

alogons) within the human genome. Phylogenetic analysis revealed that TMEM16E and TMEM16F constitute a subfamily among TMEM16 family proteins. On the basis of these facts, we concluded that the *TMEM16E* and *TMEM16F* genes are paralogs within the human genome (Katoh and Katoh 2004b).

Tsutsumi et al. (2004) suggested that the human GDD1 protein showed no significant similarity to any other known proteins or protein classes except GDD1 orthologs in other species. They also reported that the human GDD1 protein showed 79%, 56%, 40%, and 41% identity with mouse, zebrafish, fruit fly, and mosquito orthologs (or homologs), respectively.

However, TMEM16E is identical to GDD1, as mentioned above, and BLAST programs reveal that TMEM16E (GDD1) is homologous to other members of the TMEM16 family, such as TMEM16F, TMEM16A, TMEM16B, TMEM16C, and TMEM16D. Human TMEM16E (GDD1) shows 50.3% total amino acid identity with human TMEM16F (Katoh and Katoh 2004b). Human TMEM16E (GDD1) is more homologous to human TMEM16F than to fruit fly or mosquito *Tmem16e* homologs.

Cys 356 of TMEM16E (GDD1) is substituted with Arg or Gly in patients with gnathodiaphyseal dysplasia (Tsutsumi et al. 2004). Because Cys 356 is conserved among members of the TMEM16 family (Katoh and Katoh 2004b), we can now predict that Cys residues might also be essential for the biological function of members of the TMEM16 family. In the postgenome era, comprehensive identification of related genes within the human genome is important for the progression of genome science and medical science.

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Electronic-Database Information

The URLs for data presented herein are as follows:

HUGO Gene Nomenclature Committee, <http://www.gene.ucl.ac.uk/nomenclature/>

Online Mendelian Inheritance in Man (OMIM), <http://www.ncbi.nlm.nih.gov/Omim/> (for gnathodiaphyseal dysplasia, *TMEM16E*, and *TMEM16F*)

References

Katoh M, Katoh M (2003) *FLJ10261* gene, located within the *CCND1-EMS1* locus on human chromosome 11q13, encodes the eight-transmembrane protein homologous to *C12orf3*, *C11orf25* and *FLJ34272* gene products. *Int J Oncol* 22:1375–1381

——— (2004a) Identification and characterization of human *TP53I5* and mouse *Tp53i5* genes *in silico*. *Int J Oncol* 25: 225–230

——— (2004b) Identification and characterization of *TMEM16E* and *TMEM16F* genes *in silico*. *Int J Oncol* 24: 1345–1349

Schwab M (1998) Amplification of oncogenes in human cancer cells. *Bioessays* 20:473–479

Tsutsumi S, Kamata N, Vokes TJ, Maruoka Y, Nakakuki K, Enomoto S, Omura K, Amagasa T, Nagayama M, Saito-Ohara F, Inazawa J, Moritani M, Yamaoka T, Inoue H, Itakura M (2004) The novel gene encoding a putative transmembrane protein is mutated in gnathodiaphyseal dysplasia (GDD). *Am J Hum Genet* 74:1255–1261

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Response to Katoh and Katoh

To the Editor:

Gnathodiaphyseal dysplasia (GDD [MIM 166260]) is a syndrome characterized by bone fragility, sclerosis of tubular bone, and cemento-osseous lesions of the jawbone. We have mapped the GDD locus to an 8.7-cM interval on chromosome 11p14.3–15.1 by linkage analysis of a Japanese family with GDD (Tsutsumi et al. 2003). We studied a cDNA (GenBank accession number AL833271) in the candidate region, and, early in 2003, we detected a missense mutation (C356R [MIM 608662.0001]) in the affected members of the family. The gene was named “*GDD1*” (MIM 608662) and was submitted to the National Center for Biotechnology Information (NCBI) database on October 28, 2003 (GenBank accession number AB125267). The mouse homolog was also cloned and was submitted to the NCBI database on November 4, 2003 (GenBank accession number AB125740). We found cellular localization of the GDD1 protein to the endoplasmic reticulum, as well as another missense mutation (C356G [MIM 608662.0002]), in the affected members of an African American family with GDD. Overexpression of *GDD1* genes with both of the mutations found in the patients with GDD dramatically changed the cellular characteristics. Our study containing these results was electronically published in *The American Journal of Human Genetics* on April 29, 2004 (Tsutsumi et al. 2004).

On the other hand, Katoh and Katoh independently reported that they had found, through an *in silico* anal-

ysis, that *FLJ10261*, *C12orf3*, *C11orf25*, and *FLJ34272* are genes that share a structural homology (Katoh and Katoh 2003). They then reported the other members of the gene family (GenBank accession numbers AL833271 and AL832340) in the May 2004 issue of *The International Journal of Oncology* (Katoh and Katoh 2004b). In that study, they named these genes “*TMEM16A*”–“*TMEM16F*” (MIM 608663). They claimed to name AL833271 “*TMEM16E*,” whereas we designated it “*GDD1*.”

As they point out in their letter to the editor (Katoh and Katoh 2004a [in this issue]), it is now clear that *GDD1* belongs to a structurally related family of eight-transmembrane proteins, although cellular localizations of these genes are not known, except in the human *GDD1* protein, which is localized to the endoplasmic reticulum. Functional analysis of these proteins will reveal the mechanisms of pathogenesis of GDD.

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Electronic-Database Information

Accession numbers and URLs for data presented herein are as follows:

GenBank, <http://www.ncbi.nlm.nih.gov/Genbank/> (for the cDNA of *GDD1* [accession numbers AL833271 and AB125267], the *GDD1* ortholog amino acid sequence of

mouse [accession number AB125740], and another member of the gene family [accession number AL832340])
Online Mendelian Inheritance in Man (OMIM), <http://www.ncbi.nlm.nih.gov/Omim/> (for GDD, *GDD1* C356R, *GDD1*, *GDD1* C356G, and *TMEM16A*–*TMEM16F*)

References

- Katoh M, Katoh M (2003) *FLJ10261* gene, located within the *CCND1-EMS1* locus on human chromosome 11q13, encodes the eight-transmembrane protein homologous to *C12orf3*, *C11orf25* and *FLJ34272* gene products. *Int J Oncol* 22:1375–1381
- (2004a) *GDD1* is identical to *TMEM16E*, a member of the *TMEM16* family. *Am J Hum Genet* 75:927–928 (in this issue)
- (2004b) Identification and characterization of *TMEM16E* and *TMEM16F* genes *in silico*. *Int J Oncol* 24:1345–1349
- Tsutsumi S, Kamata N, Maruoka Y, Ando M, Tezuka O, Enomoto S, Omura K, Nagayama M, Kudo E, Moritani M, Yamaoka T, Itakura M (2003) Autosomal dominant gnathodiaphyseal dysplasia maps to chromosome 11p14.3-15.1. *J Bone Miner Res* 18:413–418
- Tsutsumi S, Kamata N, Vokes TJ, Maruoka Y, Nakakuki K, Enomoto S, Omura K, Amagasa T, Nagayama M, Saito-Ohara F, Inazawa J, Moritani M, Yamaoka T, Inoue H, Itakura M (2004) The novel gene encoding a putative transmembrane protein is mutated in gnathodiaphyseal dysplasia (GDD). *Am J Hum Genet* 74:1255–1261

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