

## Estrogen Signaling Shared By Invertebrates

➤ Estrogen receptors (ERs) control development, behavior, and reproduction in vertebrates. These hormone-activated transcription regulators of the steroid receptor family were once considered unique to vertebrates. In recent years, however, genes that descend from the same ancestral gene as ERs have been isolated in mollusks and cephalochordates. Surprisingly, these receptors are not activated by estrogen or other ligands.

How did steroid receptor function evolve in vertebrates and invertebrates? Could invertebrates be sensitive to endocrine disruptors? To explore these

questions, June Keay, B.S., and Joseph W. Thornton, Ph.D., at the University of Oregon in Eugene, isolated and characterized ERs from two annelids, *Platynereis dumerilii* and *Capitella capitata*, choosing these models because annelids are a sister phylum to mollusks and have been shown to produce and respond to estrogen. The researchers present their results in an upcoming issue of *Endocrinology*.\*

The researchers found that *P. dumerilii* ER recognized classic estrogen response elements, bound estrogen with high affinity, and specifically activated transcription when treated with low levels of estradiol. *C. capitata* ER was also highly sensitive to estrogens.

The annelid ERs were

activated or antagonized by some of the same synthetic and plant-derived xenoestrogens that disrupt vertebrate ERs, although not always predictably based on their effects on human ER. In some cases, these substances acted on annelid ERs at nM or sub-nM concentrations, raising the possibility that xenoestrogens in the environment might alter development and reproduction of annelids and some other invertebrates.

This is the first report of a hormone-activated invertebrate ER. The existence of an estrogen-sensitive steroid receptor in annelids suggests that



“estrogen signaling via the ER is as ancient as the ancestral bilaterian animal and [indicates] that all steroid receptors evolved from an ancestral estrogen-sensitive protein,” the researchers say. As a result, the taxonomic scope of endocrine disruption by xenoestrogens could be much broader than previously thought. ■

\* Keay J and Thornton JW. Hormone-activated estrogen receptors in annelid invertebrates: implications for evolution and endocrine disruption. *Endocrinology*, in press.