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Human lysozyme and lactoferrin therapeutic proteins also have been implicated in pathological condition

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Recently crop plants modified with the therapeutic proteins lysozyme and/or lactoferrin have been tested in the field. Rice modified with lysozyme and lactoferrin has been put forward for commercial production(1). Lysozyme protects us from the danger of bacterial infection. It is an enzyme that attacks the protective cell walls of bacteria. Bacteria build a tough skin of carbohydrate chains, interlocked by short peptide strands, that braces their delicate membrane against the cell's high osmotic pressure. Lysozyme breaks these carbohydrate chains, destroying the structural integrity of the cell wall. The bacteria burst under their own internal osmotic pressure. Lysozyme is present in bacteria and animals alike, birds egg lysozyme is a powerful food allergen but human lysozyme is less likely to cause allergy. Lactoferrin is a protein that participates in regulation of immune functions and controls pathogens by binding iron required for bacterial growth. Both lysozyme and lactoferrin are present in mother's milk and both are used to treat infections. In spite of their value in controlling infection there are pathological conditions associated with the proteins or genetic variants of the proteins. These pathological associations seem to have been overlooked by the promoters of the biopharmaceutical applications of proteins. However, the pathological side effects should have been considered because food crops may become polluted with the genes for the proteins and the proteins. The references below may provide useful information for those questioning the production of the proteins in food crops.

Lysozyme provides effective control of many infections but the protein may, as well, contribute to the pathology of pulmonary emphysema by binding to elastic fibers which undergo breakdown in the disease (2). Hereditary systemic amyloidosis is caused by mutant forms of cell proteins deposited as amyloid fibrils, the mutant cell proteins include lysozyme or apolipoprotein or fibrinogen (3). The lysozyme related disease was provoked by a single mutation of tryptophane to arginine. The disease is inherited as dominant gene and frequently leads to death at mid-life (4). A lactoferrin mutant has been implicated as a cause of amyloidosis accompanied by trichiasis (a common vision threatening condition of the eyelid). The lactoferrin mutant resulted from a single change from glutamic to aspartic acid near the end of the protein molecule (5). Lactoferrin has also been found to be implicated in forms of autoimmune diseases including systemic lupus erythematosus and rheumatoid arthritis (6) or in rheumatoid arthritis associated with vasculitis (inflammation of blood vessels) (7). Along with the effects related to pathology of the immune system, the wild type lactoferrin and lysozyme proteins are associated with amyloid formation related to diseases such as Alzheimer's disease, Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease) or Down's Syndrome. Lactoferrin is associated with other proteins in amyloid (8,9), while lysozyme alone is a precursor for amyloid fibrils (10). An extensive number of different proteins have been identified amyloid fibrils and consequences of feeding elevated human lysozyme and lactoferrin, or for that matter the other amyloid precursor proteins have not been reported.

Production of human lysozyme and lactoferrin in food crops such as rice, barley or maize has been promoted as if the products purely beneficial without harmful side-effects. However, there is evidence that both normal and mutant forms of the proteins are associated with serious detrimental human diseases. In particular the synthetic forms of the human genes used in crop modification are modified both in codons and frequently amino acids to enhance production of the proteins in plants and these alterations are seldom thoroughly tested. Mutations of the human genes in the plants are not normally identified unless they eliminate production of the protein. There seems to be a culture that puts optimism ahead of experiment and distains labeling of products, crop production or field tests so that deleterious side effects of the crops or their products cannot be identified.

Why is the evidence of harmful side effects and dangerous mutant forms presented at the safety evaluation of field tests and production sites? The answer seems to be that both proponents and regulators do not wish to alarm the public. Indeed, if and when the matter is brought up regulators and proponents will unleash teams of vicious lawyers whose job is to shift the burden of proof to those who mention harmful or dangerous side effects. Nevertheless, if and when the dangerous tests or crop productions are undertaken people who are effected should begin to notice amyloidosis or autoimmune diseases including lupus and arthritis. The main geographical areas of concern are California where biopharmaceutical rice is being “tested” on a large scale and in Washington state where large plots of biopharmaceutical barley are being “tested”.

References

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