About the NineTeen Complex The nineteen complexis a non-snRNA containing protein complex involved in splicing of nuclear RNAs via the spliceosome. It was originally isolated as a complex containing Prp19p and at least eight other proteins that complemented the splicing defect of extracts from prp19 mutant cells. Subsequent work has identified the genes encoding the additional members of the complex: NTC20, SNT309, ISY1, SYF2, CWC2, PRP46, CLF1, CEF1, and SYF1. The complex appears to be conserved as mammalian cells contain a functional equivalent called the Prp19/CDC5 complex composed of a similar, though not identical, set of proteins. The nineteen complex associates with the assembling splicesosome during or after the dissociation of the U4 snRNA, stabilizes the U5 and U6 snRNAs in the activated spliceosomal complex that is catalytic for the first step of splicing, and remains through the second step of splicing. Following disassembly of the spliceosome, members of the nineteen complex have been found in association with the excised intron.The nineteen complex also appears to be involved in control of fidelity and efficiency of splicing. Mutations in isy1 suppress the relaxed fidelity of recognition of the conserved branchpoint sequence conferred by mutations in prp16, an ATP-dependent RNA helicase required for the second step of splicing, and an isy1 null mutation decreases accuracy of 3'-splice site usage. In addition, cells with mutations in prp45, a protein found in association with NineTeen complex members, are defective in splicing of introns with non-canonical sequences at the branchpoint or the 5' or 3' splice sites. Splicing efficiency of various transcripts is differentially affected by mutations in spliceosomal components, such as PRP19, suggesting that the spliceosome can distinguish between individual transcripts and possibly use these differences to specifically regulate gene expression via control of splicing. Interestingly, the Drosophila crooked neck proteinregulates glial cell differentiation by facilitating the splicing of specific target genes.Mutational and genetic analysis of several nineteen complex subunits has suggested involvement in other cellular processes in addition to splicing, such as cell cycle regulation, cytoskeletal structure, DNA repair, and vesicular transport. In most cases it appears that the primary defect is in splicing and the other defects are the result of failure to remove an intron from the transcript of a gene involved in that process. However Clf1p, and possibly also Prp19p, may have other direct roles in addition to splicing. About CLF1 CLF1 was originally identified as the ortholog of the Drosophila crooked neckgene which when mutated causes embryonic lethality and severe developmental defects. It is composed almost entirely of fifteen tandem repeats of a 34 amino acid tetratricopeptide repeatmotif often involved in protein-protein interactions, with short non-TPR amino and carboxyl terminal sequences. CLF1 is essential and cells depleted of Clf1p arrest in G2/M and are defective in spliceosome assembly, specifically in the step of adding the tri-snRNP to the spliceosomal complex. In addition to interacting directly with a number of nineteen complex members, Clf1p interacts with the U1 proteins Prp40p and Mud2p.Clf1p-depleted cells arrest as large-budded cells, but with intact, fully formed spindles suggesting that failure to splice the TUB1 and TUB3 genes encoding tubulin is not the primary defect, unlike what is seen in other nineteen complex mutations that produce cell cycle arrest. This is further confirmed by genetic analysis with a mad2 spindle checkpoint mutant indicating that the arrest does not depend on an intact spindle checkpoint. CLF1 appears to have a direct role in initiation of DNA replication as clf1-1 mutants fail to initiate DNA replication, Clf1p interacts directly with the Orc2p component of the Origin Recognition Complex, and Clf1p localizes to chromatin and replication origins in an ORC-dependent manner. Clf1p also interacts with Csm1p, a protein involved in meiotic chromosome segregation and spore formation.