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Research advances of sex determination and differentiation related genes in molluscs

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Abstract Sex determination and differentiation are the basic events of development and the mechanisms of sex determination and differentiation are the hot issues of life science researches. There are diverse types of sexual systems existing amongst molluscs, such as hermaphroditism, gonochorism, protandry and sex reversal, which makes them the ideal animal groups to study the mechanisms of sex determination and differentiation, and their evolution processes of invertebrates. It is of great significance for revealing the molecular mechanisms of sex determination and differentiation in molluscs to explore the regulatory genes of sex determination and differentiation and clarify the regulatory role of related genes. In this review, we introduced the research progress and the prospects of sex determination and differentiation related genes in molluscs, which would provide some information for studying the mechanisms of sex determination and differentiation, reproductive operation and genetic improvement in molluscs.

Key words molluscs; sex determination; sex differentiation; genes

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Tab.1 Candidate genes related to sex determination and differentiation screened by omics in molluscs

species	technologies	gene name	references
<i>C. gigas</i>	microarray	<i>Bindind py-30 foxL2 nanos3 cd63 vitellogenin</i>	[13]
	RNA-Seq	<i>SoxH FoxL2 Dsx DmrtA2 Sh3kbp1 Malrd1-like Trophoblast glycoprotein-like Protein PML-like Protein singed-like PREDICTED: paramyosin</i>	[14-16]
	Genome-wide screening	<i>nanos piwi dax1 5-HT receptor</i>	[17]
	Genotyping-by-Sequencing	<i>proteasome subunit beta type-3 G-protein coupled estrogen receptor 1</i>	[10]

<i>C. hongkongensis</i>	RNA-Seq	<i>nanos piwi ATRX FoxL2 beta-catenin</i>	[18]
<i>Chlamys farreri</i>	RNA-Seq	<i>FSHR GABBR MTR CYP17 Vtg4 Wnt10a Htr4 PTGR1 Zar1</i>	[11]
<i>Patinopecten yessoensis</i>	RNA-Seq	<i>Foxl2 SoxH Dmrt1</i>	[19-20]
<i>C. nobilis</i>	RNA-Seq	<i>Foxl2 -Catenin 5-HT receptor Vitellogenin Dmrt2 SRY fem-1 Sfp2 Sa6 AMY-1 vasa nanos sox9</i>	[21-22]
<i>Nodipecten subnodosus</i>	RNA-Seq	<i>dmrt2 wnt4 sex-1 sfrp2 sox9</i>	[23]
	Suppressive Subtraction Hybridization and Pyrosequencing	<i>dmrt1 clk-2 fkbp52</i>	[24]
<i>Pinctada fucata</i>	Genome-wide screening	<i>vasa nanos dmrt 5-HT receptors vitellogenin estrogen receptor</i>	[25]
<i>P. margaritifera</i>	RNA-Seq	<i>Dmrt fem-1 foxl2 vitellogenin</i>	[26]
<i>Hyriopsis cumingii</i>	RNA-Seq	<i>DMRT1 SOX9 SF1 FOXL</i>	[27]
<i>H. schlegelii</i>	RNA-Seq	<i>wnt4 rspo1 fem1 tra1 Sry Dmrt1 Dmrt2 Sox9 GATA4 WT1 Wnt4 Rspo1 Foxl2 -catenin</i>	[28-29]
<i>Sinonovacula constricta</i>	RNA-Seq	<i>DmrtA2 Sox9 Fem-1b Fem-1c Vg CYP17A1 SOHLH2 TSSK</i>	[30]
<i>Tegillarca granosa</i>	RNA-Seq	<i>Foxl2 Sox -catenin CBX Sxl</i>	[31]
<i>Mactra chinensis</i>	RNA-Seq	<i>3 -HSD 17 -HSD LH CYP17 CYP1A1 CYP1B1 Estrogen vitellogenin</i>	[32]
<i>Haliotis rufescens</i>	RNA-Seq	<i>VTG fusion protein tektin lysin SOX</i>	[33]

2

2.1 *Dmrt*

<i>Dmrt</i>	doublesex and mab-3 related transcription factor	DM
DM	<i>Drosophila melanogaster</i>	<i>Doublesex Dsx</i>
<i>Caenorhabditis elegans</i>	<i>Maleabnormal-3 mab-3</i>	
[34-35]	Raymond [36]	DM
<i>Dmrt1</i>	<i>Oryzias latipes</i> [37]	<i>Daphnia magna</i> [38]
[6]	<i>Dmrt</i>	<i>Dmrt</i>
	<i>Dmrt1</i>	Y
		<i>DMY</i> [39]

2.5 *Dax1* -catenin

Dax1 DSS-AHC critical region on chromosome X gene 1 *Nr0b1* Nuclear receptor
 subfamily 0 group B member 1 nuclear receptor *Dax1*
 [87-88] -catenin *Xenopus laevis*
Wnt [89] -catenin
 [90] *Dax1* -catenin
Dax1 [91]
 -catenin
catenin [74, 92] Li [93] querceti -
catenin *Dax1* -catenin *Dax1*

2.6 *Fem-1*

Fem-1 ferminazation-1
Fem-1 ANK ankyrinrepeat
Fem-1 [96] *Fem-1* *Fem-1a* *Fem-1b* *Fem-1c*
 [97] *Fem-1b* *Fem-1c* [94-95]
 [98] *Fem-1c*
Fem-1c *Fem-1c*
Fem-1c

