Role of L1 cell adhesion molecule (L1CAM) in the metastatic cascade: promotion of dissemination, colonization, and metastatic growth.

Expression of the L1 cell adhesion molecule (L1CAM) is frequently increased in cancer patients compared to healthy individuals and also linked with bad prognosis of solid tumours. Previously, we could show that full-length L1CAM promotes metastasis formation via up-regulation of gelatinolytic activity in fibrosarcoma. In this study, we aimed to extend this finding to haematogenous malignancies and carcinomas, and to specifically elucidate the impact of L1CAM on major steps of the metastatic cascade. In a well-established T-cell lymphoma spontaneous metastasis model, silencing of L1CAM significantly improved survival of the mice, while intradermal tumour growth remained unaltered. This correlated with significantly decreased spontaneous metastasis formation. L1CAM suppression abrogated the metastatic potential of T-cell lymphoma as well as carcinoma cells as demonstrated by reduced migration and invasion in vitro and reduced formation of experimental metastasis in vivo. At the molecular level, silencing of L1CAM led to reduced expression of gelatinases MMP-2 and -9 in vitro and decreased gelatinolytic activity in primary tumours and metastases in vivo. In accordance, knock down of L1CAM had similar suppressive effects on migration, invasion and in vivo-gelatinolytic activity as treatment.
with the specific gelatinase inhibitor SB-3CT. This newly discovered impact of L1CAM on distinct steps of the metastatic cascade and MMP activity highlights the potential of possible L1CAM-directed therapies to inhibit metastatic spread.