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The Oligopeptide Transporters: A Small Gene Family with a Diverse Group of Substrates and Functions?

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ABSTRACT Genes in the Oligopeptide Transport family encode integral membrane proteins that are believed to translocate their substrates from either the extracellular environment or an organelle into the cytosol. Phylogenetic analyses of plant transporters have revealed two distant clades: the Yellow Stripe-Like (YSL) proteins and the so-called Oligopeptide Transporters (OPTs), for which the family was named. Three categories of substrates have been identified for this family: small peptides, secondary amino acids bound to metals, and glutathione. Notably, the YSL transporters are involved in metal homeostasis through the translocation of metal-chelates, indicating a level of conservation both in biological function as well as substrates. In contrast, the functions of OPT proteins seem to be less defined and, in this review, I will examine the supporting and contradictory evidence for the proposed roles of OPTs in such diverse functions as long-distance sulfur distribution, nitrogen mobilization, metal homeostasis, and heavy metal sequestration through the transport of glutathione, metal-chelates, and peptides.

Key words: Molecular transport; nutrient and metal transport; transporters; Oligopeptide Transporters.

INTRODUCTION

In plants, the Oligopeptide Transporters (OPTs) comprise a small gene family (pFAM designation: PF03169) whose products transport substrates synthesized from amino acids including small peptides, secondary amino acids that can complex with metals, and the modified tripeptide glutathione (Koh et al., 2002; Curie et al., 2001; Bogs et al., 2003). These integral membrane proteins are predicted to have 12 transmembrane domains and are characterized by several signature motifs (Wiles et al., 2006). It is widely accepted that these transporters are proton-coupled symporters that translocate their substrates in the cytosolic direction (Hauser et al., 2000; Bogs et al., 2003; Schaaf et al., 2004; Osawa et al., 2006). Phylogenetically they can be divided into two groups—the Yellow Stripe-Like (YSL) and Oligopeptide Transporter (PT) clades (Figure 1)—and in the *A. thaliana* genome, there are eight and nine of each, respectively (DiDonato et al., 2004; Koh et al., 2002). Notably, plant genes in the PT clade are closer in homology to their fungal orthologs than they are to YSL genes in the same organism (Yen et al., 2001).

The YSL genes have been found in archaea, eubacteria, plants, and fungi but not animals and their function in plants appears to be the transport of metal-chelates (Curie et al., 2001; DiDonato et al., 2004; Roberts et al., 2004; Koike et al., 2004; Murata et al., 2006) consisting of mugeneic acids or nicotianamine, both of which are synthesized from three S-adenosyl methionines. On the other hand, PT genes have only been found in plants and fungi and have been implicated in the transport of small peptides, glutathione, and metal-chelates (Koh et al., 2002; Bogs et al., 2003; Vasconcelos et al., 2008; Table 1). What is striking about the OPT family is the level of function and substrate conservation in the YSL transporters and the level of divergence in the PT clade. The YSL proteins appear to be involved in metal-chelate translocation at all possible levels including intracellular transport, long distance mobilization, and soil scavenging. The PT transporters, on the other hand, seem not to have a common biological function but rather this group may be involved in four different processes: long-distance metal distribution, nitrogen mobilization, heavy metal sequestration, and glutathione transport. This review will focus on the evidence for and

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against the PT proteins contributing to these four biological functions.

Even though the gene family is named the OPT family, PT-type genes are usually named and referred to as OPTs while yellow stripe-like genes are typically called YSLs. Furthermore, in animals, the acronym OPT has been used to describe members of the Peptide Transport (PTR) superfamily (also known as the Proton-coupled Oligopeptide Transporter (POT) family). In this review, the use of OPT will refer exclusively to genes from the PT branch of the Oligopeptide Transporter family and not YSL or PTR genes.

