SHAP potentiates hyaluronan-CD44 interaction

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[Aim] In inflammatory sites, the synthesis and secretion of hyaluronan are often upregulated, which contributes to the regulation of infiltration of leukocytes bearing CD44, the hyaluronan receptor. We previously found that SHAP (Serum-derived Hyaluronan-Associated Protein), the heavy chains of the plasma inter-a-trypsin inhibitor (IaI) family molecules, is able to form a covalent complex with hyaluronan. Significant elevation of serum level of the SHAP-hyaluronan complex has been observed in patients suffering from inflammatory diseases such as arthritis and hepatitis.

[Methods] We purified the SHAP-hyaluronan complex from synovial fluid collected from rheumatoid arthritis patients and examined the effect of SHAP on hyaluronan-CD44 interaction.

[Results and Discussion] Under either static or flowing condition, Hut78, a CD44-positive T leukemia cell line, binds much more strongly to the SHAP-hyaluronan complex than to the free hyaluronan molecules that were immobilized on HABP (hyaluronan-binding protein)-precoated dishes. The strong binding of Hut78 cells to the SHAP-hyaluronan complex was inhibited in the presence of hyaluronan but not IaI, and was completely abolished when the cells were pretreated with anti-CD44 monoclonal antibodies (Ab-4 and IM7). Furthermore, the preferring binding to the SHAP-hyaluronan complex was also observed in CD44-negative Jurkat cells after the transfection with CD44 cDNA. These results suggest that the formation of the SHAP-hyaluronan complex may underlie the regulation of inflammation response via the enhancement of the interaction between CD44-bearing leukocytes and hyaluronan-bearing local tissue cells.

Key words: Hyaluronan, SHAP, CD44, Inflammation, Leukocytes