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正常マウス乳腺上皮細胞の産生するシンデカン-1 および-4 のコンドロイチン硫酸鎖は、構造および機能的に異なり、ヘパラン硫酸と協調して増殖因子と結合する Sarama Sathyaseelan Deepa¹, ○山田 修平¹, 雑喉 正泰², Olga Goldberger³, 菅原 一幸¹ (¹神戸薬大・生化,²愛知医大・眼科,³米国・ハーバード大)

Objective: Syndecans are the major cell-surface proteoglycans (PGs) expressed by virtually all epithelial cells. The majority of glycosaminoglycan chains of syndecans are the heparan sulfate (HS) type, although syndecan-1 and syndecan-4 are modified by chondroitin sulfate (CS) chains as well. Recently, it has been demonstrated that syndecans-1 and -4 synthesized simultaneously by normal mouse mammary gland epithelial cells bear HS chains that are structurally indistinguishable. In this study, we addressed whether the CS chains of syndecan-1 and -4 are structurally similar, like their HS counterparts, and what functions the CS chains of these hybrid PGs play.

Methods: The purified ectodomains of syndecan-1 and -4 were exhaustively digested with CS lyases and the released disaccharides were fluorescently labeled and analyzed by HPLC on an amine-bound silica column. The kinetic parameters for the binding of midkine (MK), pleiotrophin (PTN) and basic fibroblast growth factor (bFGF) to the intact syndecans-1 and -4 were analyzed using a surface plasmon resonance biosensor.

Results and Discussion: The CS chains of the two syndecans were significantly different, with a higher degree of sulfation for syndecan-4. Functional analysis using a BIAcore system showed that bFGF specifically bound only to the HS chains of both syndecans, whereas MK and PTN bound not only to the HS but also to the CS chains. Intriguingly, removal of the CS chains decreased the association and dissociation rate constants of MK, PTN and bFGF for both syndecans, suggesting the simultaneous binding of these growth factors to both types of chains, producing a ternary complex that transfers the growth factors to the corresponding cell surface receptors more efficiently as compared with the HS chains alone.