The LIM and SH3 domain protein family: structural proteins or signal transducers or both?

LIM and SH3 Protein 1 (LASP-1) was initially identified from a cDNA library of metastatic axillary lymph nodes (MLN) more than a decade ago. It was found to be overexpressed in human breast and ovarian cancer and became the first member of a newly defined LIM-protein subfamily of the nebulin group characterized by the combined presence of LIM and SH3 domains. LASP2, a novel LASP1-related gene was first identified and characterized in silico. Subsequently it proved to be a splice variant of the Nebulin gene and therefore was also termed LIM/nebulette. LASP-1 and -2 are highly conserved in their LIM, nebulin-like and SH3 domains but differ significantly at their linker regions. Both proteins are ubiquitously expressed and involved in cytoskeletal architecture, especially in the organization of focal adhesions. Here we present the first systematic review to summarize all relevant data concerning their domain organization, expression profiles, regulating factors and function. We compile evidence that both, LASP-1 and LASP-2, are important during early embryo-and fetogenesis and are highly expressed in the central nervous system of the adult. However, only LASP-1 seems to participate significantly in neuronal differentiation and plays an important functional role in migration and proliferation of certain cancer cells while the role of LASP-2 is more structural. The increased expression of LASP-1 in breast tumours correlates with high rates of
nodal-metastasis and refers to a possible relevance as a prognostic marker.