Gene Section
Short Communication

TGM2 (transglutaminase 2)
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Abstract
Short Communication on TGM2, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity
Other names: G-ALPHA-h, GNAH, TG2, TGC
HGNC (Hugo): TGM2
Location: 20q11.23

DNA/RNA
Description
The gene encompasses 36838bp; 13 exons; a dense CpG island engulfs exon 1 and the transcriptional start site; negative strand.

Transcription
Two transcript variants 1) 3937bp; 2) 2326bp (C-terminal truncation exons 11-13); induced by NFkB, retinoic acid, IL-6, TGF-beta1, HRE, AP-1 and GRE.

Protein
Description
687 amino acids; 78 kilodaltons; monomer.

Expression
Ubiquitously expressed.

Localisation
Mostly intracellular (cytosol, nucleus and cell membrane); extracellular.

Function
Multifunctional enzyme with transglutaminase crosslinking activity (catalyze covalant bonds between the ε-amino group of a lysine and the γ-carboxyl group of a glutamine residue) stabilizing the extracellular matrix (ECM) and cell-ECM interaction; require Ca2+ for catalytic activity; inhibited by GTP; under stress (loss of Ca2+) may play a role in apoptosis; involved in wound healing and inflammation; aberrant overexpression of TG2 is linked to chemotherapeutic drug resistance.

Mutations
Germinal
No germinal mutations have been identified; low frequency of SNPs.

Somatic
No somatic mutations have been identified in cancer; can be transcriptionally silenced by CpG methylation in cancer (breast and brain); overexpression in many cancers; 3 missense mutations identified in early-onset type 2 diabetes patients (c.989T>G, c.992T>A, c.998A>G).
**Breast cancer**

**Oncogenesis**
Overexpression renders culture mammary epithelial cells resistant to doxorubicin, associated with invasive phenotype and epithelial-to-mesenchymal transition; epigenetic silencing has been documented in many breast cancer cell lines and patient samples. In 30 patients, TG2 overexpression was found more often in lymph node metastases than primary tumors.

**Ovarian cancer**

**Prognosis**
Overexpression of TG2 is associated with negative survival in 93 patients (p=0.007).

**Oncogenesis**
Overexpression renders ovarian cancer cells resistant to cisplatin and is associated with higher tumor stage.

**Pancreatic cancer**

**Prognosis**
Overall survival of stage II pancreatic ductal adenocarcinoma (PDAC) patients with TG2-mediated loss of PTEN was poor (20.7 months) compared to 68.6 months for TG2 negative and PTEN positive patients.

**Oncogenesis**
Overexpression; resistance to gemcitabine; in 51 PDAC tumor samples overexpression of TG2 was associated with loss of PTEN expression.

**Non-small cell lung cancer (NSCLC)**

**Prognosis**
In 429 Korean patients, TG2 expression was associated with shorter disease free survival and correlated with recurrence.

**Oncogenesis**
Overexpression ; cisplatin resistance.

**Celiac disease**
Autoantibodies against TG2; autoantibodies are deposited in the small-bowel mucosa; TG2 crosslinks gliadin peptides (gluten) derived.

**References**


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