

## **HIM-8 and the family of HIM-8-related C2H2 zinc finger proteins modulate transcription factor activity in multiple tissues during *C. elegans* development**

Hongliu Sun<sup>2</sup>, Brian L. Nelms<sup>1</sup>, and **Wendy Hanna-Rose**<sup>1, 2</sup>; <sup>1</sup>Department of Biochemistry and Molecular Biology, <sup>2</sup>Intercollege Graduate Degree Program in Genetics, The Pennsylvania State University, University Park, PA 16802

Mutation of the *C. elegans* *him-8* gene causes hermaphrodites to produce a high incidence of male progeny due to meiotic nondisjunction of the X chromosome. HIM-8 is a C2H2 zinc finger protein that is encoded in an operon with three similar ZIM (zinc finger in meiosis) proteins. HIM-8 binds to the X chromosome pairing center and associates with the nuclear periphery in meiotic cells, likely recruiting the pairing center to the vicinity of the nuclear envelope<sup>1</sup>. HIM-8 promotes pairing and subsequent synapsis of X chromosomes during meiosis<sup>1</sup>, while each ZIM protein promotes pairing of a specific set or sets of autosomes<sup>2</sup>.

We have identified a novel function for HIM-8 and the ZIM proteins in regulating the activity of transcription factors in somatic tissues during development. Mutation of *him-8* or the *zim* genes suppresses defects caused by mutations in the DNA binding domain of EGL-13, a Sox domain transcription factor. Furthermore, mutation of HIM-8 can suppress phenotypes caused by mutation of the DNA binding domain of the HMG box TCF/LEF protein POP-1, the Sp1-like zinc finger protein SPTF-3, and the PAX protein EGL-38. While HIM-8 and the ZIM proteins play primarily chromosome-specific roles during meiosis, their effects in the soma do not appear to depend on the chromosomal location of the suppressed gene. HIM-8 can modulate the activity of proteins encoded on autosomes and the X chromosome.

We mostly observe phenotypic suppression, but we have observed robust phenotypic enhancement as well. While some phenotypes caused by a specific DNA binding domain mutation in EGL-38 are suppressed, others are strongly exacerbated. Modulation by HIM-8 appears to be specific to proteins with DNA binding domain mutations. Phenotypes caused by null alleles of *egl-13* are not affected by mutation of *him-8*, a non-null allele that doesn't alter the DNA binding domain of the LIM domain protein LIN-11 is not suppressed, and nonnull alleles in genes that do not encode transcription factors are not suppressed. Our results suggest broad regulation of transcription factor activity by HIM-8 and that this activity may be shared among the HIM-8 family of ZIM proteins.

1 Phillips, *et. al* (2005) *Cell* 123: 1051-1063.

2 Phillips, C.M., and A.F. Dernburg (2006) *Dev Cell* 11: 817-829.

Email: xxx@xxx