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New serological markers for celiac disease diagnosis: Anti-neo-epitope human and microbial transglutaminases antibodies

Background: The guidelines of ESPGHAN for the diagnosis of pediatric celiac disease (PCD) rely on anti-human tissue transglutaminase (tTg) as the prime and unique antibody for screening PCD population. Microbial Tg (mTg) is a family member of human tissue transglutaminase (tTg). Both enzymes tTg and mTg complexed to gliadin present neo-epitopes and antibodies against these complexes are called tTgneo-epitope and mTg neo-epitope. mTg is capable of cross-linking numerous molecules. Despite declarations of mTg safety, direct evidence for immunogenicity of the enzyme is lacking. The reliability of those antibodies in CD was evaluated.

Materials & Methods: The serological activity of mTg, tTg, mTg neo-epitope and tTg neo-epitope were studied in: 95 pediatric celiac patients (CD), 99 normal children (NC) and 79 normal adults (NA). Sera were tested by ELISAs, detecting IgA, IgG or both IgA and IgG: *AESKULISA®* tTg (tTg, RUO), *AESKULISA®* tTg New Generation (tTg neo-epitope (tTg-neo)), *AESKULISA®* mTg(RUO) and *AESKULISA®* mTg neo-epitope (mTg-neo, RUO). Marsh criteria were used for the degree of intestinal injury.

Results: Comparing pediatric CD patients with the 2 normal groups: mTg-neo IgA, IgG and IgA+IgG antibody activities exceed the comparable mTg ones ($p<0.0001$). All mTg-neo and tTg-neo levels were higher ($p<0.001$). tTg IgA and IgG+IgA were higher than mTg IgA and IgA+IgG ($p<0.0001$). The levels of tTg-neo IgA/IgG were higher than tTg IgA/IgG ($p<0.0001$). The sequential antibody activities reflecting best the increased intestinal damage were: tTg-neo IgG≥mTg-neo IgG>mTg-neo IgA+IgG>tTg-neo IgA. Taken together, mTg-neo IgG and tTg-neo IgG correlated best with intestinal pathology ($r^2=0.989$, $r^2=0.989$, $p<0.0001$, $p<0.0001$, respectively).

Conclusion: mTg is immunogenic in children with CD and by complexing to gliadin its immunogenicity is enhanced. It represents a new serological marker for CD and matches the performance of the tTg neo-epitope. Both antibodies correlate with intestinal damage to the same degree. The neo-epitope tTg and mTg are new powerful serological markers for CD diagnosis. Further studies are needed to explore the pathogenic potential of those antibodies in CD.

Biography

Aaron Lerner after receiving his MD from the Sakler school of medicine, Tel-Aviv University (1976), Professor Lerner specialized in Pediatrics (1982), Pediatric Gastroenterology and Nutrition (1984) and Adult Gastroenterology (1987). Took several senior positions as head of Department of pediatrics (1995-2005) and head of Pediatric Gastroenterology and Nutrition unit, at the Carmel Medical Center, Haifa, Israel. Finished his Medical Management degree M.H.A, at Ben- Gurion University, Beer-Sheba, Israel (1999), spent research sabbaticals in Hahnemann University, Philadelphia, PA, USA (1991), State University of North Carolina, Chapel Hill, N.C,U.S.A (2005) and currently, in an extended scientific sabbatical in Aesku. Kipp Institute, Wendelsheim, Germany.(2014-16). Prof. Lerner presented in numerous international congresses, mainly of pediatrics, nutrition and autoimmunity, published 250 manuscripts in peer reviewed journals and is on the editorial board of 14 international journal.