The Sm and Sm-likeproteins are a highly conserved family of ancient origin, found in bacteria, archaea, and eukaryotes. These proteins were first characterized in humans with systemic lupus erythemathosus, where autoantibodies were found that recognize an antigen called Sm. The Sm antigen was characterized as a domain present in a group of eight small proteinsthat associated with four of the five snRNAsinvolved in splicing of nuclear pre-mRNAs. The S. cerevisiae genome contains 16 proteins containing an Sm, or Sm-like, domain. Seven genes encode proteins corresponding to the human Sm antigen proteins: SMB1, SMD1, SMD2, SMD3, SME1, SMX3, and SMX2. An additional eight genes, LSM1, LSM2, LSM3, LSM4, LSM5, LSM6, LSM7, and LSM8 also encode proteins containing Sm domains and are thus named LSMproteins. These proteins are more closely related to individual Sm proteins than to each other. MAK31 has also been reported to contain an Sm domain.Crystal structures of human Sm proteins, in pairs or with U1 snRNA, indicate that the seven core Sm proteins form a heteroheptameric ring with a small central hole. The Sm site, the conserved uridine rich sequence found near the 3-prime ends of the U1, U2, U4, and U5 snRNAs, appears to form contacts along the inner surface of the ring complex and it is suggested that the RNA may pass through the hole. Experiments in S. cerevisiae indicate that a similar seven-membered ring containing one copy of each of the seven Sm proteins exists in yeast. Similarly to the Sm proteins, the Lsm proteins also form heteroheptameric rings. In S. cerevisiae, as well as in other eukaryotes, two different Lsm ring complexes exist, containing Lsm2p-7p and either Lsm1p or Lsm8p.The Lsm proteins are found in two distinct heteroheptameric complexes. Each complex contains Lsm2p, Lsm3p, Lsm4p, Lsm5p, Lsm6p, Lsm7p, and a seventh protein, either Lsm1p or Lsm8p. By analogy with the Sm proteins, it is thought that the Lsm proteins also form a seven-membered ring structure.The complex containing Lsm8p localizes to the nucleus, associates with multiple snRNP complexes containing the U6 snRNAand by binding directly to the U6 snRNA, plays a role in the biogenesis and stability of the U6 snRNP and U4/U6 snRNP complexes and thus in splicing of nuclear mRNAs. The Lsm2-8 proteins bind specifically to the 3'-terminal U-tract of the U6 snRNA and facilitate the binding of the splicing factor Prp24p. It is also thought that the Lsm2-8 complex plays a role in the degradation of nuclear RNA substrates by targeting them for decapping.The complex containing Lsm1-7p is cytoplasmic and mutations in LSM1-7 all cause defects in mRNA degradation. Lsm1-7p are found in association with the Pat1p decapping enzyme and Xrn1p exoribonucleases; thus the Lsm1-7 complex is thought to be involved in mRNA degradation via the decapping step.There may be yet another Lsm complex, containing at least six members, as these six proteins, but not Lsm1p or Lsm8p, have been found in association with the pre-RNase P RNAand with the box H/ACA snoRNA snR5.Because it has been observed that cells depleted of any of the essential Lsm proteins, are defective in processing of tRNA, rRNA, and snoRNA, it has been suggested that the Lsm proteins may have the additional role of directly processing these classes of RNAs. However, it has also been observed that these phenotypes are alleviated by overexpression of the U6 snRNA, so it may be that these other RNA processing defects are downstream effects of lowering U6 levels and thus inhibiting splicing.