T : Transglutaminase substrates, reactive sites, cellular localizations, and possible involvement in human physiology/diseases.

TG substrate	Reactive site	Localization	Physiology/disease
Acetylcholine esterase	Glutamine	Intracellular	Neurological diseases [ ]
Actin	Glutamine and lysine	Intracellular	Cytoskeleton regulation [ ]
Aldolase	Reactive glutamine present but specic residue is unknown	Intracellular	Genetic disease, endocrine and metabolic diseases, autoimmune and inammatory diseases [ ]
Androgen receptor		Intracellular (nuclear receptor)	Endocrine and metabolic diseases [,]
Annexin I (lipocortin I)	Glutamine	Intracellular	Autoimmune and inammatory diseases, cytoskeleton regulation [ ]
Calgizzarin-S100 protein-MLN 70	Glutamine and lysine	Keratinocyte cornied envelope	Endocrine and metabolic diseases, dermatological diseases [ ]
Collagen alpha (III)	Glutamine	Extracellular	Extracellular matrix interaction and stabilization, autoimmune and inammatory diseases [ ]
-B-crystallin	Lysine	Intracellular	Cell life and death, cytoskeleton regulation, protein stabilization [ ]
-A crystallin	Glutamine	Intracellular	Cell life and death, cytoskeleton regulation, protein stabilization [ ]
-B crystallin	Glutamine	Intracellular	Cell life and death, cytoskeleton regulation, protein stabilization [ ]
-Bp (beta-B) crystalline	Glutamine	Intracellular	Cell life and death, cytoskeleton regulation, protein stabilization [ ]
Cytochrome c	Glutamine	Intracellular	Cell life and death [ ]
Fibronectin	Glutamine	Extracellular	Protein stabilization, extracellular matrix interaction and stabilization [ ]
Fibrinogen A alpha	Glutamine and lysine	Extracellular	Extracellular matrix interaction and stabilization, autoimmune and inammatory diseases [ ]
Glutathione S transferase	Glutamine, lysine, and uorescein	Intracellular	Extracellular matrix interaction and stabilization [ ]
Gluten proteins	Glutamine	Extracellular	Celiac disease []
Glyceraldehyde phosphate dehydrogenase	Lysine	Intracellular	Neurological diseases [ ]
H1 histone	Glutamine	Intracellular	Cell life and death [ ]
H2 histone	Glutamine	Intracellular	Cell life and death [ ]
H4 histone	Glutamine	Intracellular	Cell life and death [ ]
H histone	Glutamine	Intracellular	Cell life and death [ ]
Importin alpha		Nuclear transport protein	Cell life and death [ ]
-Ketoglutarate dehydrogenase	Lysine	Intracellular	endocrine and metabolic diseases [ ]
Latent TGF-beta binding protein-(LTBP-)		Extracellular	Carcinogenesis, autoimmune, and inammatory diseases [ ]
--Macroglobulin receptor-associated protein	Glutamine	Extracellular	autoimmune and inammatory diseases [ ]
Microtubule-associated protein tau-isoform Tau-F (Tau-)	Glutamine and lysine	Intracellular	Cytoskeleton regulation, neurological diseases [ ]
Myosin		Intracellular	Cytoskeleton regulation [ ]
Nidogen	Glutamine	Extracellular	Extracellular matrix interaction and stabilization [ ]

that could enable them to alternately assume such roles in the event of TG absence.

Similarly, TG -mediated integrin- bronectin interaction is critical to many physiological events in the cell, including cell adhesion, growth, migration, di erentiation, programmed cell death, and ECM assembly [ ]. Such interaction is vital to many cellular processes and serves as one of the major routes for extracellular survival, signalling activation, and consequent apoptotic evasion. It is nonenzymatic and independent of TG transamidation and cross-linking activities. Consequently, it is unlikely that any other member of the transglutaminase family can successfully compensate for this function in the event of TG absence.

6 Conclusions

e abundance of TG in various cell types, its specialized structural conformation, and its broad substrate speci city are some of the key factors justifying the enzyme•s implication in myriads of biological events. From this review, it is evident that besides its calcium-dependent activities, TG can enzymatically or nonenzymatically mediate key cell physiological events. However, it has been increasingly suggested that in the event of TG absence its biological functions could be successfully compensated for by other members of the transglutaminase family. ese suggestions have been made without recourse to the distinguishing features of TG among the transglutaminase family. It is necessary to carry out further investigations to ascertain the main reasons why TG knockout is not embryonic lethal, instead of relying on the assertion that its functions are compensated for by other transglutaminase enzymes. Finally, it is also our view that a systematic investigation should be carried out to establish, with certainty, the possibility of and premise for the replacement of TG function by any other member of the transglutaminase family.

Conflict of Interests

ere is no con ict of interests.

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