

## Scientists made a six-legged mouse embryo – here's why

This six-legged animal isn't an insect: it's a mouse with two extra limbs where its genitals should be (A. Lozovska *et al.* *Nature Commun.* 15, 2509; 2024).

Developmental biologist Moisés Mallo, at the Gulbenkian Science Institute in Oeiras, Portugal, and his colleagues were studying one of the receptor proteins, *Tgfb1*, in a signalling pathway that is involved in many aspects of embryonic development.

The scientists inactivated the *Tgfb1* gene in mouse embryos about halfway through development to see how the change affected spinal-cord development.

One of the resulting

bioengineered embryos had genitals that looked similar to two extra hind limbs.

Researchers have long known that, in most four-limbed animals, both the external genitalia (penis or clitoris) and hind limbs develop from the same primordial structures. When Mallo's team looked further into the six-legged mouse phenomenon, they found that *Tgfb1* directs these structures to become either genitalia or limbs by altering the way that DNA folds in the structure's cells. Deactivating the protein changed the activity of other genes, resulting in extra limbs and no true external genitalia.



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