# Exploring the *xol-1*-independent role of *sex-1* in dosage compensation

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## Dosage compensation in *C. elegans*

Transcription from the two X chromosomes is reduced by half to match the gene output from single X in male.

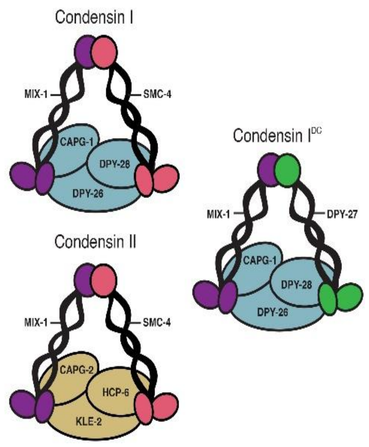
⇩XX⇩ XO

## Mechanisms of dosage compensation

There are multiple redundant pathways used by the dosage complensation complex (DCC) to repress and condense the X chromosome

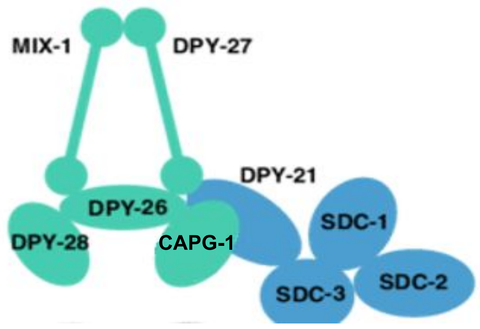
| Human Condensin I | *C. elegans* Condensin I | *C. elegans* Condensin $I^{DC}$ |
|---|---|---|
| SMC 2/hCAP-E | MIX-1 | MIX-1 |
| SMC 4/hCAP-C | SMC-4 | DPY-27 |
| hCAP-D2 | DPY-28 | DPY-28 |
| hCAP-G | CAPG-1 | CAPG-1 |
| hCAP-H | DPY-26 | DPY-26 |

| Human Condensin II | *C. elegans* Condensin II |
|---|---|
| SMC 2/hCAP-E | MIX-1 |
| SMC 4/hCAP-C | SMC-4 |
| hCAP-D3 | HCP-6 |
| hCAP-G2 | CAPG-2 |
| hCAP-H2 | KLE-2 |




Taken from Lau et al, 2015

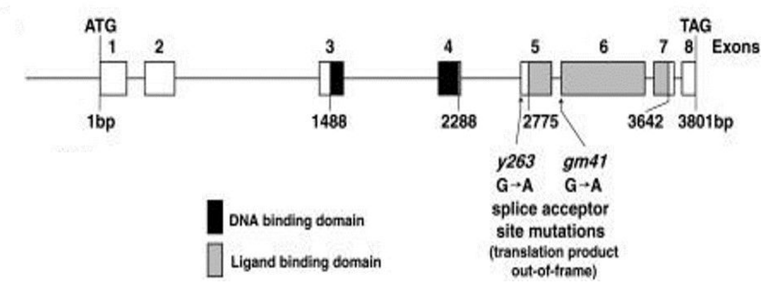
- Condensin $I^{DC}$ is a complex that loads onto the hermaphrodite X chromosomes and reduces the expression of genes by half.
- Condensin $I^{DC}$ is a powerful experimental model to study the mechanisms of interphase gene regulation by condensin complexes Condensin I and Condensin II.




Taken from Ercan et al, 2009

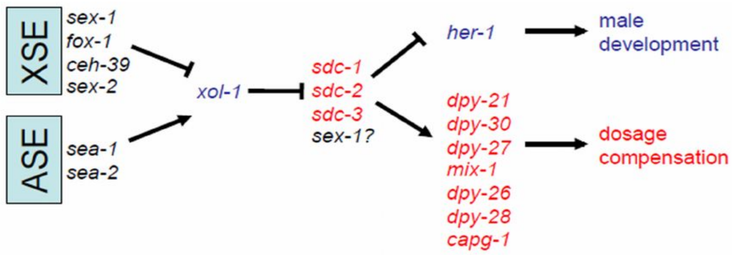
- The dosage compensation complex (DCC) carries out dosage compensation in C. elegans.
- The DCC is comprised of the Condensin $I^{DC}$ complex along with proteins such as DPY-21, SDC-1, SDC-2 and SDC-3.

