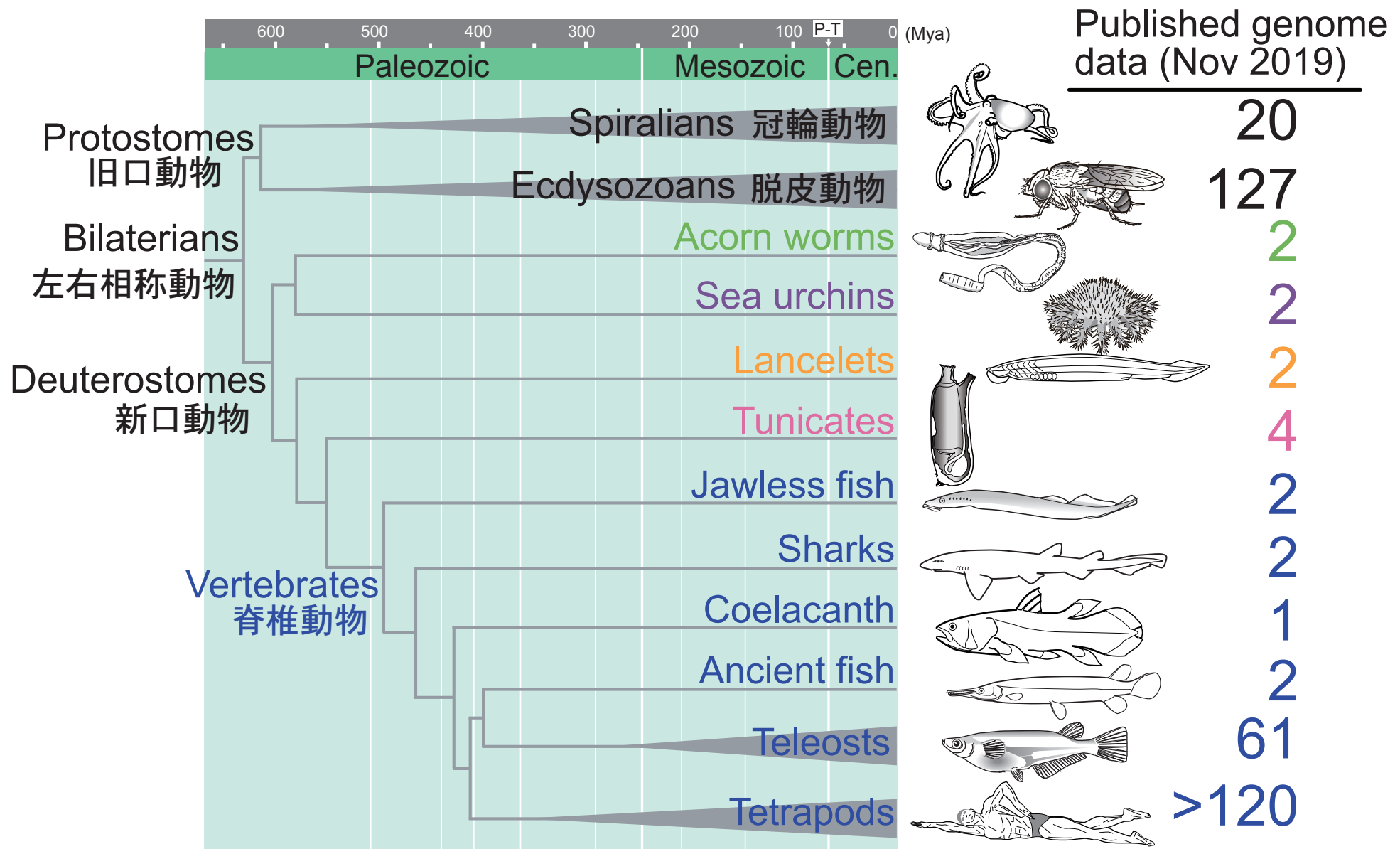


ORTHOSOCPE

遺伝子の起源と機能を推定するウェブツール

2021/4/21
井上潤

Genome data are accumulating



Difficult to identify gene with the same function

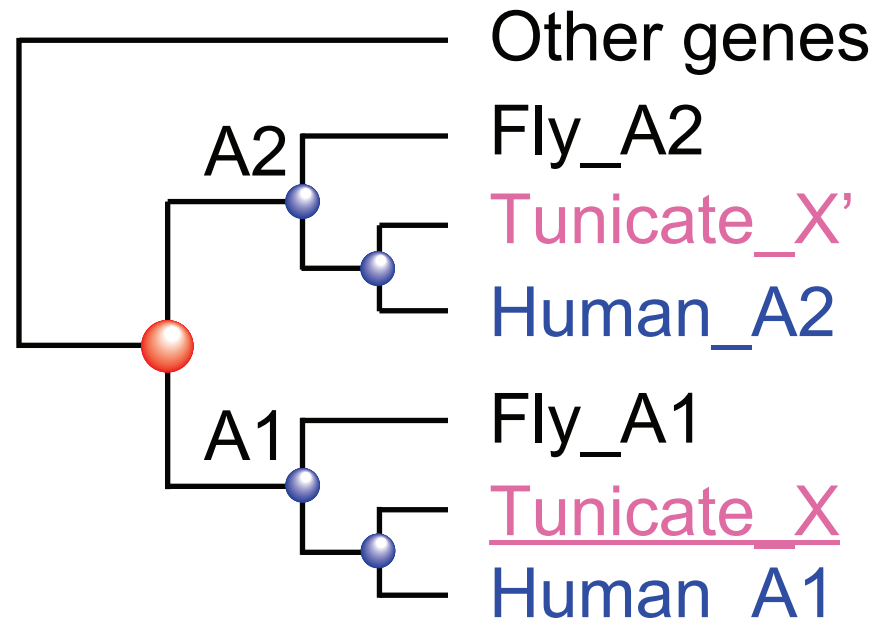
Why difficult

- > 20,000 genes in each species
- > Sequence is similar,
but different function

Inferring functions using orthogroups

Duplication and deletion of genes
=>
Orthogroup (オーソグループ):

Considering
Fly, Human and Tunicate,



Other genes

Fly_A2

Tunicate_X'

Human_A2

Fly_A1

Tunicate_X

Human_A1

Deuterostome
A1 orthogroup

Pairwise similarity
(BLAST)

Single ortholog
オーソログ1組

Orthogroup

Difficult to
identify,
A1 or A2 ?

Not enough,
A1 ?

Easy to
identify,
A1

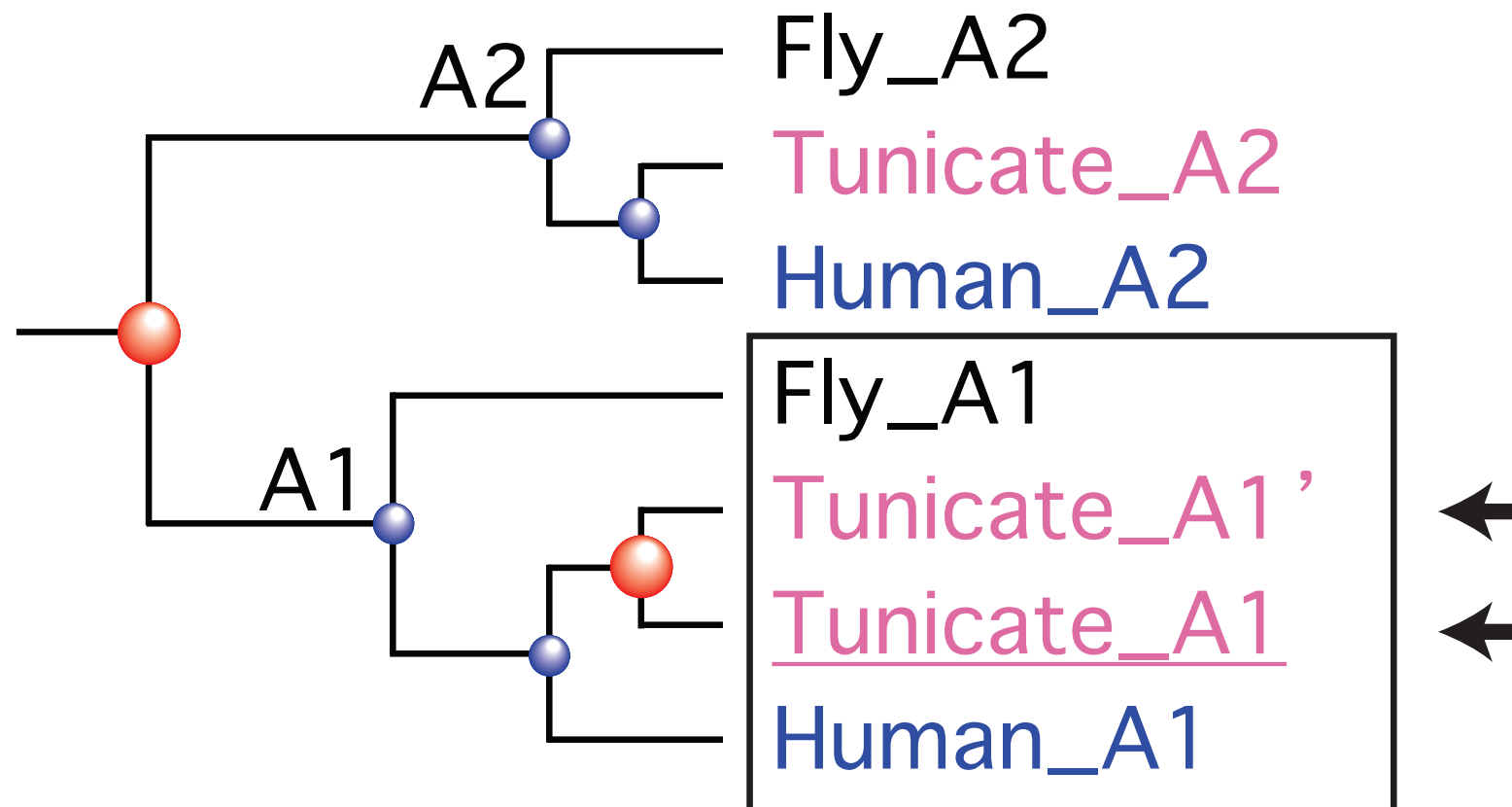
Orthogroup clearly shows function candidates