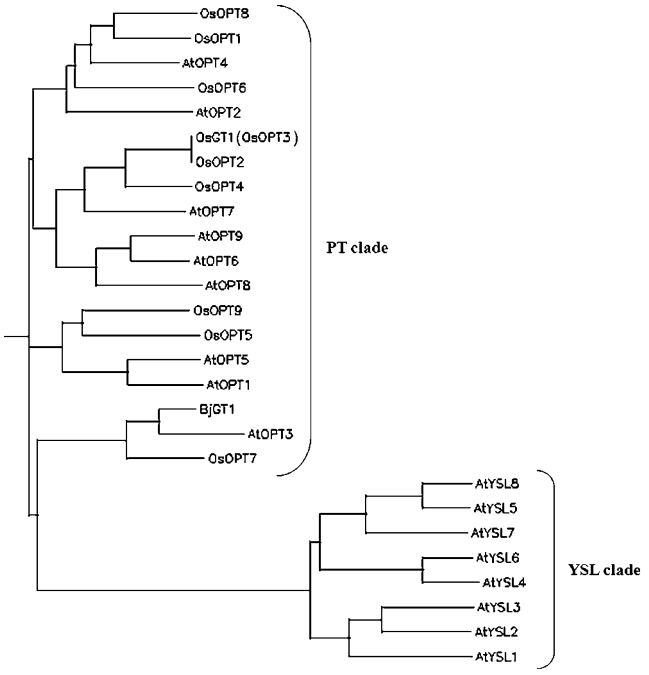

Figure 1. Phylogenetic Tree Illustrating the YSL and PT Clades Found in the OPT Family in Plants.

The tree was constructed from a ClustalW alignment comprising all 17 *A. thaliana* OPT family members, all nine PT *O. sativa* transporters, and BjGT1 from *Brassica juncea*.

SEVERAL OPTs EXHIBIT CHARACTERISTICS OF IRON TRANSPORTERS

Transporters from several different families have been shown to play a role in iron (Fe) trafficking and there is evidence from both a model monocot and dicot that a subset of the OPTs are involved in iron and possibly other metal transport (Wintz et al., 2003; Vasconcelos et al., 2008). Iron-transporting OPTs have been described in *A. thaliana* and *Oryza sativa*, with the *A. thaliana* transporter AtOPT3 being the best characterized of these. While expression and mutant analyses all suggest that AtOPT3 transports iron, actual translocation of an iron-chelate by this protein has not been demonstrated.

Several expression studies have revealed a regulatory regime for *AtOPT3* that is consistent with long-distance iron transport and partitioning. First, four studies found that *AtOPT3* expression was induced by iron deficiency and the increase in expression was shown to be more than an order of magnitude in roots and twofold in leaves (Wintz et al., 2003; Stacey et al, 2006, 2008; Buckhout et al., 2009). Second, loss-of-function mutants in *POPEYE* (*PYE1*), which encodes a key bHLH transcription factor that regulates iron homeostasis, had increased *AtOPT3* expression regardless of iron availability (Long et al., 2010). Additionally, the same study found that *PYE1* and *AtOPT3* are co-regulated. Third, a meta-analysis of 58 microarray datasets showed that *AtOPT3* is in the same regulatory network as other iron-partitioning genes, including the iron transporter encoded by *AtNRAMP4* and the iron reductase encoded by *AtFRO3* (Long et al., 2010). Finally,

Table 1. Summary of Proposed Functions and Substrates of Characterized OPTs.

Transporter	GenBank accession number	Proposed functions	Proposed* or demonstrated substrates	Reference
AtOPT3	AT4G16370	Long-distance iron transport or signaling	Fe-chelate*	Stacey et al., 2008
AtOPT4	AT5G64410	Loading vasculature with peptides at source tissues	Broad range of peptides	Koh et al., 2002; Stacey et al., 2006
AtOPT5	AT4G26590	Possibly mediates heavy metal phytotoxicity	Unknown	B. Ahner, personal communication
AtOPT6	AT4G27730	Long-distance GSH mobilization through loading of asculature and mediating heavy vmetal phytotoxicity	GSH, GSH-Cd, PC_n-metal*, and peptides of 4–13 amino acids	Pike et al., 2009; Cagnac et al., 2004
BjGT1	CAD91127	GSH transport from leaves and hypothesized role in mediating heavy metal phytotoxicity	GSH, GSH-Cd*, PC_n-metal*	Bogs et al., 2003
OsOPT1	BAB89477	Undetermined role in iron homeostasis	Fe–NA	Vasconcelos et al., 2008
OsGT1 (OsOPT3)	NP_001056651.1	Long-distance GSH transport	GSH	Zhang et al., 2004; Wang et al., 2007
OSOPT4	NP_001056665.1	Undetermined role in iron homeostasis	Fe–NA	Vasconcelos et al., 2008
OsOPT7	AAO32313	Undetermined role in iron homeostasis	Fe–NA	Vasconcelos et al., 2008