CHANNELS
2017, VOL. 11, NO. 1, 8–10
http://dx.doi.org/10.1080/19336950.2016.1222760

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AUTOCOMMENTARY

GDP-L-fucose transport in plants: The missing piece

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ARTICLE HISTORY Received 4 August 2016; Accepted 7 August 2016

KEYWORDS Golgi apparatus; nucleotide sugars

The monosaccharide fucose is an important deoxyhexose occurring in plants, fungi and animals. Fucose is mainly found as a component of glycan structures such as *N*- and *O*-linked glycans, glycolipids and in cell wall polysaccharides such as fucoidan, xyloglucan, rhamnogalacturonan II. The biosynthesis of these glycan structures is mediated by glycosyltransferases and typically occurs within the endomembrane system. Fucosylation reactions require an activated sugar in the form of GDP-L-fucose (GDP-Fuc) which is either biosynthesized *de novo* or can also be salvaged from fucose in the cytosol. This partitioning necessitates active GDP-Fuc transport into the endomembrane system for glycosylation reactions. To date, GDP-Fuc transporters have been characterized in mammals (*Homo sapiens*), insects (*Drosophila melanogaster*) and nematodes (*Caenorhabditis elegans*), reviewed in.[1] However, given the importance of fucose containing structures in plants, the absence of a characterized GDP-Fuc transporter has, until recently, been a dilemma. Thus, the recent identification of a GDP-Fuc transporter (GFT1) in the reference plant *Arabidopsis thaliana* represents the final missing piece of GDP-Fuc metabolism in plants.[2]

Considering the identification of a functional endomembrane GDP-Fuc transporter occurred over 15 y ago,[3] it is intriguing that it has taken this long for the plant ortholog to be identified. This fact is even more surprising when we consider that the plant GDP-sugar transporter clade was elucidated in the same year with the identification of GONST1, the Arabidopsis GDP-mannose (GDP-Man) transporter.[4] While in the intervening period members of the plant GDP-sugar (GONST) clade have been assessed for their capacity to transport GDP-Fuc,[5] no candidate was identified. There are a number of reasons for this lack of success, but 2 main issues are likely responsible. First, nucleotide sugar transporters are antiporters and thus require an exchange substrate, and in the case of GDP-Fuc, there is a requirement for GMP.[2] Unfortunately, the majority of transport assays undertaken with the nucleotide sugar transporter family do not use pre-loaded vesicles and assume that endogenous substrates (e.g. UMP or GMP) are present in excess and will drive transport *in vitro*. Second, the identification of candidate plant GDP-Fuc transporters using bioinformatic approaches is likely problematic; it is now clear that plant GDP-Fuc members (clade II) form a distinct clade when compared to their experimentally determined orthologues in animals (clade III, Fig. 1). This is in contrast to the GDP-Man clade where both the plant and fungal orthologues appear to form a tighter group (clade I).

The recent identification of a fucose salvage pathway in the fungus *Mortierella alpina* as well as the identification of GDP-Fuc in metabolic extracts,[6] supports the likelihood that a GDP-Fuc transporter is present in some fungal species. This observation could be readily confirmed with the addition of the top BLAST match for *Mortierella* sp. and *Scleroderma* sp to the phylogenetic tree and their subsequent homology to the characterized animal GDP-Fuc transporters

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Autocommentary to: Rautengarten C, et al. The Arabidopsis Golgi-localized GDP-L-fucose transporter is required for plant development. Nat Commun. 2016 Jul 6;7:12119; PMID: 27381418; http://dx.doi.org/10.1038/ncomms12119.

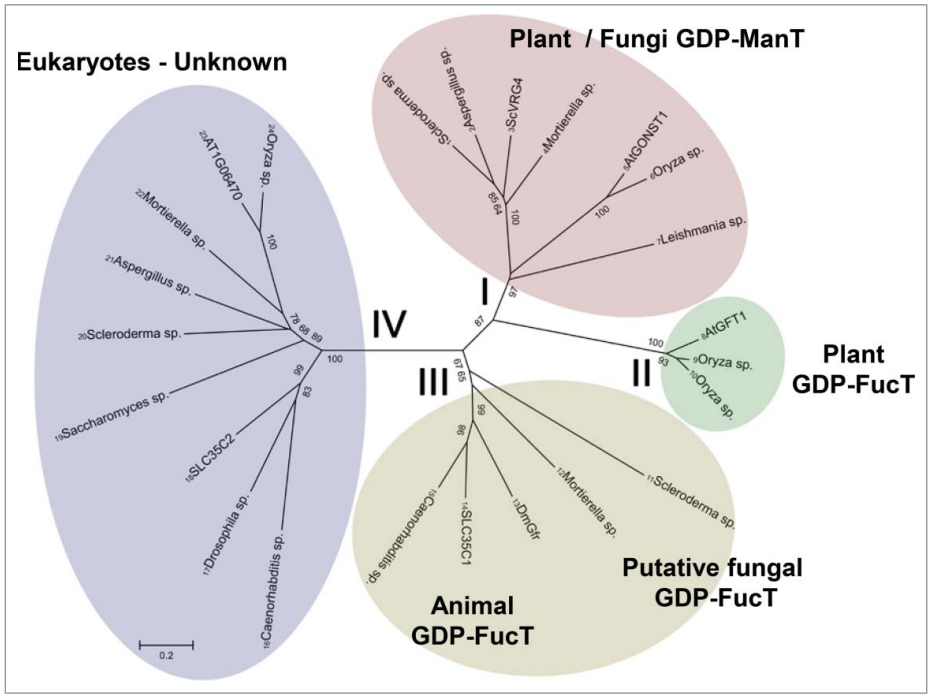

Figure 1. Phylogenetic tree of functionally characterized GDP-Fuc and GDP-Man transporters from eukaryotes. The protein sequences were obtained from GenBank and BLAST and the phylogenetic analysis of sequences was conducted using MEGA7. The clades were arbitrarily assigned a number. Bootstrap values are shown at branch points.

(Fig. 1). Since we have now demonstrated that highly homologous nucleotide sugar transporters are functional orthologues,[7] there is a high likelihood that these fungal candidates are authentic GDP-Fuc transporters. Overall, the above observations support the notion that GDP-Fuc transport arose separately from GDP-Man transport in both the plant and animal/fungi lineages and that the requirement for GDP-Man transport in animals was subsequently lost (clade I, Fig. 1).

The last apparent conundrum for the GDP-Fuc transporter family is connected to the human SLC35C2 nucleotide sugar transporter. While there would appear to be some biochemical evidence for its association with fucosylation of endomembrane targets in mammalian cells,[8] it forms a clade separate to all other characterized GDP-Fuc transporters (clade IV, Fig. 1). Interestingly, this clade appears to comprise a distinct group of unknown nucleotide sugar transporter family members that seem to be highly conserved throughout the major eukaryotic lineages. Since there is evidence to suggest SLC35C2 is unable to directly transport GDP-Fuc [8] and that there is now a clearly defined GDP-Fuc transporter in plants with little homology to this protein, it would seem unlikely that SLC35C2 has a direct role in the transport of GDP-Fuc and its effects on fucosylation need to be further investigated.

Taken together the characterization of the first plant GDP-Fuc transporter resolves an obvious omission in the transport of GDP-Fuc into the endomembrane in eukaryotes. Its identification has enabled us to survey the extent to which this transporter has been conserved between lineages and has provided a clear mechanism to confidently ascertain likely orthologues in fungi as well as other plant species.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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