What ORTHOSCOPE can do?

By identifying orthogroups,

- Gene functions/names can be estimated.

=> Count the number of genes



ORTHOSCOPE v1.5.1

Gene tree and orthogroup estimation using a species tree (< 5 min as default).

7 Apr. 2021

[Instructions](#), [Species tree](#)

Support: Safari(except for v14), Firefox, Chrome

Mirror: [SAKURA AORI](#)

Focal group

[Actinopterygii](#)

[Mammalia](#)

[Vertebrata](#)

[Deuterostomia](#)

[Protostomia](#)

[Acropora](#)

[Plants](#)

Status

Ready.

Execute

Mode

☒ Tree Search Only
(Estimating gene tree only)

☐ Search/Rearrangement
(Comparing gene and species trees)

Upload file

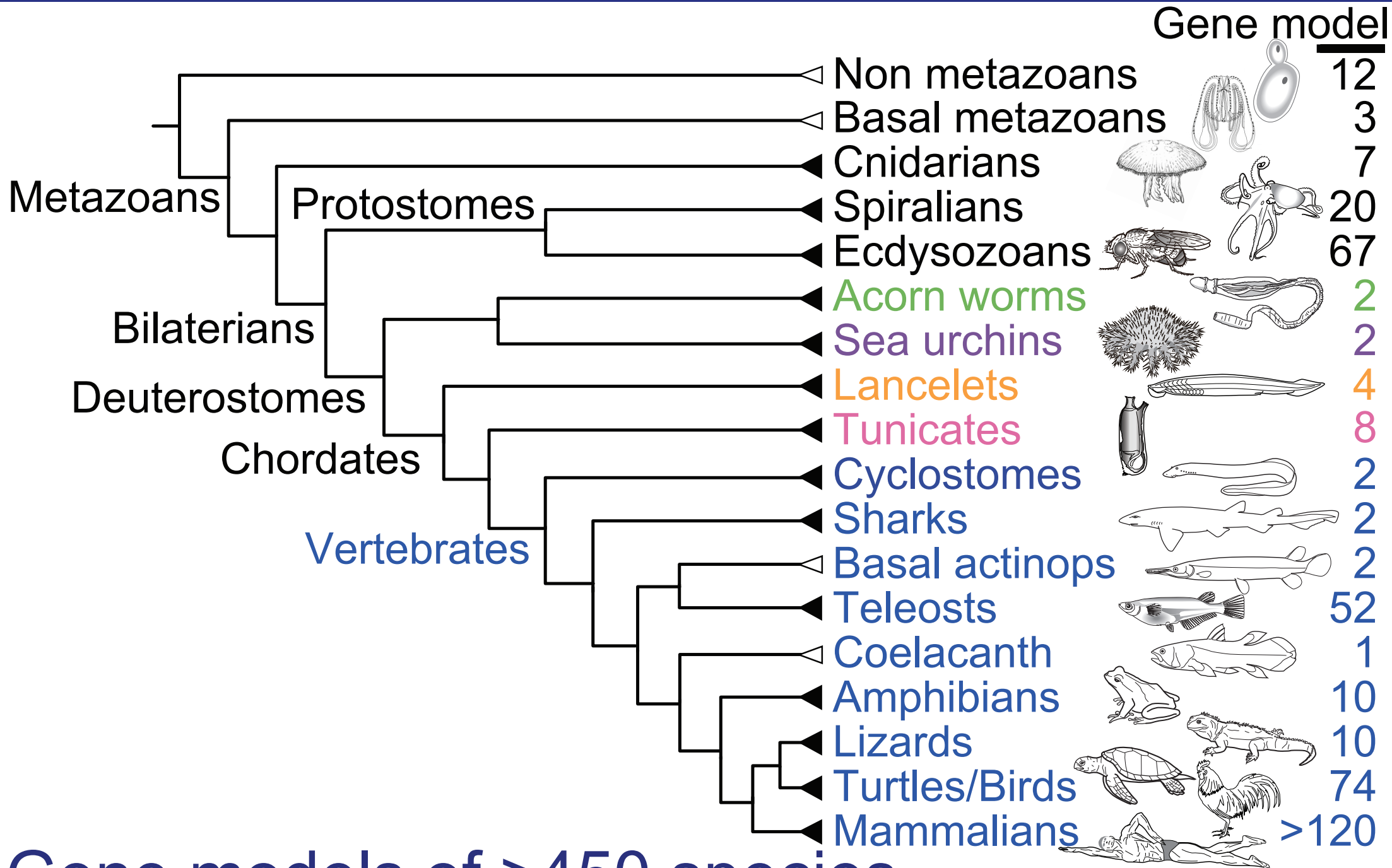
Sequences (fasta): ☒ DNA ☐ Amino acid

Example: [fasta file](#)

