A novel marker for assessment of liver matrix remodeling: An enzyme-linked immunosorbent assay (ELISA) detecting a MMP generated type I collagen neo-epitope (C1M)

A competitive enzyme-linked immunosorbent assay (ELISA) for detection of a type I collagen fragment generated by matrix metalloproteinases (MMP)-2, -9 and -13, was developed (CO1-764 or C1M). The biomarker was evaluated in two preclinical rat models of liver fibrosis: bile duct ligation (BDL) and carbon tetra chloride (CCL4)-treated rats. The assay was further evaluated in a clinical study of prostate-, lung and breast-cancer patients stratified according to skeletal metastases. A technically robust ELISA assay specific for a MMP-2, -9 and -13 neo-epitope was produced and seen to be statistically elevated in BDL rats compared to baseline levels as well as significantly elevated in CCL4 rats stratified according to the amount of total collagen in the livers. CO1-764 levels also correlated significantly with total liver collagen and type I collagen mRNA expression in the livers. Finally, the CO1-764 marker was not correlated with skeletal involvement or number of bone metastases. This ELISA has the potential to assess the degree of liver fibrosis in a non-invasive manner.

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