

## **A new strategy for protection of skin senescence by utilizing adhesion molecules**

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SHPS-1 is a transmembrane protein whose extracellular region interacts with CD47 and whose cytoplasmic region undergoes tyrosine phosphorylation and thereby binds the protein tyrosine phosphatase SHP-2. Formation of this complex is implicated in regulation of cell migration by an unknown mechanism. A CD47-Fc fusion protein or antibodies to SHPS-1 inhibited migration of human melanoma cells or of CHO cells overexpressing SHPS-1. Overexpression of wild-type SHPS-1 promoted CHO cell migration, whereas expression of the SHPS-1-4F mutant, which lacks the phosphorylation sites required for SHP-2 binding, had no effect. Antibodies to SHPS-1 failed to inhibit migration of CHO cells expressing SHPS-1-4F. SHPS-1 ligands induced the dephosphorylation of SHPS-1 and dissociation of SHP-2. Antibodies to SHPS-1 also enhanced Rho activity and induced both formation of stress fibers and adoption of a less polarized morphology in melanoma cells. Our results suggest that engagement of SHPS-1 by CD47 prevents the positive regulation of cell migration by this protein. The CD47-SHPS-1 system and SHP-2 might thus contribute to the inhibition of cell migration by cell-cell contact.