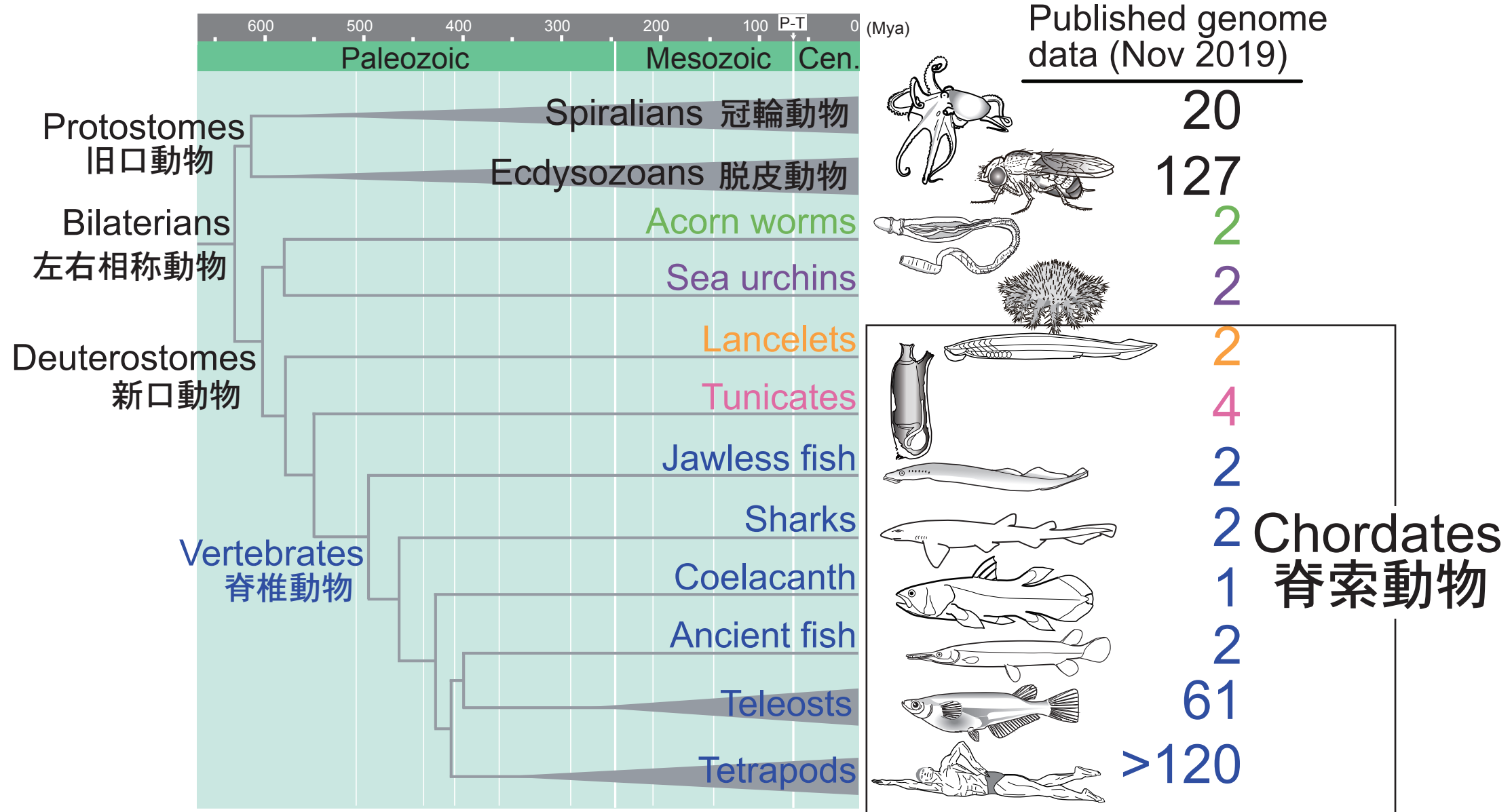
Species tree (newick): ファイル未選択

If not selected, [this tree](#) is used.

ORTHOSCOPE database



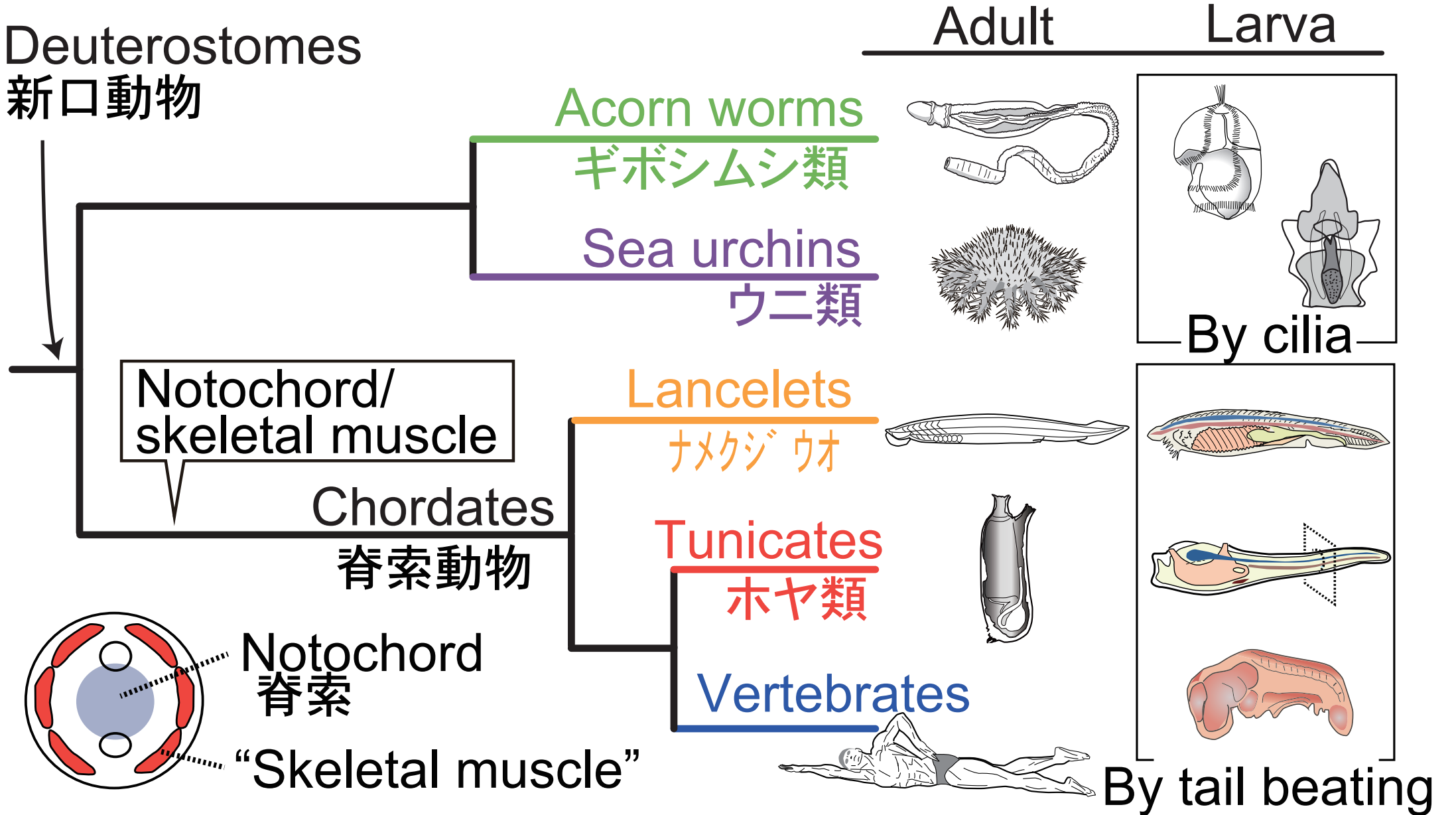
Example study: chordates



3 chordate lineages are dramatically different.

Chordate characteristics

Deuterostomes
新口動物



Fish-like larvae enabled chordate ancestors to swim by beating a tail with notochord.

