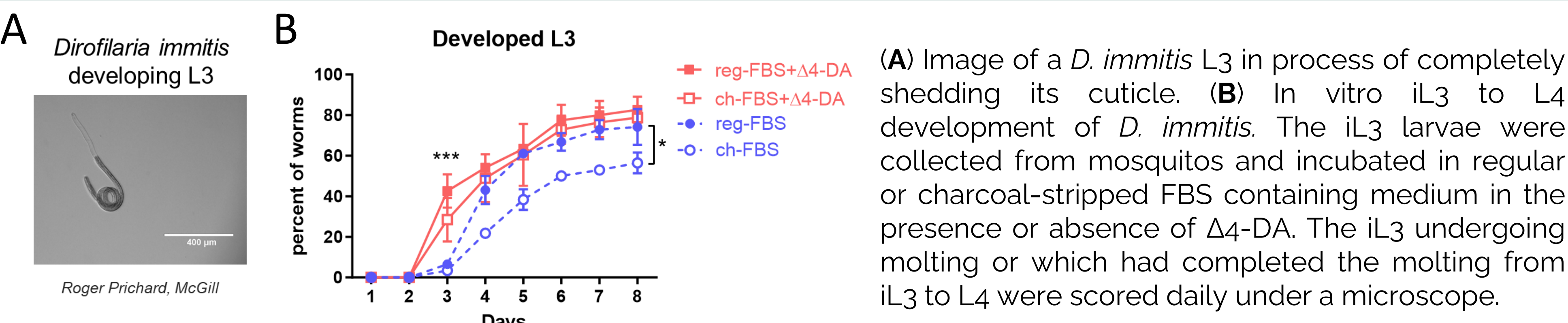
## SPECIFICITIES OF FILARIAL DAF-12 ACTIVATION



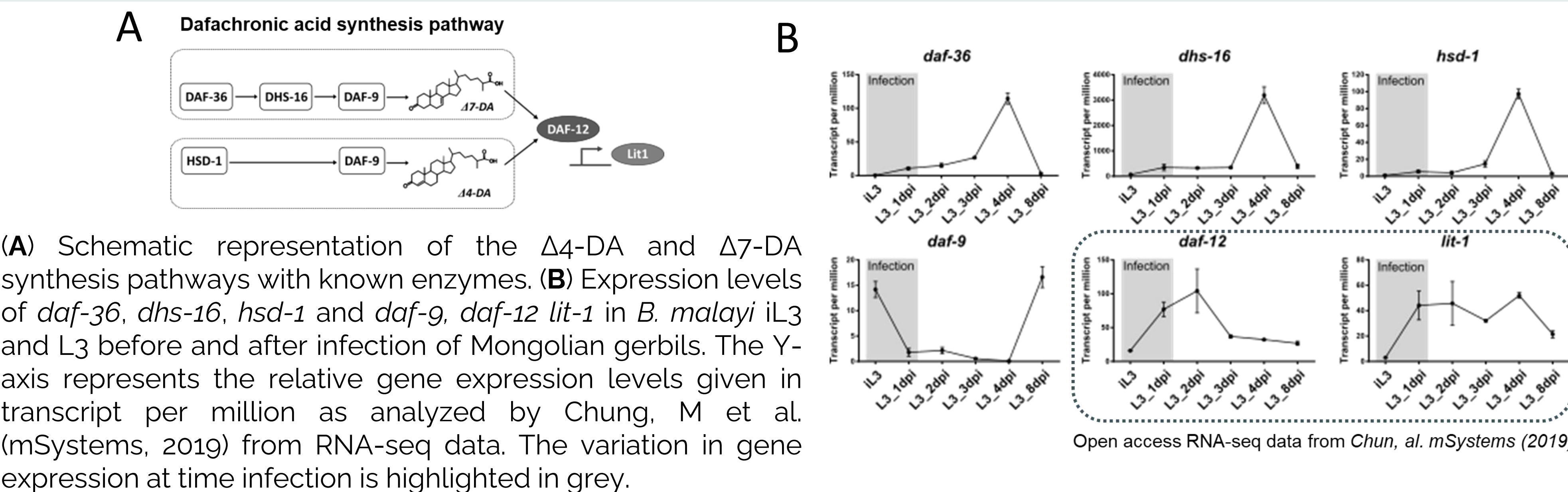
## MAMMALIAN SERA CONTAIN DAF-12 LIGANDS



## DAF-12 ACTIVATION STIMULATES D. IMMITIS IL3 DEVELOPMENT

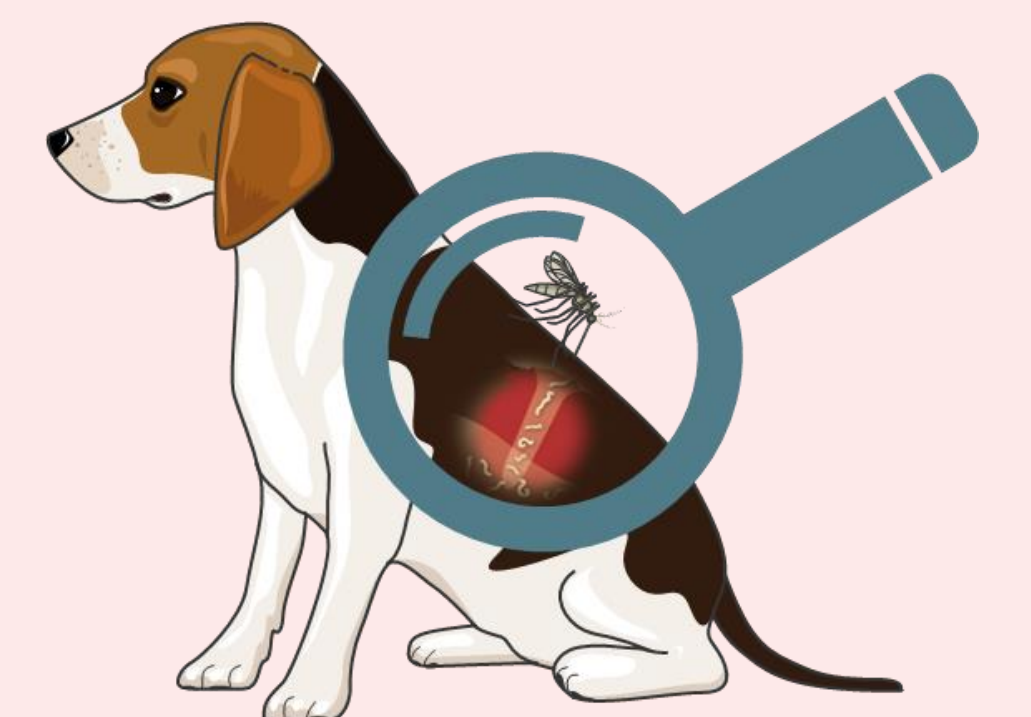


## DAF-12 LIGANDS BIOSYNTHESIS ENZYMES ARE DOWN-REGULATED IN THE FILARIAL NEMATODE BRUGIA MALAYI AT THE TIME OF INFECTION



## CONCLUSIONS

- Filarial DAF-12s are hypersensitive to their ligands
- Host serum contains DAF-12 ligands, including  $\Delta 4$ -dafachronic acid
- These DAF-12 ligands support *D. immitis* larval development
- The expression of genes involved in DA biosynthesis is very low during the early days of infection



**daf-12 may have evolved in filarial parasites to sense the host environment through its ligands and promptly trigger parasite development and growth upon infection.**