Molecular Plant • Volume 6 • Number 3 • Pages 665–674 • May 2013 REVIEW ARTICLE

Rice MtN3/Saliva/SWEET Family Genes and Their Homologs in Cellular Organisms

Meng Yuan and **Shiping Wang**[1]

National Key Laboratory of Crop Genetic Improvement, National Center of Plant Gene Research (Wuhan), Huazhong Agricultural University, Wuhan 430070, China

ABSTRACT **The MtN3/saliva/SWEET-type genes, existing either alone or in a family group, are found in diverse organisms, from monocellular protozoa to higher eukaryotes, indicating their importance in cellular organisms. These genes encode polytopic membrane proteins that feature an MtN3/saliva domain, also known as a PQ loop repeat. The rice MtN3/saliva/SWEET gene family consists of 21 members and is among the largest families in sequenced organisms. Accumulating data suggest that these genes are involved in multiple physiological processes, including reproductive development, senescence, environmental adaptation, and host–pathogen interaction, in different species. In rice, some members of the family, including *Xa13/Os8N3/OsSWEET11*, which is essential for reproductive development, are used by the pathogenic bacterium *Xanthomonas oryzae* pv. *oryzae* to invade its host. Emerging data have also revealed that at least some MtN3/saliva/SWEET-type proteins may regulate different physiological processes by facilitating ion transport via interaction with ion transporters or as sugar transporters. The accumulating knowledge about MtN3/saliva/SWEET-type genes will help to elucidate the molecular bases of their function in different organisms.**

Key words: MtN3/saliva; PQ loop repeat; membrane protein; SWEET; transporter.

INTRODUCTION

The genes involved in basic cellular and development processes are usually conserved during evolution, and they are ubiquitous in living organisms. If genes occur as highly conserved gene families and have redundant functions, they may contribute to the physiological processes that are essential for survival. Examples are the *RecA*/*RAD51* gene family involved in DNA repair, DNA homologous recombination, and genome stability and the *MutS* and *MutL* gene families involved in the DNA mismatch repair system; these gene families are present from protozoa to high eukaryotes (Lin et al., 2006, 2007; Kou et al., 2012).

The MtN3/saliva/SWEET-type genes are an evolutionally conserved group of genes that are prevalent in higher eukaryotes, and they are also found in protozoa, metazoa, fungi, bacteria, and archaea (Hamada et al., 2005; Saier et al., 2006). These genes encode membrane proteins harboring the MtN3/saliva domain. This domain is also named the PQ loop repeat, and it comprises a pair of repeats, each spanning two transmembrane helices connected by a loop based on the description of the Conserved Domain Database (www.ncbi.nlm.nih.gov/cdd). The first gene of this type to be identified was *MtN3*, a root nodulin-related gene in *Medicago truncatula* that is associated with different stages of *Rhizobium*-induced nodule development (Gamas et al., 1996). A homologous gene of *MtN3*, the *saliva* gene, was later found in *Drosophila*, in which it is expressed in salivary glands during embryonic development (Artero et al., 1998). Lately, some proteins of this family in animals and plants were found to function as glucose transporters and thus they were named SWEET (Chen et al., 2010).

Although a distinct type of genes based on *MtN3* and *saliva* has been identified, the exact biological functions of *MtN3* and *saliva* themselves remain to be determined. The only known domain or motif of MtN3/saliva/SWEET-type proteins is the MtN3/saliva domain, and the biochemical function of this domain is unknown. However, accumulating data have shown that *MtN3/saliva/SWEET* genes are involved in multiple biological processes, and recent studies have revealed the biochemical functions of selected MtN3/saliva/SWEET proteins. These advances provide clues for exploring the biological roles of these proteins in different organisms.

---

[1] To whom correspondence should be addressed. E-mail swang@mail.hzau.edu.cn, tel. 86–27–8728–3009, fax 86–27–8728–7092.

doi:10.1093/mp/sst035, Advance Access publication 21 February 2013

Received 8 December 2012; accepted 9 February 2013

MTN3/SALIVA/SWEET-TYPE GENES ARE PREVALENT IN CELLULAR ORGANISMS

Based on the results of key word searches using 'MtN3' and 'saliva' as queries, and BLASTN, BLASTP, and TBLASTN searches using the sequences of genes and proteins of human RAG1AP1 (also named HsSWEET1 or SLC50A1; Chen et al., 2010), rice Xa13 (also named Os8N3 or OsSWEET11; Chu et al., 2006; Yang et al., 2006; Chen et al., 2010), and *Ciona intestinalis* Ci-Rga (also named CiSWEET1; Chen et al., 2010) as queries against the databases in the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov), the MtN3/saliva/SWEET-type genes are widely distributed in cellular organisms (Table 1). In the Transporter Classification Database (TCDB, www.tcdb.org), the MtN3/saliva/SWEET-type proteins are grouped in the 9.A.58 family (Saier et al., 2006). The number of members of MtN3/saliva/SWEET gene family varies by species (Table 1). Interestingly, a large number of MtN3/saliva/SWEET genes existing within a species is not associated with the evolutionary complexity of the species. Plants have a much greater number of MtN3/saliva/SWEET-type genes than other species. Mammals (human, olive baboon, rat, and mouse) have only one MtN3/saliva/SWEET-type gene. In addition, chordates (*Ciona intestinalis*, *Danio rerio*, and *Xenopus laevis*) and bacteria (*Mycoplasma arthritidis*, *Prochlorococcus marinus*, *Fusobacterium mortiferum*, and *Leptospira interrogans*) also have only one MtN3/saliva/SWEET-type gene. However, an arthropod (*Drosophila melanogaster*) has two MtN3/saliva/SWEET-type genes, and an aschelminthe (*Caenorhabditis elegans*) has seven MtN3/saliva/SWEET-type genes. This feature suggests that this gene type may play more diverse roles in plants than in animals (Baker et al., 2012).