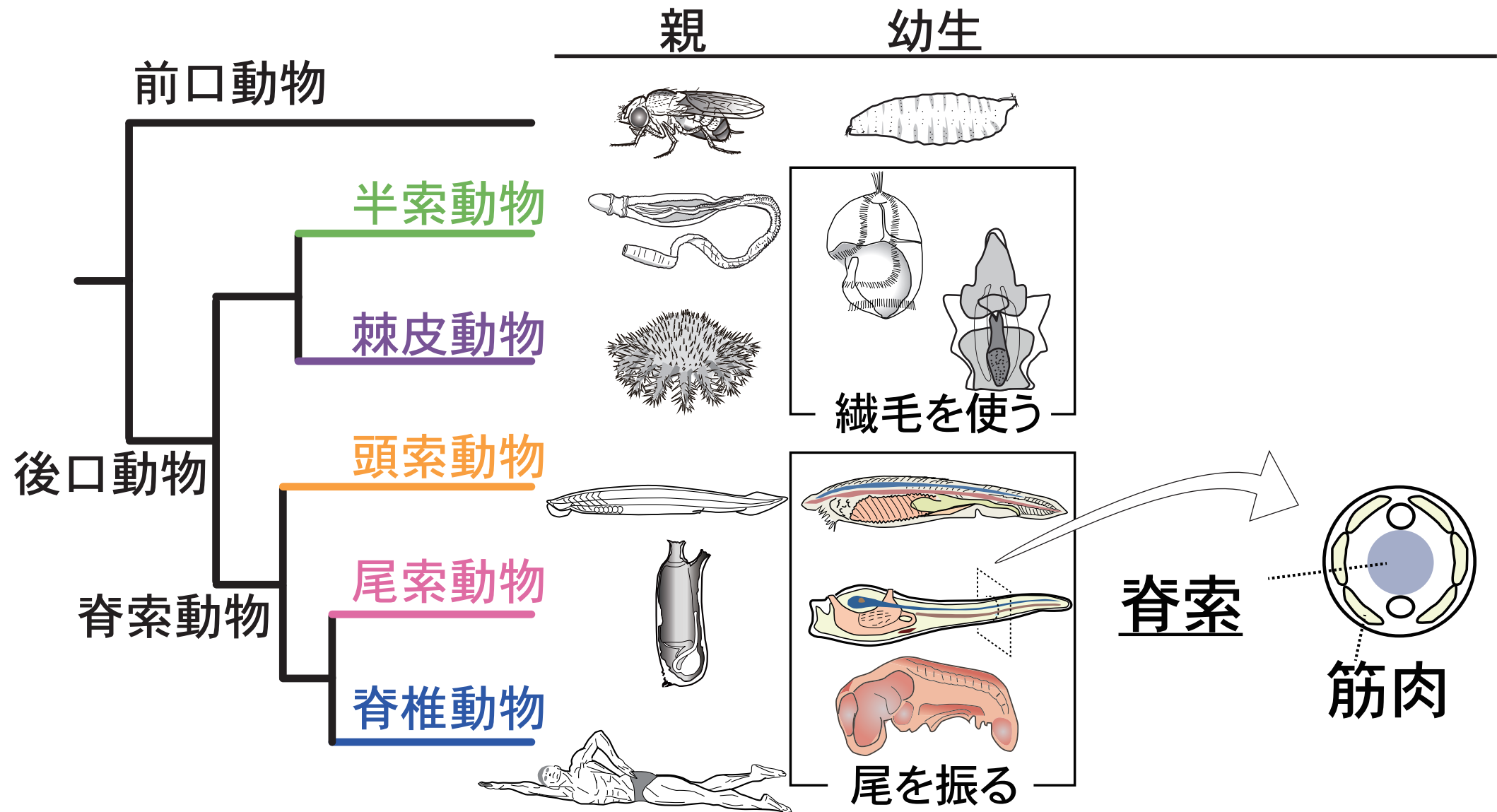
By tail beating
Fish-like larvae

ORTHOSCOPE の利用例

脊索動物の出現を可能にした遺伝子： ブラキウリ遺伝子

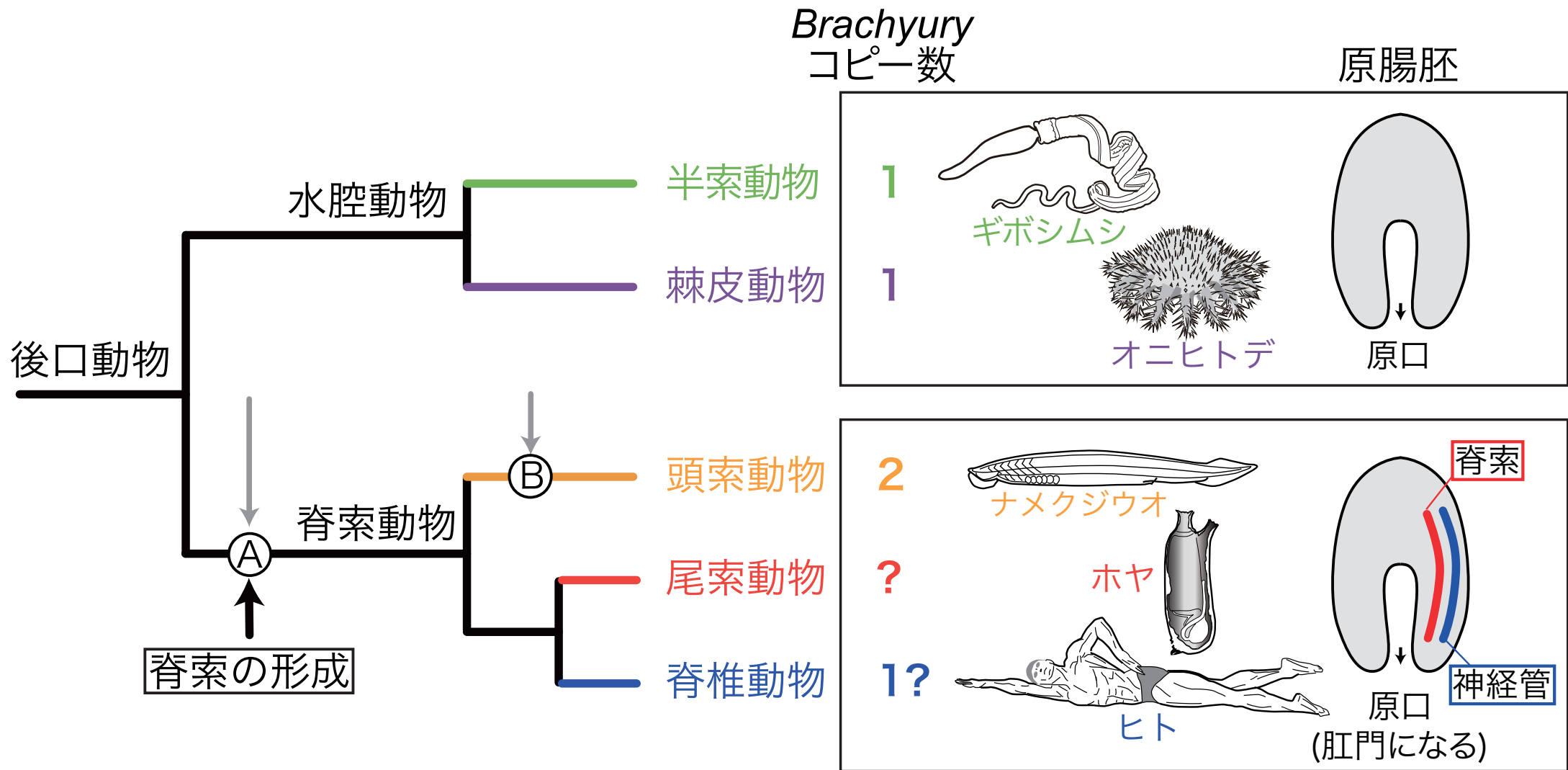
Inoue J, Yasuoka Y, Takahashi H, Satoh N. 2017.
Zoological Letters. 3: 4.

ブラキウリの役割



ブラキウリは脊索の形成に重要

Brachyury の役割：原腸胚と脊索の形成



A, B どっちで 2 つになった?

ORTHOSCOPE v1.0.2

Gene tree and orthogroup estimation using a species tree (< 5 min as default).

29 Nov. 2019

[Instructions](#), [Species tree](#)

Support: Safari(latest), Firefox, Chrome

Mirror: [N](#), [O](#), [S](#)

Focal group

[Actinopterygii](#)

[Mammalia](#)

[Vertebrata](#)

[Deuterostomia](#)

[Protostomia](#)

Status

Ready.

Execute

Mode

☒ Tree Search Only
(Estimating gene tree)

☐ Search/Rearrangement
(Comparing gene and species trees)

Upload file

Coding or amino acid sequence set
(fasta)

☐ Amino acid ☒ DNA [Example](#)

Species tree
(newick)

If not selected, [this tree](#) is used.

