
The L1 cell adhesion molecule is implicated in the control of proliferation, migration, and invasion of several tumor cell types in vitro. Recently, L1 overexpression was found to correlate with tumor progression of ovarian carcinoma, one of the most common causes of cancer-related deaths in gynecologic malignant diseases. To evaluate L1 as a potential target for ovarian cancer therapy, we investigated the effects of anti-L1 monoclonal antibodies (chCE7 and L1-11A) on proliferation and migration of L1-positive human SKOV3ip ovarian carcinoma cells in vitro and the therapeutic efficacy of L1-11A against i.p. SKOV3ip tumor growth in nude mice. In vitro, both anti-L1 antibodies efficiently inhibited the proliferation of SKOV3ip cells as well as other L1-expressing tumor cell lines (renal carcinoma, neuroblastoma, and colon carcinoma). On two cell lines, hyper-cross-linking of L1-11A with a secondary antibody was necessary for significant inhibition of proliferation, indicating that cross-linking of L1 is required for the antiproliferative effect. L1-negative prostate carcinoma cells were not influenced by antibody treatment. Biweekly treatment of ovarian carcinoma-bearing mice with L1-11A led to a dose-dependent and significant reduction of tumor burden.
(up to -63.5%) and ascites formation (up to -75%). This effect was associated with reduced proliferation within the tumors. L1-directed antibody-based inhibition of peritoneal growth and dissemination of human ovarian carcinoma cells represents important proof-of-principle for the development of a new therapy against one of the leading gynecologic malignant diseases.