# Human Atherosclerotic Plaques Contain Gamma-Glutamyl Transpeptidase Enzyme Activity

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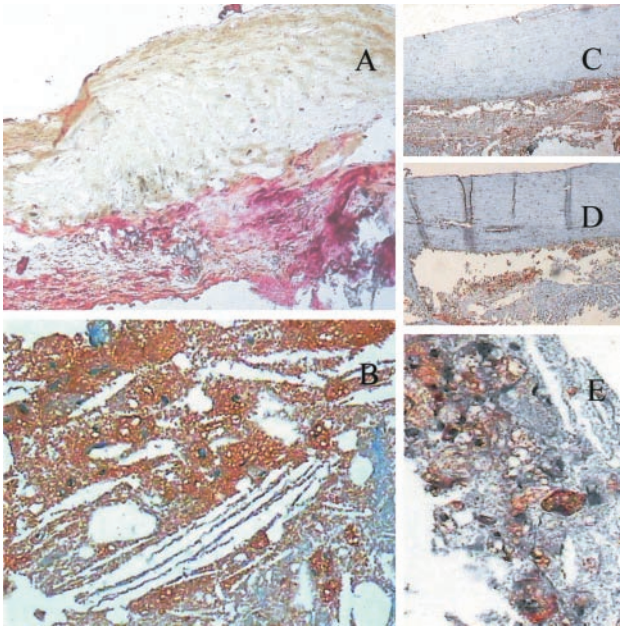
During the last decade, growing evidence has shown that serum gamma-glutamyl transpeptidase (GGT) is an independent prognostic marker for cardiac death and reinfarction, both in unselected populations and in patients with coronary artery disease. Clinical and epidemiological evidence indicates that the prognostic value of GGT is largely independent of other risk factors for cardiovascular disease and alcohol consumption. The catalytic activity of GGT, which is present on the surface of cell membranes and in serum, is responsible for the extracellular catabolism of the antioxidant glutathione. Cysteinyl glycine deriving from the hydrolysis of glutathione performed by GGT has been found to trigger iron-dependent production of reactive oxygen species as well as low-density lipoprotein oxidation in vitro. The localization of GGT within the coronary plaque (Figure) provides a pathological basis for the hypothesis of a direct participation of GGT in low-density lipoprotein oxidation within the plaque and in atherogenesis and coronary artery disease progression.




Histochemical and immunohistochemical demonstration of GGT enzyme activity within a frozen section of coronary atheroma from endarteriectomy in vivo. Histochemical reaction for GGT enzyme activity was performed by using the specific substrate gamma-glutamyl-4-methoxy-2-naphtylamide and the diazonium salt Fast Garnet GBC as a chromogen. A strong GGT activity (the red stain) is selectively present in correspondence of the core of the atheroma, while the fibrous cap stains negative (A, magnification 20×). The identification of the enzyme was confirmed immunohistochemically using a polyclonal antibody directed against the heavy chain of human GGT, which marked the same part of the atheroma (B and C, magnification 40× and 10×, respectively). The homogeneous immunostaining of oxidized lipid-containing foam cells by the antibody is evident at higher magnification (B). For the sake of confirming the localization of GGT activity, another section of the same specimen was immunostained with an antibody directed against CD 68+ cells (ie, macrophages), selectively identifying foam cells (D and E, magnification 10× and 40×, respectively).

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