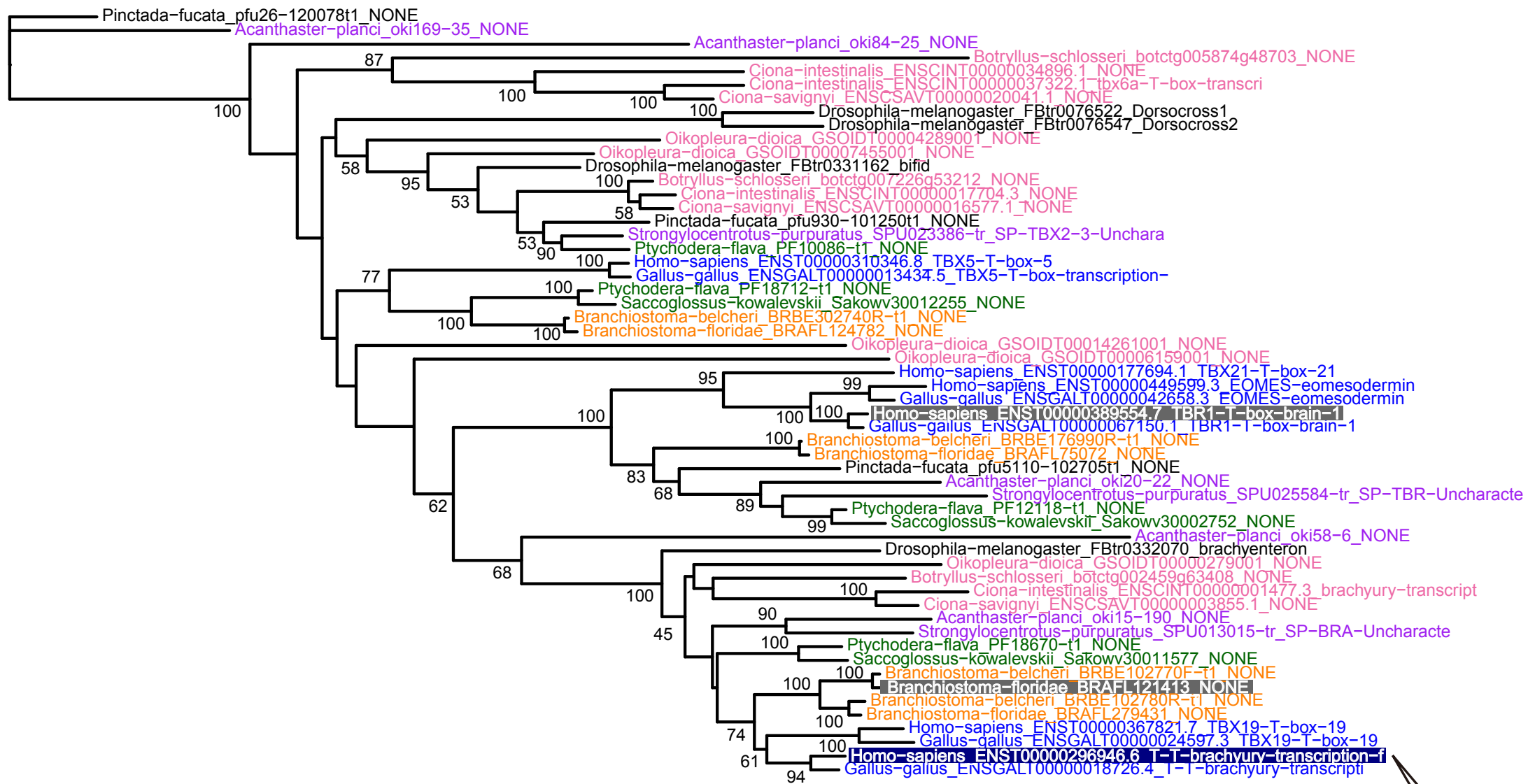
The first query

```
DeuterostomeBra.fas.txt Free Mode
~/Downloads/DeuterostomeBra.fas.txt
1 >Homo-sapiens_XXX1
2 ATGAGCTCCCCTGGCACCGAGAGCGCGGGAAAGAGCCTGCAGTACCGAGTGGACCACCTGCTGAGC
3 >Branchiostoma-floridiae_XXX
4 ATGAAGCAGACACCGGACCAGTTCTCGGTTAGCCACCTCCTGAGCGCCGTGGAGAGCGAGATCTCG
5 >Homo-sapiens_ENST00000389554.7_T-box-brain-1
6 ATGCAGCTGGAGCACTGCCTTTCTCCTTCTATCATGCTCTCCAAGAAATTTCTCAATGTGAGCAGC
```

L: 1 C: 1 Text File Unicode (UTF-8) Unix (LF) Saved: 2019/05/31 11:11:20 4,767 / 12 / 7 100%

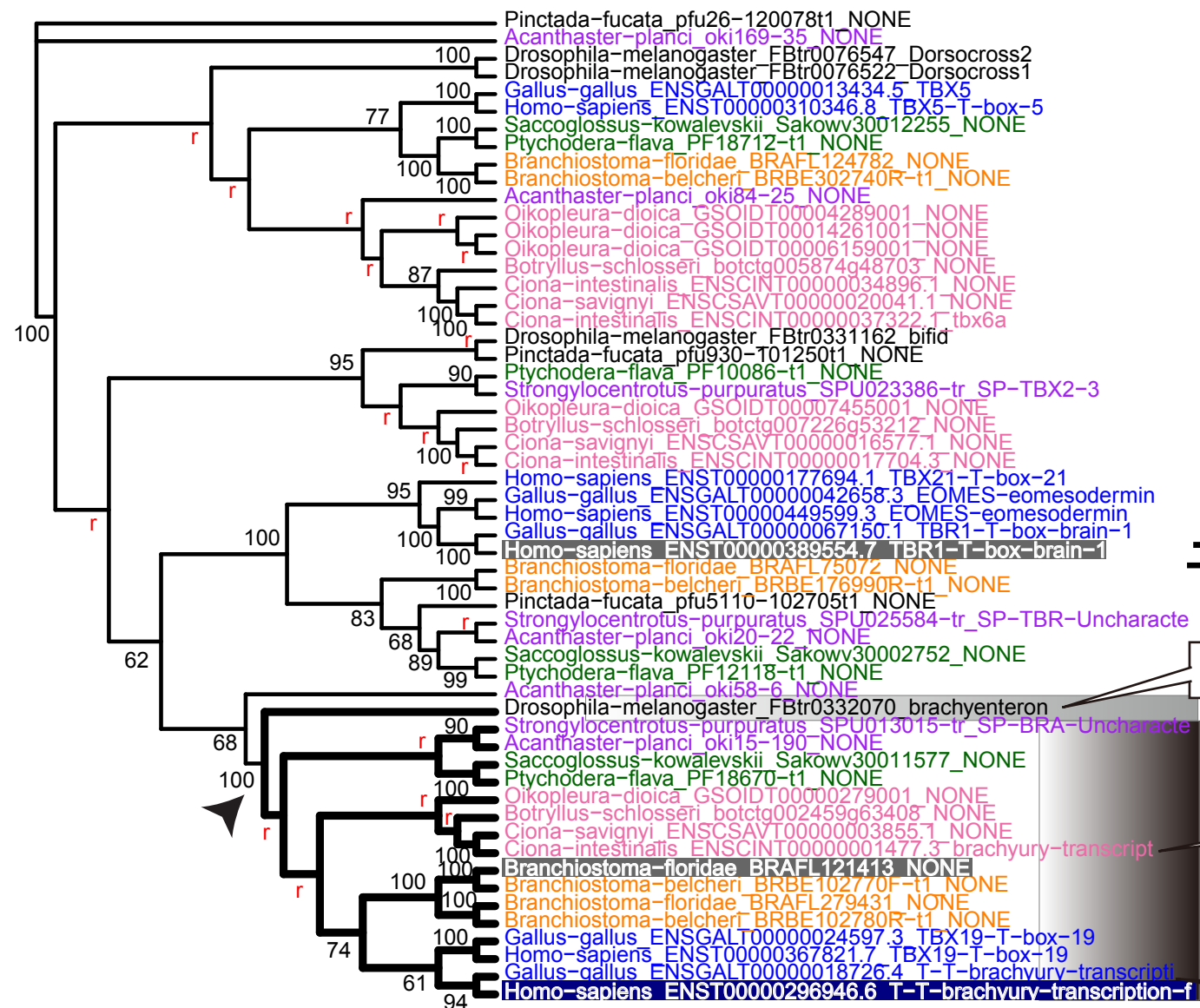
Several queries can be used.

結果: NJ tree



第 1 クエリ

ユーザーによる結果の解釈



モデル生物の情報を参照

Drosophila: Brachyenteron

Ciona: Brachyury

Human: Brachyury

Transcript ID

Drosophila-melanogaster_FBtr0332070_brachyenteron

Ensembl (<http://www.ensembl.org>)

Search

All species  for

FBtr0332070 

e.g. **BRCA2** or **rat 5:62797383-63627669** or **rs699** or **coronary heart disease**



