Nature makes impressive use of a relatively small number of proteins. The same signaling pathways and transcription factors are often reused in different contexts to direct diverse developmental processes, and understanding how proteins show the right activity at the right time and place is a fundamental question for developmental biologists. Lee et al. reveal how the small ubiquitin-like modifier SUMO changes the function of the SoxE family of transcription factors during neural crest development (1).

Neural crest cells are stem cell–like progenitors that arise from the embryonic ectoderm, undergo an epithelial–mesenchymal transition, and disperse throughout the embryo before they differentiate into a variety of different lineages (2). “They’re a unique and fascinating cell population,” says Carole LaBonne from Northwestern University in Evanston, Illinois. “There are a handful of key factors that play multiple roles in neural crest development. For example, SoxE transcription factors are critical for the initial formation of the stem cell population, but then, counterintuitively, they direct the stem cells’ differentiation into a subset of neural crest derivatives, namely glial cells, melanocytes, and cartilage cells.”

SoxE transcription factors are best known as transcriptional activators (3). In 2005, LaBonne and graduate student Kimberly Taylor-Jaffe found that SoxE’s function in the neural crest of *Xenopus* embryos was regulated by SUMOylation (4). Non-SUMOylatable forms of SoxE induced the formation of neural crest stem cells, whereas constitutively SUMOylated SoxE blocked neural crest development and promoted ear formation instead. “So we knew that SUMO had a profound influence, but we didn’t understand the mechanism,” recalls LaBonne, who says that *Xenopus* embryos are ideal for these studies because of their amenability to both cell biological and biochemical approaches.

SoxE factors are functioning...