## *sex-1* and its role in dosage compensation



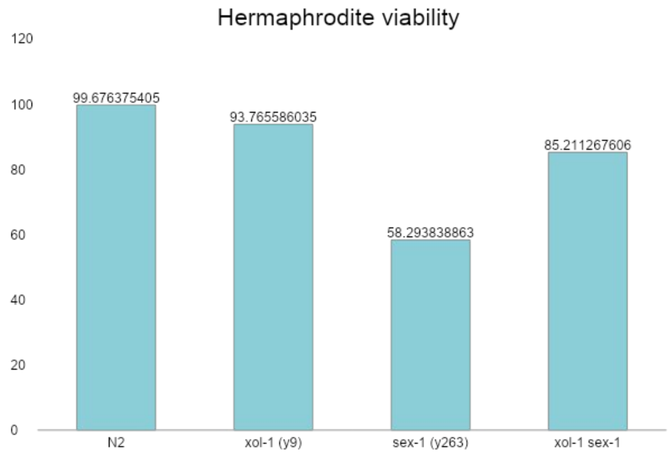

Taken from Carmi et al, 1998

- SEX-1 is a nuclear hormone receptor with a DNA binding domain and an AF-2 domain.
- It directly binds DNA and represses the transcription of genes. The presence of an AF-2 domain suggests that it acts in conjunction with a co-repressor for this function.



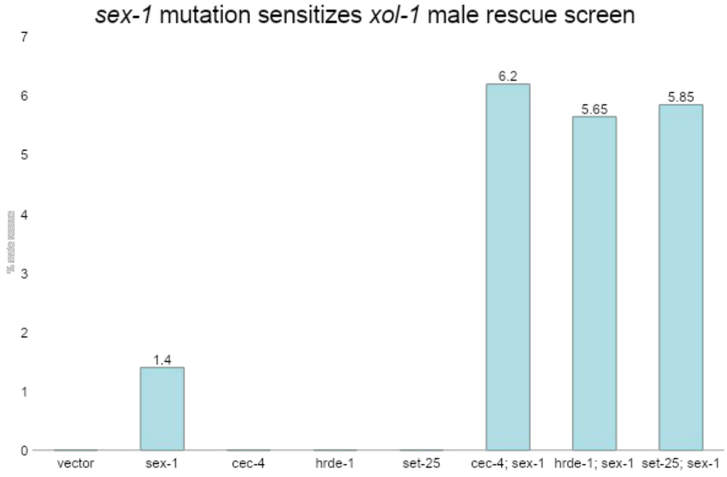

- *xol-1* is a master regulator of both the male developmental pathway and dosage compensation.
- SEX-1 binds directly to the promoter region of *xol-1* and represses its transcription.

## Does *sex-1* have a downstream role?




- SEX-1 mutations reduce hermaphrodite viability.
- This is not completely rescued by introducing a mutation in *xol-1*.

## *sex-1* mutation sensitizes *xol-1* male rescue screen




- *xol-1* inhibits the dosage compensation machinery and prevents it from turning on in males.
- In *xol-1* mutant strains, the DCC is turned on inappropriately in males which leads to male-specific lethality.
- Mutations in genes that carry out dosage compensation should rescue these males. This screen is used to detect such genes.
- However, due to multiple redundant pathways in dosage compensation, male rescue cannot always be detected.
- SEX-1 partial loss of function mutant *sex-1 (y263)* sensitizes this screen by disrupting dosage compensation through an unknown mechanism.
- Figure: Genes involved in dosage compensation such as *cec-4* aren't able to rescue males on their own. With a *sex-1* mutation in the background, ~7% of the males are rescued (more than *sex-1* or *cec-4* alone).
- This experiment is done in a *xol-1* deletion background, suggesting that *sex-1* has a *xol-1*-independent role in dosage compensation

## Future Directions

- How does *sex-1* perform dosage compensation independent of *xol-1* ?
- What is the mechanism of *xol-1*-independent *sex-1*-mediated transcriptional regulation ?

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