FB2019_03, released Jun 11, 2019

Gene: Dmel\byn

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J2G ▾

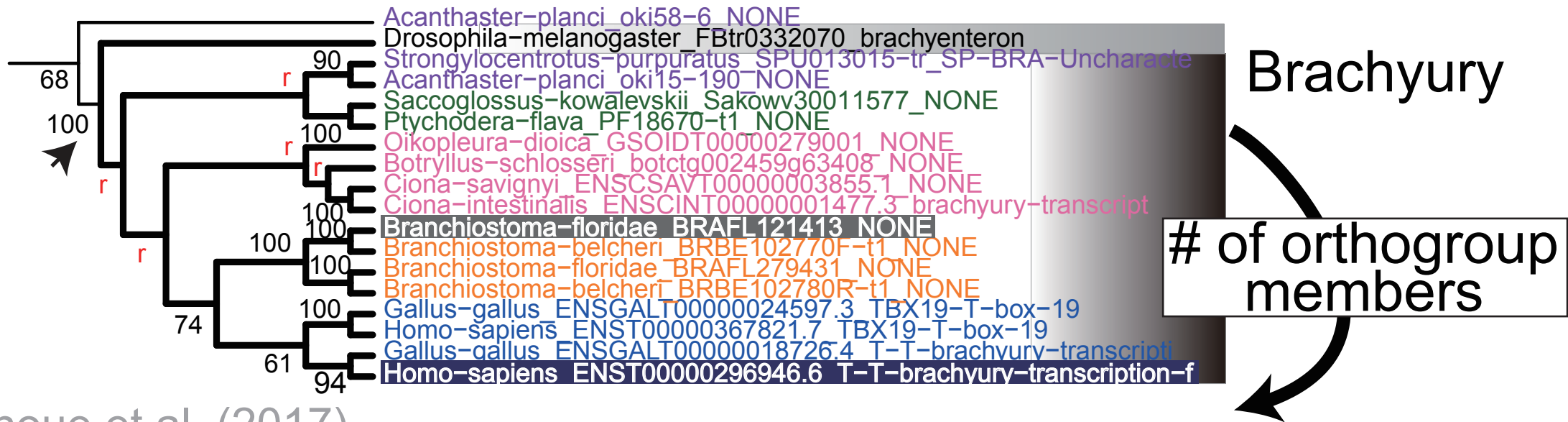
Jump

General Information

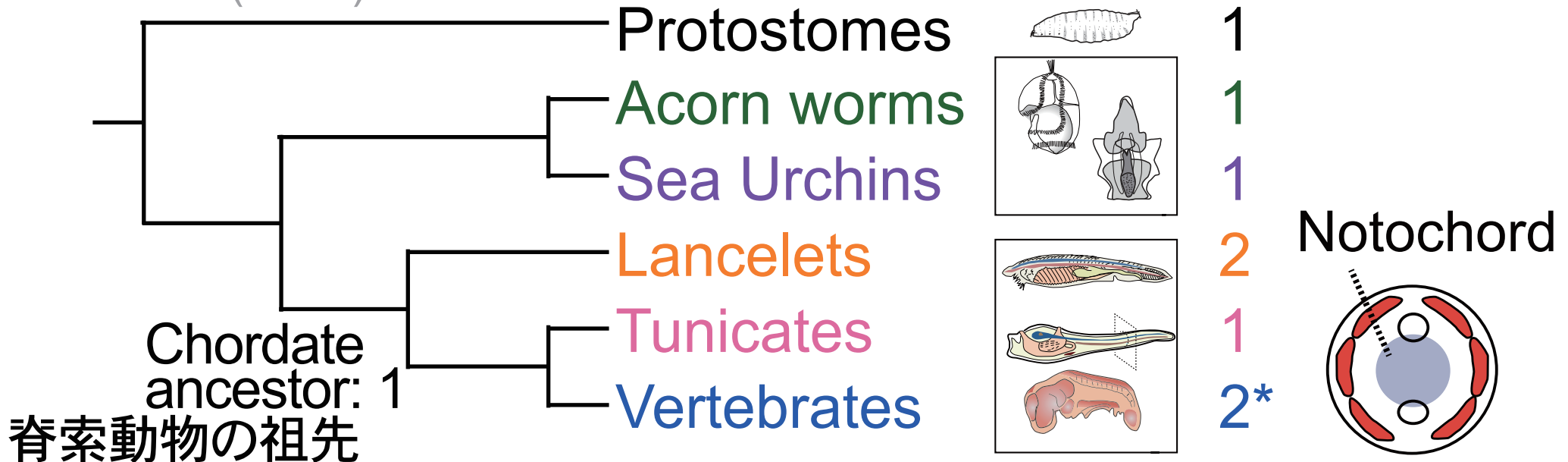


Symbol	Dmel\byn	Species	<i>D. melanogaster</i>
Name	brachyenteron	Annotation Symbol	CG7260
Feature Type	protein_coding_gene	FlyBase ID	FBgn0011723
Gene Model Status	Current	Stock Availability	6 publicly available
Gene Snapshot	brachyenteron (byn) encodes a T-domain transcriptional activator that acts in developmental specification, in particular it specifies posterior gut structures and a subset of posteriorly derived visceral muscles. [Date last reviewed: 2019-03-07]		

How to use ORTHOSCOPE results

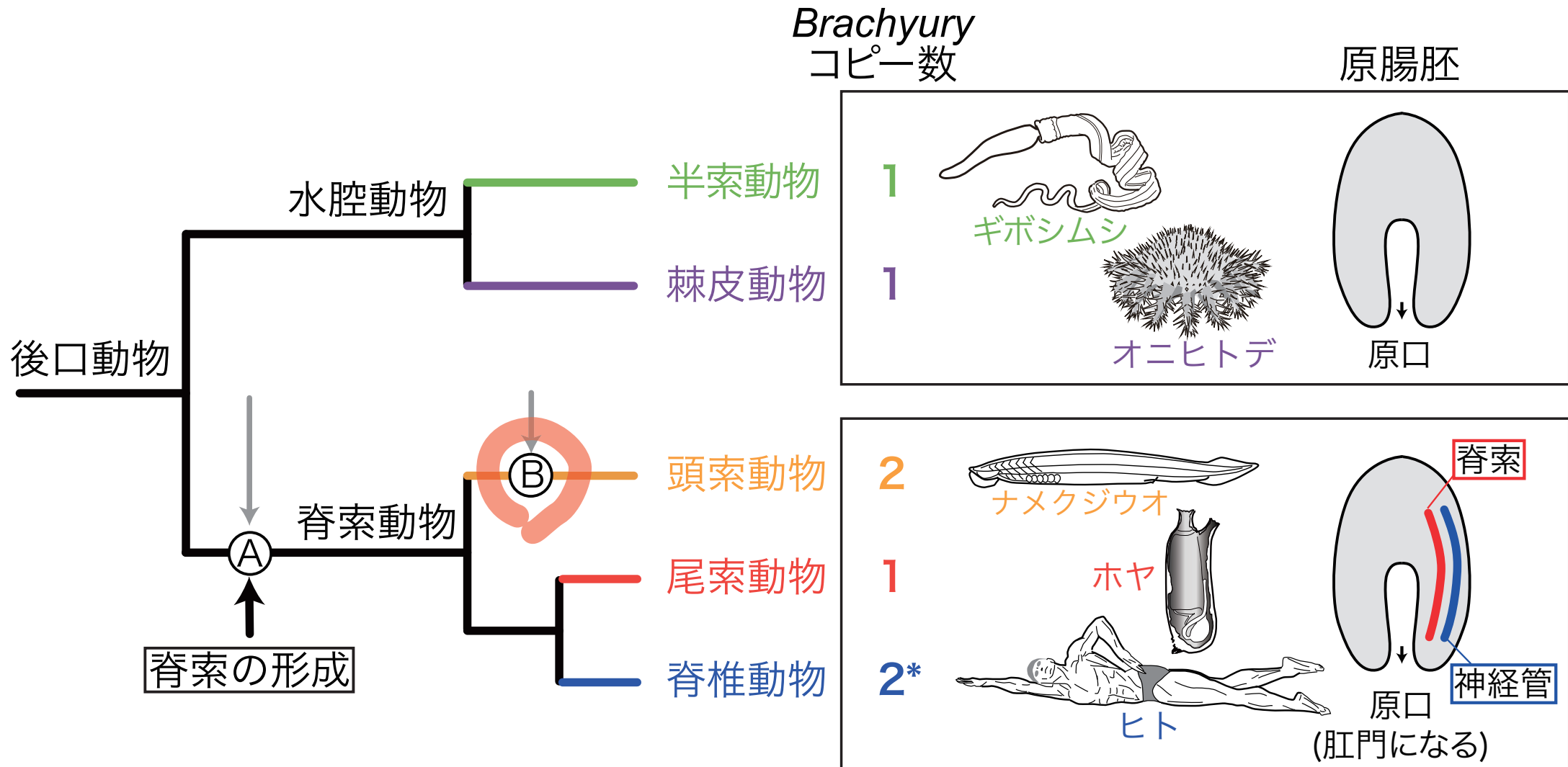


Inoue et al. (2017)



