Cancer attacks immune cells
A balance between cancer and anti-metastasis defense in the metastasis-target organs is a key factor in the process of metastasis formation. HMGB1 is a bifunctional protein; a chromatin component regulating transcriptional gene expression and DNA repair, and an inflammatory cytokine worsening endotoxic shock. HMGB1 is released from nuclei under chromatin histone acetylation or cell necrosis. In cancer cells, HMGB1 activates its receptor, RAGE (receptor for advanced glycation end products), which is a multifunctional membrane protein, to accelerate proliferation, motility, invasion, angiogenesis, and metastasis. In macrophages and dendritic cells, HMGB1 induces apoptosis at high concentration via JNK phosphorylation. HMGB1-induced apoptosis inhibits macrophage infiltration into the tumors. HMGB1 also affects resident macrophages in the lymph nodes and liver. HMGB1 secreted from colon cancer cells in the primary tumors reaches the metastasis-target organs via portal or lymphatic flow, and suppresses the resident macrophages to reduce resistance on cancer cell embedding. The effect of cancer-derived cytokines on the metastasis-target organs might be a pivotal scenario in cancer metastasis.

Sasahira T, Sasaki T, Kuniyasu H: Interleukin-15 and transforming growth factor α are associated with


