Cloning and characterization of two multifunctional proteins, MSW and p190 B, involved in DNA binding and the Ras signaling pathway. Yoshihiko Yamada, Atsushi Utani and Peter Burbelo, Laboratory of Developmental Biology, National Institute of Dental Research, NIH, Bethesda, Maryland 20892.

Extracellular agents such as growth factors and the extracellular matrix influence cellular behavior by controlling transcription, DNA replication, and cytoskeleton structure via signal transduction pathways. We report the cloning of two multifunctional transcription/DNA binding factors, MSW (A-p145) and p190 B. MSW was cloned by its activity to bind a region from the bidirectional promoter of the α1(IV) and α2(IV) collagen chain genes. The middle portion of this 1,131 amino acid DNA binding protein has a region homologous to bacterial DNA ligase, and the more carboxyl part contains several domains homologous to smaller subunits of a DNA replication factor complex, Activator 1. Western blotting revealed that MSW is the 145 kDa component of the purified A1 complex. Gel shift assay using recombinant MSW indicated that the carboxyl portion of the DNA ligase domain is responsible for DNA binding activity. Since DNA binding of MSW shows sequence specificity, MSW may function for both DNA replication and transcription, similar to many other DNA replication proteins.

p190 B consists of about 1,500 amino acids with 51% amino acid sequence identity to the previously reported p190 A, a GAP binding protein which is involved in the control of the Ras signal pathway and cytoskeleton. p190 B is a multidomain protein with several potential protein motifs including a RNA splicing factor domain, a GTPase domain, two zinc finger transcription factor like domains, four SH3 binding domains, a nuclear targeting sequence and a Rho-GAP domain. We found that p190 B bind to Src and that the Rho-GAP domain of p190 B accelerates the GTPase activity specifically for Rho and Rac which have been implicated in the control of the actin cytoskeleton. Similar to the proposed function of p190 A, p190 B may be an effector to control cytoskeleton and cell adhesion to the extracellular matrix.