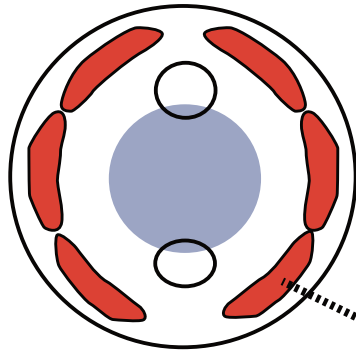
Chordate ancestor possessed only 1 copy of Bra gene

Brachyury の役割：原腸胚と脊索の形成



A, B どっちで 2 つになった？ => B
=> A で 1 つの Bra に 2 つの機能が追加

ORTHOSCOPE example

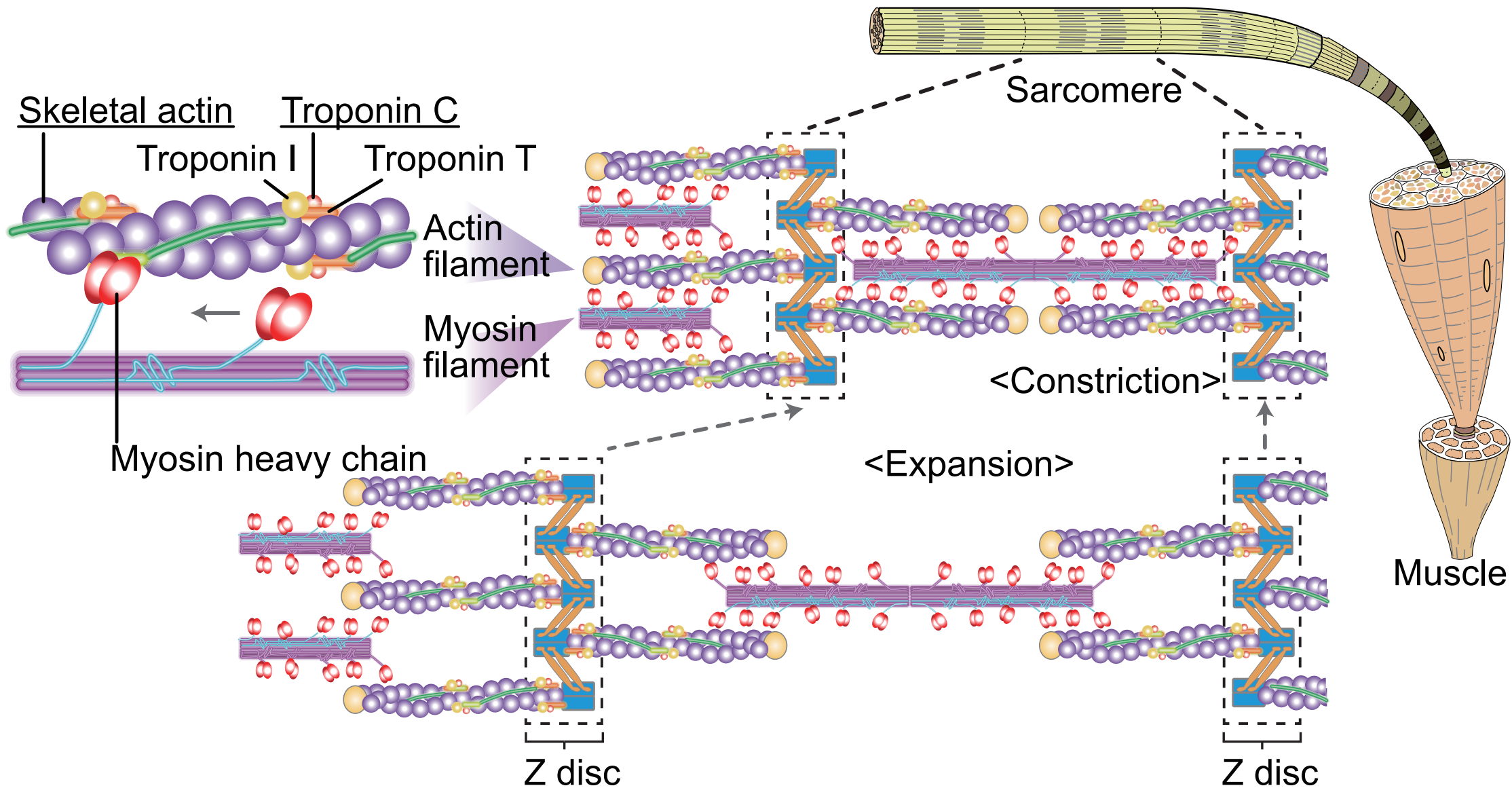


“Skeletal muscle”

Origins of muscle proteins

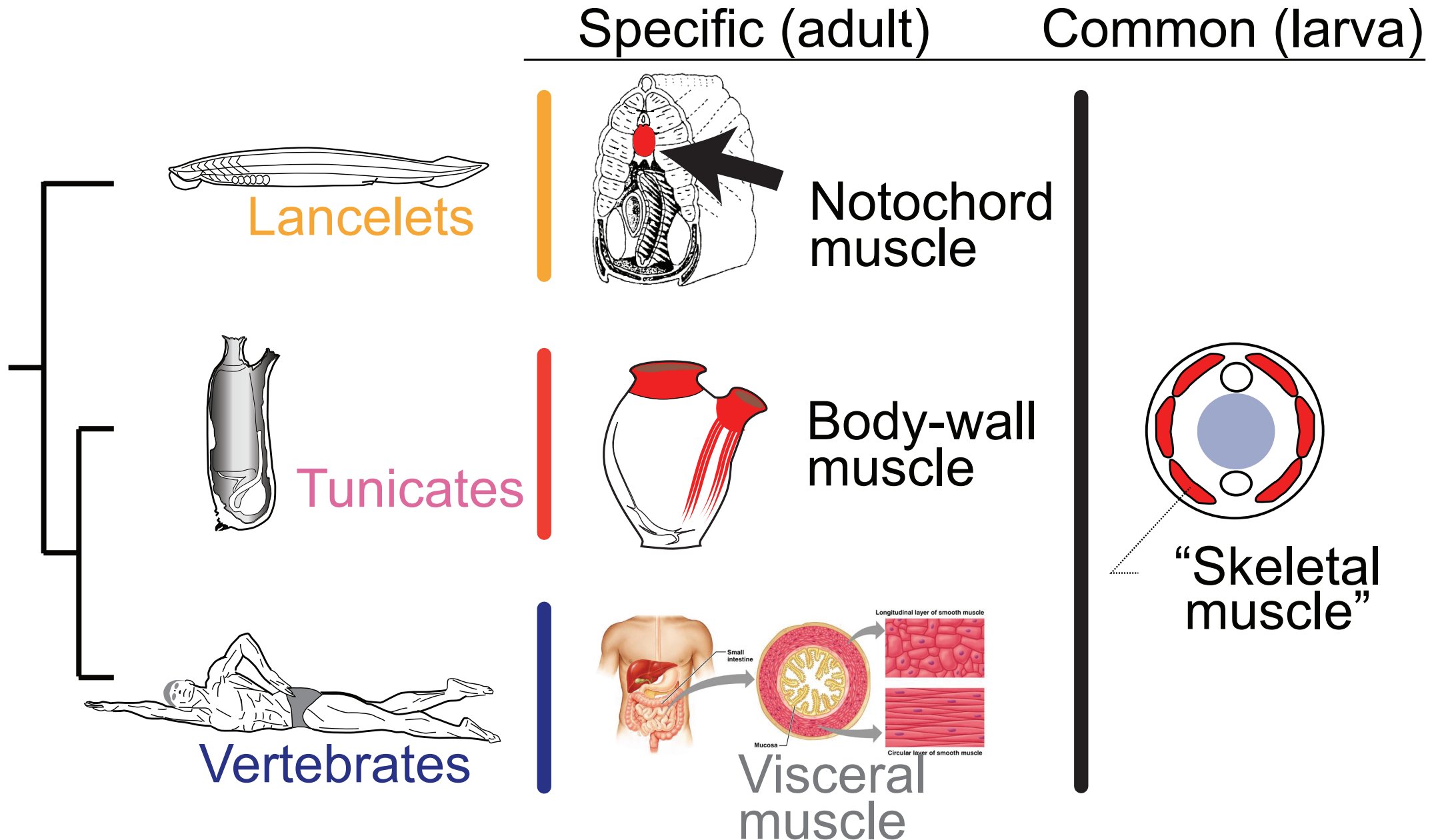
Inoue J, Satoh N. 2017.
Mol. Biol. Evol. 35:914–924

