Two recent publications reveal how cancer-associated mutations in ING1 and ING4 genes impair their tumour suppressor activity

A collaborative work between the groups of Ignacio Palmero (Instituto de Investigaciones Biomédicas-CSIC) and Francisco J Blanco (CIC bioGUNE) has unveiled the molecular implications of mutations in two of the tumor suppressors detected in cancers. ING1 mutations that impair the recognition of the histone H3 H3K4me3 result in loss of ING1 ability to induce senescence. The N214D ING4 mutant loses its ability to stop cell proliferation, although its recognition of H3K4me3 is unchanged. This mutation causes protein destabilization due to increased proteasome mediated degradation.

These results demonstrate that ING1 is a critical epigenetic regulator of cellular senescence and highlight the importance of ING4 function in the prevention of tumorigenesis.

Links to the published articles:

http://www.ncbi.nlm.nih.gov/pubmed/21078114
http://www.ncbi.nlm.nih.gov/pubmed/20705953

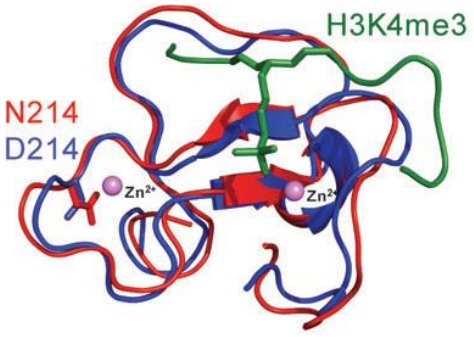

Figure: Superimposition of the structures of the wild-type (red) and N214D mutant (blue) ING4-PHD fingers. Depicted in green is the backbone structure of the H3K4me3 peptide, with the trimethylated lysine residue shown in sticks, as seen in the crystal structure of its complex with the wild-type ING4-PHD. The two Zn2+ cations bound to the PHD are shown as pink spheres.