

## **LINKING STRESS SIGNALING TO CHROMATIN REMODELING THROUGH THE ING FAMILY OF TUMOR SUPPRESSORS**

Karl Riabowol

Faculty of Medicine, University of Calgary, Canada

Stresses such as DNA damaging agents initiate damage response pathways, block cell cycle progression and induce apoptosis. These biological responses act in a concerted fashion and remain functionally linked through mechanisms not completely understood. Interestingly, hyperacetylation of histone proteins, which alters transcription patterns and appears linked to DNA repair, also induces apoptosis suggesting that aspects of chromatin modification link these very distinct processes. Modulating chromatin structure in the absence of any DNA lesions also activates key DNA damage signaling proteins, further supporting the role of higher order chromatin structure in mediating stress responses. Five different ING genes (ING1-5) encoding proteins with highly conserved plant homeodomain (PHD) motifs, and several splicing isoforms of the ING1 and ING2 gene have been identified that link stress signals to chromatin modification. Following stress, rare and ephemeral phosphatidylinositol phosphates (PtdInsPs) are produced which bind members of the ING family through their conserved PHD domain, resulting in localization of INGs to chromatin and in the case of ING1b, to sites containing proliferating cell nuclear antigen (PCNA). Recent phylogenetic analysis of the evolutionarily conserved ING family has identified a region that may serve to regulate and/or target histone acetyltransferase/deacetylase (HAT/HDAC) complexes thus linking the activation of INGs by stress to chromatin remodeling via altering histone acetylation.