Skeletal muscle of vertebrates



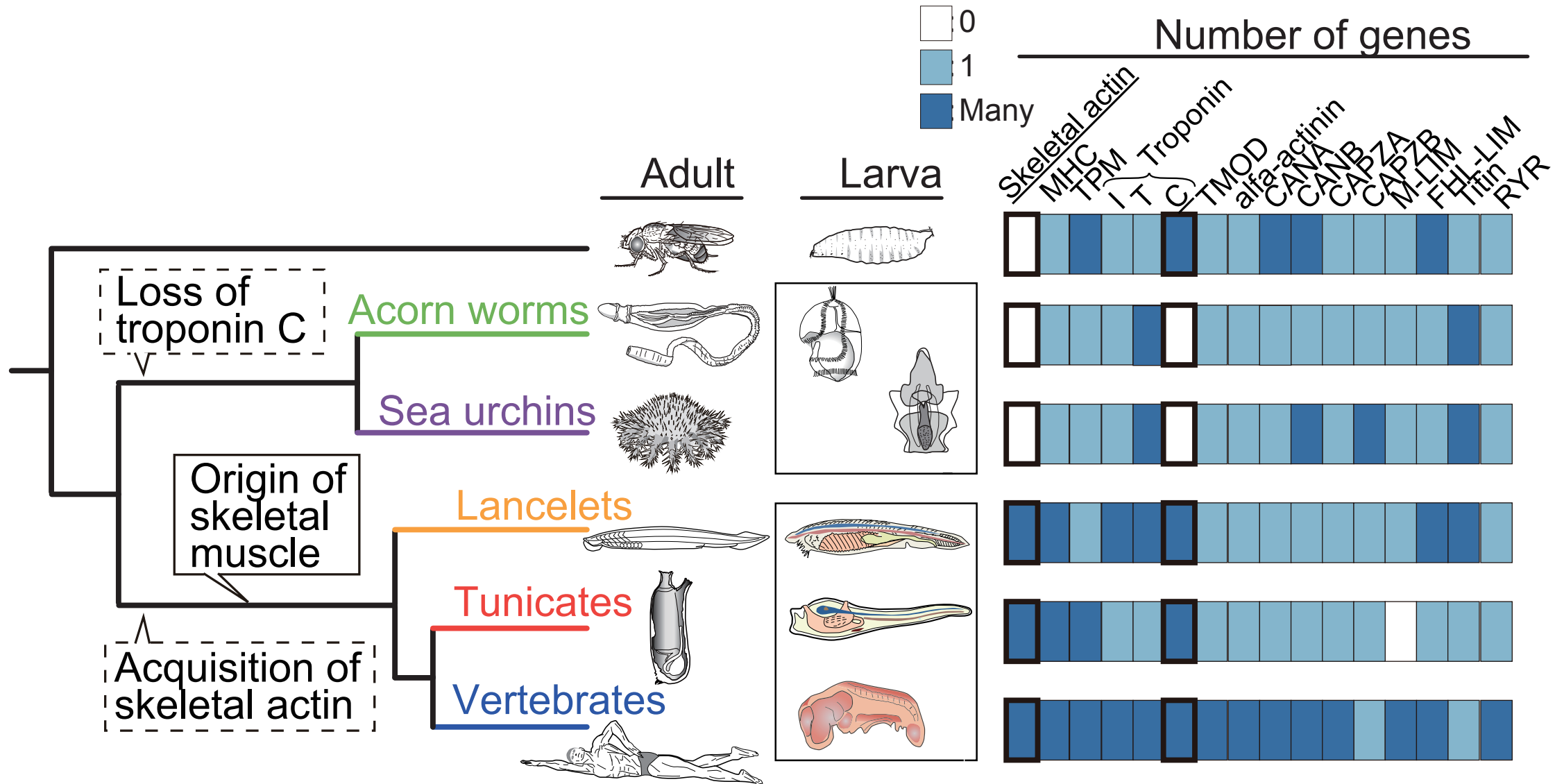
Estimating origin of each protein

Lineage-specific muscles



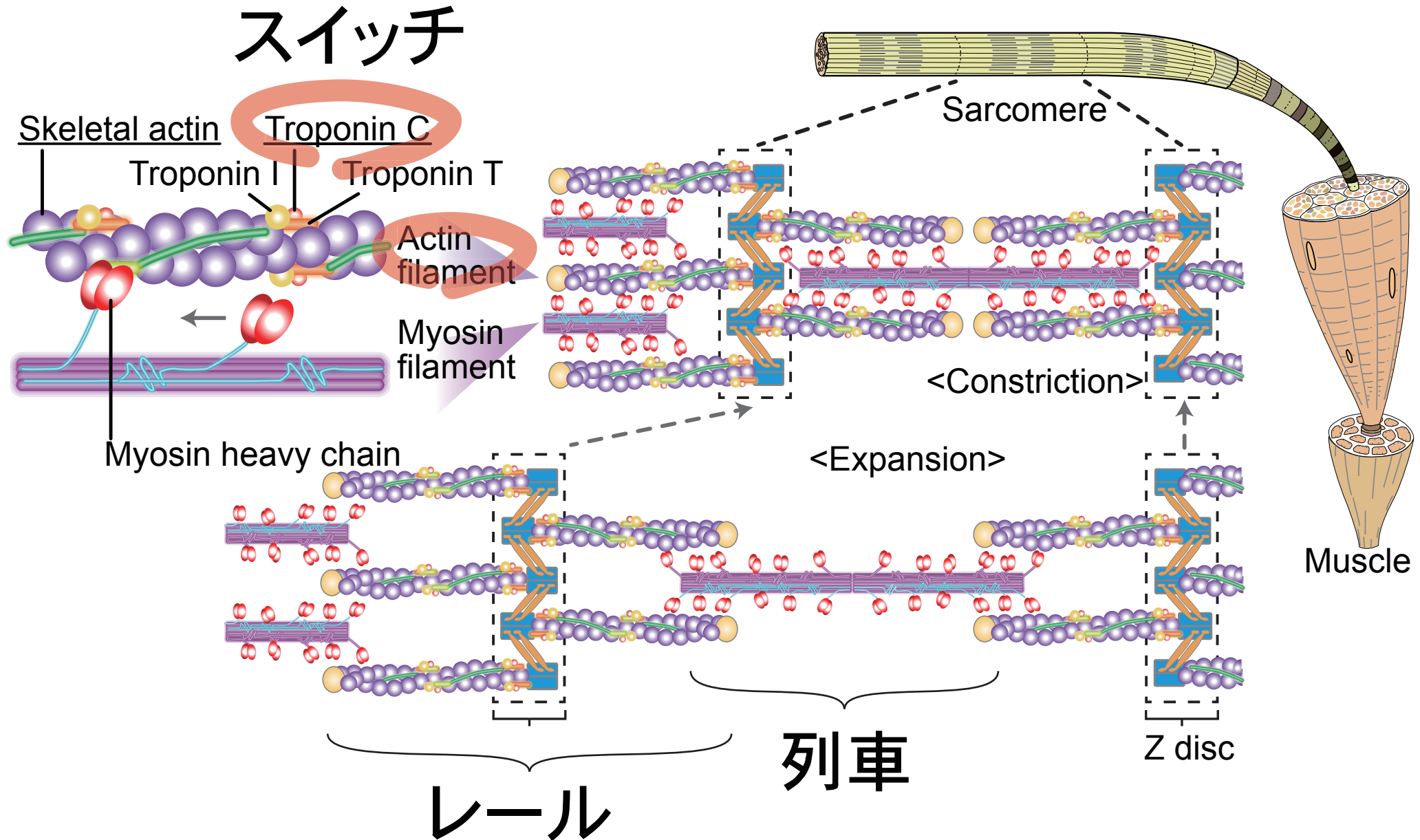
How fast “Skeletal muscle” emerged?

Results: Pre/abs of orthogroup members



Skeletal muscle was acquired by using 2 proteins
Skeletal actin and Troponin C.

Skeletal muscle of vertebrates



新しいルールとスイッチの導入して速くなった

Summary of ORTHOSCOPE

Significance:

- Origin of genes
- User friendly and quick

Ishikawa et al. 2019 Science

Shiraishi et al. 2019 PNAS etc.

Problem:

- Gene function of model organisms
=> Needs to be confirmed

ORTHO
オーソログを

SCOPE
一つの遺伝子で詳しく検証