Medical significance of cysteine protease inhibitors in mammalian secretory fluids

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Abstract: New cysteine protease inhibitors in human tears and milk and their medical significance are reviewed in this paper. As protective components against bacterial infection in the eyes, we detected four kinds of anti-bacterial proteins in normal human tears including lysozyme and three kinds of cysteine protease inhibitors. Using our reverse zymography of normal tears, three kinds of cysteine protease inhibitors were found to be 78kDa, 20kDa and 15kDa and were determined to be lactoferrin, Von Ebner's Gland (VEG) protein and cystatin S, respectively. All of them belong to the cystatin super family and VEG protein and cystatin S are well known cysteine protease inhibitors. The C-terminus area 17mer peptide, Y_{679}-k_{695}, of lactoferrin showed strong homology with a common active domain of the cystatin family and the synthesized peptide showed inhibition of cysteine proteases. Not only were disease-specific changes found in these inhibitor profiles, but also disease-specific new inhibitors in patients tears with certain autoimmune diseases. A 35kDa inhibitor, which was detected specifically in tears with Behcet's disease, an typical autoimmune disease, was determined to be a lacrimal acidic proline-rich protein based on the N-terminus sequence analysis. A65kDa inhibitor of tears with Harada's autoimmune disease was determined to be an Ig heavy chain V-III region. In addition, lactoferrin content in Harada's disease was very low. We found two cathepsin inhibitors in bovine milk using reverse zymography, namely lactoferrin and ?-casein. The L_{133}-Q_{151}, in the human ?-casein molecule is the active inhibitory domain. They may play an important role in antiseptic and anti-infectious functions.

Author Keywords: Autoimmune disease; Behcet's disease; Cystein protease inhibitor; Human tears; Lactoferrin; Milk; Reverse zymography

Index Keywords: bacterial protein; beta casein; cystatin s; cysteine proteinase inhibitor; immunoglobulin G; lactoferrin; lysozyme; proline; unclassified drug; von ebner gland protein; autoimmune disease; bacterial infection; Behcet disease; carboxy terminal sequence; lacrimal duct; milk; protein domain; protein family; protein synthesis; review; secretion; Vogt Koyanagi syndrome; zymography; Animals; Autoimmune Diseases; Bacteria; Bacterial Infections; Caseins; Cattle; Cysteine Endopeptidases; Cysteine Proteinase Inhibitors; Enzyme Tests; Humans; Lactoferrin; Milk; Molecular Weight; Tears; Bacteria (microorganisms); Bovinae; Mammalia

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