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Self-multimerization of transglutaminase-2 mediated by the calcium binding C1 domain

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Transglutaminase 2 (TG2) is ubiquitously expressed enzyme with multiple functions. It belongs to the large TG2 family of eight isozymes including blood coagulation factor XIII and TG1-7. TG2 is present in blood, extracellular matrix and intracellular compartments. TG2 is primarily involved in deamidation of glutamine residues or covalent cross linking between glutamine and lysine residues. TG2 induces wound healing, cell growth, differentiation and apoptosis. It is thus involved in treatment of cancer, liver diseases, diabetes, fibrosis, and neurodegeneration as well as inflammatory and autoimmune disorders. TG2 is centrally involved in celiac disease by being the target for highly disease specific autoantibodies and by deamidating gluten epitopes for recognition of pathogenic T cells and B cells. It has been demonstrated that TG2 utilizes itself as a substrate that leads to the formation of TG2 multimers. Gluten peptides can be incorporated into the multimers, forming TG2-TG2-gluten complexes. Such multivalent complexes are excellent antigens both for TG2-specific and deamidated gluten specific B cells and also to lead efficient activation of gluten specific T cells. TG2 consists of an N-terminal domain, a catalytic core domain and two C-terminal domains. TG2 is a calcium dependent enzyme and its activity is mediated by calcium binding to the core domain. Previous studies have reported the binding of at least six calcium ions, out of which five have been located in the catalytic core domain. In the current study, we have identified a calcium binding site at the first C-terminal domain. We have characterized TG2 self multimerization and found that it is mediated by the calcium binding C1 domain. Our findings offer insight into the functional mechanism of TG2 and will help in development of new and improved therapeutics.

Biography

Qamar Bashir has completed his PhD and Post-doctoral studies from Leiden University, The Netherlands. Currently, he is a Researcher at University of Oslo, Norway. He has published more than 15 papers in reputed journals, with a cumulative impact factor of 76 and 340 citations.

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