

P043 Phagocytosis of collagen by fibroblasts and invading cancer cells is mediated by MT1-MMP.

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Degradation of collagen is required for the physiological remodelling of connective tissues during growth and development, as well as in wound healing, inflammatory diseases, and cancer cell invasion. In remodelling adult tissues, degradation of collagen occurs primarily through a phagocytic pathway. **While various steps in this pathway have been characterized, the enzyme** required to fragment collagen fibrils for phagocytosis has not been identified. Laser confocal microscopy, TEM, and biochemical assays were used to show that degradation of collagen substrates by fibroblasts correlated with the expression of the membrane-bound matrix metalloproteinase MT1-MMP. The MT1-MMP was localized to sites of collagen cleavage on the cell surface and also within the cells. **In contrast to MT1-MMP, the gelatinase MMP-2 was not required for collagen phagocytosis.** Similar analyses of several ovarian cancer, breast cancer and fibrosarcoma cells indicated that highly metastatic cells also degrade collagen through a phagocytic pathway that is mediated by MT1-MMP. Collectively, these studies demonstrate a pivotal role for catalytically active MT1-MMP in preparing collagen fibrils for phagocytic degradation by normal and transformed cells. CIHR MOP-36333.