

The unknown roles of the Rvb1p/Rvb2p protein complex in eukaryotic cells – effects on DNA repair and galactose induced gene expression.

Hörður Guðmundsson and Zophonias O. Jónsson, (zjons@hi.is), Institute of Biology, University of Iceland, Sturlugata 7, 101 Reykjavík.

Rvb1p and Rvb2p are highly conserved nuclear proteins, essential for survival of eukaryotic cells. Together they form a double hexamer ring which interacts with numerous proteins. Rvb1p and Rvb2p both have Walker type ATPase motifs which are essential for viability. Both proteins are essential components of two chromatin remodelling machines, the Ino80 and Swr1 complexes. The Ino80 complex is a conventional chromatin remodeler which opens up chromatin by changing the topology of DNA on histone octamers. The Swr1 complex on the other hand catalyzes the exchange of histone H2A for unconventional H2A.Z.

We have shown that Rvb proteins in *Saccharomyces cerevisiae* affect the association of the Gal4p transcription factor to its cognate promoters. Plausible explanations are that they: a) maintain an open chromatin state around *GAL* promoters, b) loosen the bond between Gal4p and proteins that prevent its association with DNA, c) influence the expression or stability of *GAL4* mRNA, or the stability of Gal4p and thus control Gal4p quantity, or d) influence the localization of Gal4p inside the nucleus. The main goal of the project is to test these hypotheses to explain how Rvb proteins and their interactors effect galactose-induced gene expression.

Besides their functions in gene regulation, recent data from several groups have demonstrated that the Ino80 and Swr1 complexes (and therefore presumably the Rvb proteins as well) play an important role in the repair of double strand DNA breaks (DSB-repair). These roles relate to DSB-induced phosphorylation of the histone-variant H2A.X and the normal H2A histone which causes cell cycle arrest by activating cellular checkpoints and recruits various DNA repair proteins to the DSB. We have generated cold-sensitive *rvb1* mutant yeast strains which display DNA repair phenotypes. We are in the process of investigating the genetic interactions between the *rvb1-cs* mutation and various well characterized repair genes. Initial results indicate that the underlying cause of UV sensitivity in *rvb1-cs* strains may be of epigenetic nature due to the plasticity of the observed phenotype.