Transplantation of Human Amniotic Membrane in Experimental Herpes Stromal Keratitis: Modulates Matrix Metalloproteinases and Tissue Inhibitors of Metalloproteinases in the Cornea

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Purpose: To study matrix metalloproteinases (MMP) and tissue inhibitors of metalloproteinases (TIMP) in the corneas from mice with ulcerative HSK treated with amniotic membrane transplantation (AMT).

Methods: The corneas from BALB/c mice were infected with HSV-1. Mice with ulcerative HSK on day 14 after infection (p.i.) were used for the experiments. In one group of mice, the corneas were treated with AMT that was secured with a tarsorrhaphy, while a control group received a tarsorrhaphy. After 2 days, the appearance of corneal ulcers and stromal inflammation was judged clinically. Corneal sections were studied by immunohistochemistry for the expression of MMP-2, -8, 9 and TIMP-1 and -2. MMP activity in the corneas was investigated by zymography, and the expression of the enzymes was measured by the Western blot technique.

Results: At day 14 p.i., the ulcers stained intensely positive for MMP-2, -8, -9, TIMP-1 and -2. Ulceration ($p<0.001$), stromal inflammation ($p<0.01$) and inflammatory cell infiltration ($p<0.001$) markedly improved by day 2 after AMT. This was associated with reduced expression ($p<0.01$) and activity of MMP-8, -9 and increased localization of TIMP-1 ($p<0.01$), while TIMP-2 was not affected. In contrast, high levels of expression of MMP-8 and -9 remained in the cornea after tarsorrhaphy, and the TIMP-1 expression was only slightly upregulated.

Conclusions: Rapid improvement of HSV-1-induced ulcerative keratitis is noted after amniotic membrane transplantation. This may be caused by reduced expression and activity of MMP-8 and -9, increased TIMP-1 and sustained TIMP-2 expression.