

PAX3

Interacting Proteins

PAX3 interacts with the retinoblastoma tumor suppressor Rb, and shows weak interaction with the related proteins retinoblastoma-like 1 (RBL1/p107) and retinoblastoma-like 2 (RBL2/p130). Transient transfections suggest that these **Rb family member proteins can repress PAX3 transcriptional activation** (Wiggan et al., 1998).

Yeast two-hybrid analysis followed by GST pull-down experiments and co-immunoprecipitations showed that the **PAX3 homeodomain interacts with the C-terminal WD-repeat region of HIRA**, a transcriptional repressor that maps to the DiGeorge/velocardiofacial syndrome critical region and has been postulated to regulate chromatin structure. Mouse neural crest cultures demonstrated that, after 24hrs in culture, *Hira* and *Pax3* are co-expressed in the nuclei of migrating neural crest (Magnaghi et al., 1998).

PAX3 transcriptional activity is inhibited by interaction with DAXX via the homeodomain and octapeptide domain of PAX3. Of note, PAX3-FKHR is not subject to this repression (Hollenbach et al., 1999).

Mammalian-two hybrid and GST-pull down binding assays using the transcription factor **POU3F2 (also known as BRN-2 or N-OCT-3) found that POU3F2 binds to PAX3** (Smit et al., 2000).

PAX3 interacts with and is imported into the nucleus by the nuclear import protein KAP13. KAP13 also binds to PAX6, in a region of PAX6 that partially overlaps the homeodomain and is highly conserved among paired type homeodomain family members, suggesting KAP13 may regulate nuclear import of the many members of the paired type homeodomain protein family (Ploski et al., 2004).

The paired domain of PAX3 is able to confer transcriptional repression, and interacts with the corepressor protein KAP1 and heterochromatin protein 1 gamma. Chromatin immunoprecipitation assays indicated that competitive binding between these proteins appears to regulate the transcriptional repressive capabilities of PAX3 (Hsieh et al., 2006).

A variety of assays showed that **PAX3 interacts with the transcriptional co-activator TAZ, and increases PAX3 transcriptional activation** of luciferase reporter constructs that are regulated by either the endogenous *Mitf* promoter, or by artificial constructs containing basal PAX3 binding sites (Murakami et al., 2006).

Inhibition of *Mitf* expression by FOXD3 was shown by transfection into B16-F10 cells. A variety of binding assays showed that this inhibition does not occur by FOXD3 directly binding the *Mitf* promoter. Instead, the **inhibition of Mitf by FOXD3 arises from PAX3 inhibition, which occurs via FOXD3 and PAX3 protein-protein interactions** (Thomas and Erickson, 2009).

Histone deacetylase 10 (HDAC10) was shown to positively regulate PAX3 function by maintaining PAX3 in a deacetylated state. HDAC10 was shown by a variety of assays to directly complex with PAX3 and KAP1. These three proteins together were shown to bind the promoters of *Mitf*, *Dct*, and *Tyrp1* in melanocyte-derived mouse cell lines (B16F10). HDAC10 maintains the deacetylation of PAX3, resulting in PAX3's increased binding and activation of the promoters of *Mitf*, *Dct*, and *Tyrp1*. These data suggest that, when acetylated, PAX3 along with KAP1 act as repressors upon the promoters of *Mitf*, *Dct*, and *Tyrp1* (Lai et al., 2010).