Most of the characterized or predicted MtN3/saliva/SWEET proteins from different species consist of seven transmembrane helices that harbor two MtN3/saliva domains (Figure 1; Chen et al., 2010; Yuan et al., 2010). A few MtN3/saliva/SWEET proteins consist of three transmembrane helices harboring one MtN3/saliva domain (Figure 1). Phylogenetic analysis of the representative MtN3/saliva/SWEET-type proteins selected from the TCDB database reveals that they can be divided into three clades (Figure 2). Both monocots (*Oryza sativa*, *Sorghum bicolor*, *Zea mays*, and *Brachypodium distachyon*) and dicots (*Arabidopsis thaliana*, *Lotus japonicus*, *Petunia hybrida*, *Capsicum annuum*, *Lycopersicon esculentum*, *Vitis vinifera*, and *Lilium longiforum*) are distributed in clade I. Most of the proteins in clade I harbor two MtN3/saliva domains. Clade II includes MtN3/saliva/SWEET-type proteins from metazoa (*Caenorhabditis elegans*, *Drosophila melanogaster*, *Ciona intestinalis*, *Danio rerio*, and *Xenopus laevis*) and mammals (*Mus musculus*, *Rattus norvegicus*, *Papio anubis*, and *Homo sapiens*). All the clade II proteins contain two featured MtN3/saliva domains. The MtN3/saliva/SWEET-type proteins from bacteria (*Mycoplasma arthritidis*, *Prochlorococcus marinus*, *Fusobacterium mortiferum*, and *Leptospira interrogans*) and archaea (*Methanocaldococcus jannaschii*) all fall into clade III; in addition, some members of the *C. elegans* MtN3/saliva/SWEET family are also included in this clade. All the proteins from bacteria in clade III putatively feature three transmembrane helices harboring one MtN3/saliva domain. This phylogenetic analysis suggests that the widely distributed MtN3/saliva/SWEET-type proteins in cellular organisms may originate from the protein with three transmembrane helices harboring one MtN3/saliva domain in prokaryotes. In contrast, the domain duplication that occurred during eukaryotic evolution resulted in the generation of proteins with seven transmembrane helices harboring two MtN3/saliva domains.

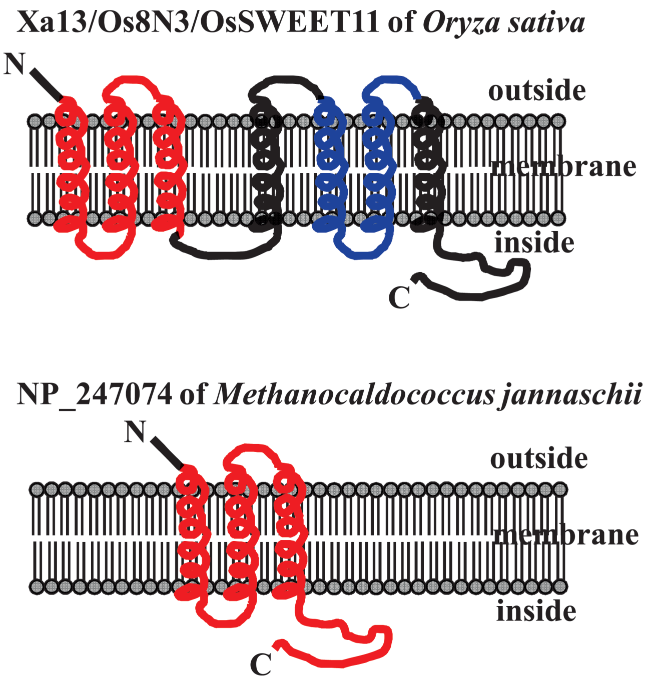

Figure 1. Structures of MtN3/Saliva/SWEET-Type Proteins.

According to the number of MtN3-saliva domains in a protein, MtN3/saliva/SWEET-type proteins can be classified into two types: those harboring two MtN3/saliva domains (shown with red and blue colors), such as rice Xa13/Os8N3/OsSWEET11 protein, and those harboring only one MtN3/saliva domain (shown with red color), such as *Methanocaldococcus jannaschii* NP_247074 protein. The topology of Xa13/Os8N3/OsSWEET11 protein is determined by analyzing a set of truncated proteins using a split-ubiquitin system for integral membrane protein (Yuan et al., 2010). The topology of NP_247074 protein is from the Transporter Classification Database (TCDB, www.tcdb.org).

MTN3/SALIVA/SWEET-TYPE GENES ARE INVOLVED IN MULTIPLE PHYSIOLOGICAL PROCESSES

Although evolutionarily conserved, MtN3/saliva/SWEET-type genes have been reported to be involved in multiple physiological processes in different species and even within