2.7 *Vasa* *Nanos*

Vasa *Nanos*
 [99-100] *Vasa* DEAD-box AspGlu- Ala-Asp DEAD-box
 RNA *mRNA* *Vasa* *Vasa*
 [99, 101-102] *Nanos* *Vasa*
Nanos1 *Nanos2* *Nanos3*
 [100, 103] *Vasa*
Octopus sinensis *Vasa* RNA *Vasa*
 [104-108] *Vasa* *Nanos*
 [109-111]

2.8 *GnRH*

GnRH " - -
 " FSH LH
 [112-114] GnRH GnRH-I GnRH-II GnRH-III
 GnRH *O. vulgaris* *Aplysia californica* *Loligo*
edulis *Ruditapes philippinarum* *Sepiella japonica*
O. minor *Sepia lycidas* *GnRH*
 GnRH [115-124]

3

[5, 73, 125-126]

master-switch gene

Danio rerio

[127]

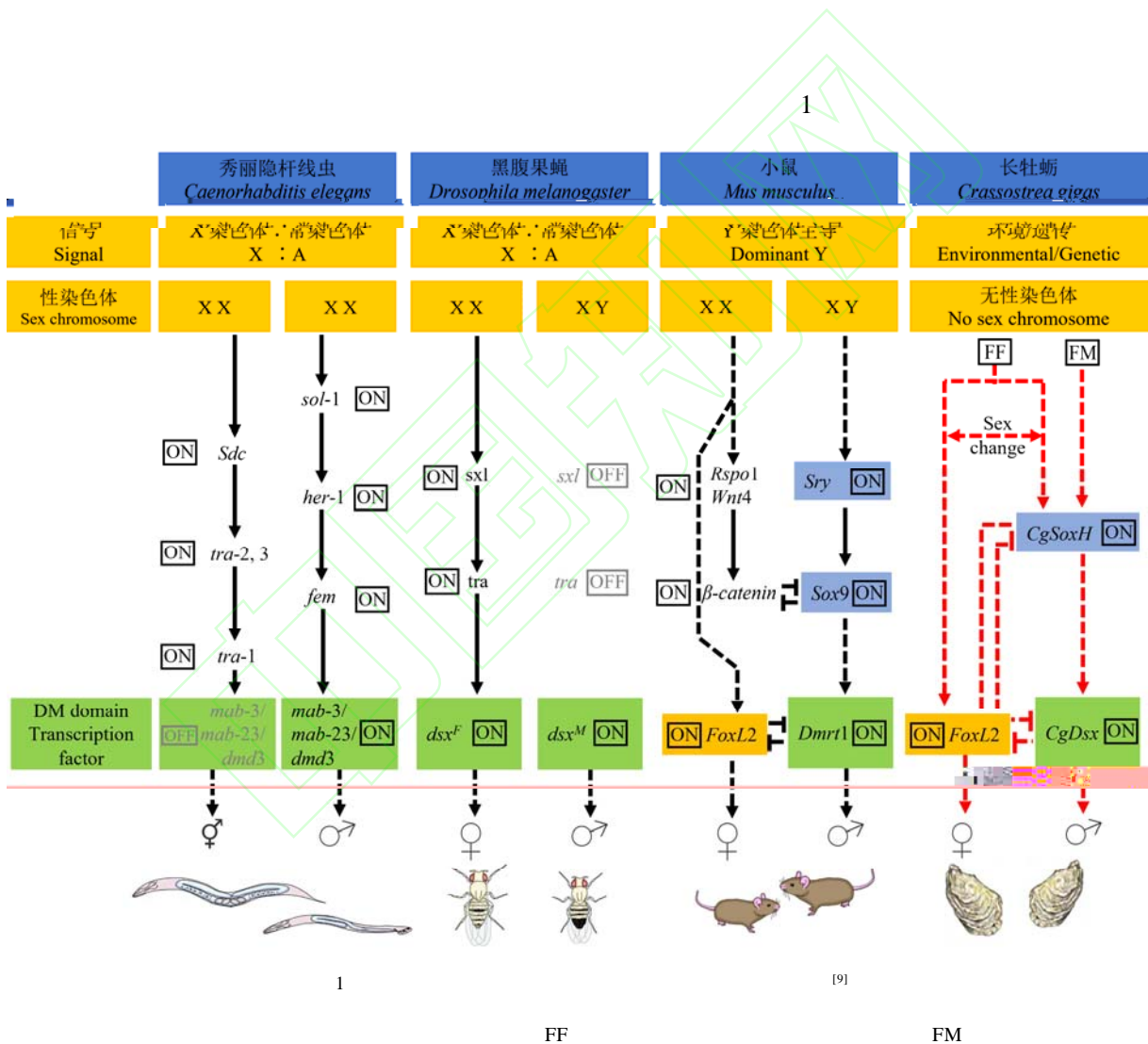


Fig.1 Comparison between putative sex determination pathway in *C. gigas* and model animals [9]

For clarity, only selected key sex-specific regulators are shown. Regulatory interactions (solid lines) are meant to indicate the regulatory logic of each pathway but do not necessarily imply direct regulation. Dashed lines indicate temporal and dashed red lines indicate hypothetical relationships based on expression data only; FF genotype is fake male and permits sex change, FM genotype is true males that do not change sexes

[128-129]

Kdm6b

[130]

DNA

[131-133]

RNA

CRISPR/Cas9

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