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CLINICAL SPECIFICATIONS

MICROBIAL TRANSGLUTAMINASE

Function:

Microbial transglutaminase (mTG), also known as thrombian, is a product added to a powder used in the food manufacturing industry to adhere smaller pieces of food together to make a decorative effect or give food a pleasing texture.[1,2] It is also used to thicken some milks, yogurts and egg whites.

Associated With:

Microbial transglutaminase immune reactivity
Celiac disease[3]

Known Cross-Reactions: $A\beta_{42}$ peptide;[4] Gliadin-Transglutaminase Complex;[3] transglutaminase-2, -3 and -6[5]

Clinical Significance:

Microbial transglutaminase (mTG) is an enzyme that is produced by a very special mold. As a biological glue, it is added to many products, including meat, in order to give the food a decorative and pleasing texture. The combination of mTG with other foods can significantly alter the native food protein,[8] making the food more antigenic to a person who may not react to the native food protein. It has been shown in celiac patients that, like tissue transglutaminase-2, mTG can deamidate gliadin.[3] Microbial transglutaminase may play a role in the integrity of the blood-brain barrier (BBB) that may arise from reactivity with mTG or cross-reactivity between enteric neuronal antigens. As a result, autoantibodies to these transglutaminases may play a role in BBB breakdown and AD neuropathology.[4] mTG antibodies were found in 24% of patients with Alzheimer's disease.[4] These circulating antibodies can contribute to amyloidogenesis, if there is a disruption of the BBB. Furthermore, using anti-$A\beta_{42}$ peptide antibody, Vojdani and Vojdani showed reaction from these antibodies with tTG2, tTG3, and particularly mTG.[4] Therefore, removal of mTG from the diet of patients with AD is recommended in order to reduce the level of these cross-reactive antibodies and their reaction with neurons.

References:

1. Kieliszek and Misiewicz. Microbial transglutaminase and its application in the food industry. A review. Folia Microbiol, 2014; 59:241-250.
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4. Vojdani and Vojdani. Amyloid-beta 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A-beta-P-42. Int J Alzheimers Dis, 2018; 2018:1672568.
5. Lerner and Matthias. "Microbial transglutaminase is a potential environmental inducer of celiac disease," in Autoantigens, Autoantibodies, Autoimmunity, Vol. 10, eds K. Conrad, E. K. L. Chan, L. E. C. Andrade, G. Steiner, G. J. M. Pruijn, and Y. Shoenfeld (Lengerich: Pabst Science Publishers), 2015:227-233.
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CLINICAL SPECIFICATIONS

TRANSGLUTAMINASE-3

Function:

Transglutaminases are a family of enzymes. They form protein polymers, like scaffolding, which are vital in the formation of barriers and stabilizing structures. Tissue Transglutaminase-3 (tTG3) is expressed mainly in the epidermis, and to a lesser extent in the placenta and the brain.[1] In the epidermis tTG3 plays a role in the formation of cell envelope barrier structures and in the hair follicle tTG3 helps in the hardening of the inner root sheath.[1,2]

Associated With:

Celiac disease[3]
Dermatitis herpetiformis[1,4]
Esophageal cancer[5]
Gluten sensitivity[4]
Huntington's disease[6]

Known Cross-Reactions: Transglutaminase-2[4,6] and -6;[7] microbial transglutaminase[8]

Clinical Significance:

Transglutaminase is an enzyme that is expressed in the epidermis, placenta, and the brain.[1] It is activated by oxidative stress, during which inflammatory cytokine production increases, specifically tumor necrosis factor-alpha and interferon-gamma.[1,4,6] Tissue Transglutaminase-3 (tTG3) has been shown to be up-regulated in a variety of degenerative diseases.[1,6] Patients with Huntington's disease have been shown to have elevated antibody levels to Transglutaminase-1, -2 and -3.[6] Transglutaminase-3 may play a role in the integrity of the BBB that may arise from reactivity with microbial transglutaminase (mTG) or cross-reactivity between enteric neuronal antigens. The production of antibodies against tTG3 indicates that barrier structures may not be stable. As a result, autoantibodies to these transglutaminases may play a role in BBB breakdown and Alzheimer's disease (AD) neuropathology.[9] Antibodies against tTG3 were found in 31% of patients with AD.[9] Furthermore, using anti-$A\beta_{42}$ peptide antibody, Vojdani and Vojdani showed reaction from these antibodies with tTG2, tTG3, and particularly mTG.[9] Therefore, removal of mTG from the diet of patients with AD is recommended in order to reduce the level of these cross-reactive antibodies and their reaction with neurons.

References:

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2. Lee et al. The proximal promoter of the human transglutaminase 3 gene. J Biologic Chem, 1996; 271(8):4561-4568.
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5. Uemura et al. Transglutaminase 3 as a prognostic biomarker in esophageal cancer revealed by proteomics. Int J Cancer, 2009; 124:2106-2115.
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CLINICAL SPECIFICATIONS

TRANSGLUTAMINASE-6

Function:

Transglutaminases are a family of enzymes. They form protein polymers, like scaffolding, which are vital in the formation of barriers and stabilizing structures. Tissue Transglutaminase-6 (tTG6) is expressed in neural tissue.[1] The tTG6 enzyme is not commonly expressed in the small intestine but can be found in mucosal antigen-presenting cells.[1]

Associated With:

Celiac disease and NCGS[1]
Cerebral Palsy[2]
Gluten Ataxia[1,3]
Gluten Ataxia with Enteropathy[1]
Idiopathic sporadic ataxia[1]
Peripheral Neuropathy[1,3]

Known Cross-Reactions: Transglutaminase-2 and -3;[1] microbial transglutaminase[4]

Clinical Significance:

Transglutaminase-6 is an enzyme that is expressed in the neural tissue. It is activated by oxidative stress, during which inflammatory cytokine production increases, specifically tumor necrosis factor-alpha and interferon-gamma.[5] Researchers speculate that autoimmunity against tTG6 may result from early brain damage and associated inflammation.[2] Patients with high levels of antibodies against tTG6 are suspected of having autoimmunity against neuronal tissue. Neuronal clinical conditions may manifest as Cerebral Palsy,[2] Gluten Ataxia[1,3] or Peripheral Neuropathy.[3] Antibodies may appear in serum before the clinical onset of symptoms. Patients with positive antibodies to tTG6 should be assessed for increased intestinal permeability or "leaky gut." Transglutaminase-6 may play a role in the integrity of the BBB that may arise from reactivity with mTG or cross-reactivity between enteric neuronal antigens. As a result, autoantibodies to these transglutaminases may play a role in BBB breakdown and AD neuropathology.[6] Furthermore, using anti-Aβ_{42} peptide antibody, Vojdani and Vojdani showed reaction from these antibodies with tTG2, tTG3, and particularly mTG.[6] Therefore, removal of mTG from the diet of patients with AD is recommended in order to reduce the level of these cross-reactive antibodies and their reaction with neurons.

References:

1. Hadjivassiliou et al. Autoantibodies in gluten ataxia recognize a novel neuronal transglutaminase. Ann Neurol, 2008; 64(3):332–343.
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