

# SOX10

## Related Genes

**The SOX gene family includes at least 30 mammalian SOX genes**, and SOX genes have also been identified in birds, reptiles, amphibians, fish, insects and nematodes. **SOX8, -9, and -10 form the SOXE family**, and all share significant structural similarity, including a C-terminal transactivation domain and two highly conserved domains flanking the HMG box that are predicted to mediate protein-protein interactions ([Bowles et al., 2000](#)).

In chick, ectopic overexpression of SOX8, -9, or -10 in the neural tube induces neural crest cells at the expense of central nervous system cells. Later in development, **SOX9 overexpression biases cells toward melanocyte and glial lineages in migratory neural crest**, including increasing SOX10 expression ([Cheung and Briscoe, 2003](#)).

*Sox9* and *Sox10* are both expressed in developing neural crest cells, however they appear to carry out different functions. **SOX9 appears to be necessary for generation of mouse trunk neural crest cells**, as the vast majority of trunk neural crest cells are missing in a conditional *Sox9* mutant. In these mutants, neural crest formation is initiated, and then cells are lost by apoptosis ([Cheung et al., 2005](#)).

In zebrafish, two different *sox9* orthologs exist, carrying out distinct functions in various embryonic regions. **The zebrafish *sox9b* gene appears to act upstream of *sox10* in the trunk during neural crest formation**, as removal of *sox9b* expression reduces the *sox10* expression domain, and *sox9a* or *sox9b* overexpression increases the *sox10* expression domain ([Yan et al., 2005](#)).

**In *Xenopus*, *sox10* and *sox9* display similar activities, both inducing formation of neural crest precursors and derivatives, including melanocytes, glia and ectopic otocysts.** Neural crest/melanocyte formation can be rescued by *sox9* when *sox10* is absent. The post-translational modifier proteins sumo1 (sumo-1 and ubc9 (ube2i)), which act to attach a SUMO polypeptide to lysine residues to regulate protein function, interact with and modify *sox9* and *sox10*. **The SUMOylation state of *sox9* and *sox10* differentially affects their activities in neural crest and in otic placode/cranial crest formation.** The authors suggest that the SUMOylation state of SOXE proteins may determine their transcriptional activities, potentially by governing protein interactions ([Taylor and Labonne, 2005](#)).

Measurement of DNA binding activities in melanocytes revealed the presence of another protein that bound to conserved Sox binding motifs, and a variety of assays demonstrated **SOX9 expression and binding activity in melanocytes**. Higher SOX9 expression was seen in pigmented melanoma cell lines as compared to unpigmented cell lines, displaying an inverse relationship to SOX10 (and BRN2) expression ([Cook et al., 2005](#)).

**Although *Sox10* and *Sox8* are closely related and display overlapping developmental expression patterns in mouse, the generation of gene replacement mice where *Sox8* was inserted at the *Sox10* locus (*Sox10<sup>Sox8ki</sup>* mice) showed that the two genes are not functionally equivalent.** Specifically, *Sox10<sup>Sox8ki</sup>* homozygotes did not survive past the first postnatal week, showed complete absence of melanin as demonstrated by a white coat, showed complete absence of *Dct*-positive melanoblasts and very few *Mitf*-positive melanoblasts at E12.5, and showed less than 10% of wildtype *Kit*-positive melanoblasts at E12.5. Therefore *Sox8* exhibits no functional redundancy with *Sox10* in the melanocyte lineage, and is unable to substitute for *Sox10* in melanocytes. The enteric ganglia defects were also not rescued in *Sox10<sup>Sox8ki</sup>* mice, however *Sox8* was able to rescue peripheral neuron and glia development ([Kellerer et al., 2006](#)).

**SOX9 is expressed in human epidermal melanocytes, and is upregulated in response to ultraviolet-B exposure.** A variety of assays showed that SOX9 directly regulates *MITF* and *DCT* expression.

**However, SOX9 does not appear to regulate SOX10 in normal human epidermal melanocytes**, as neither silencing nor overexpression of SOX9 had any affect on SOX10 protein level (Passeron et al., 2007).