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Exploration of archaeal nucleotide sugar epimerases unveils a highly promiscuous GDP-Gal4E subgroup

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PURPOSE OF THE ABSTRACT

Nucleotide sugar epimerases form a very interesting group of enzymes, as they can invert the configuration of a specific hydroxyl group through a single reaction and without prior activation or protection steps. Within this group, UDP-galactose 4- epimerase (Gal4E, EC 5.1.3.2) is by far one of the best studied members due to its essential role in the Leloir pathway in which it interconverts UDP-galactose and UDP-glucose. Gal4E deficiency is responsible for galactosemia, a hereditary disease, highlighting its vital importance. Although Gal4E was widely studied throughout all domains of life, ranging from eukaryotes to archaea, its biochemical characterization was often limited to UDP-hexoses, neglecting the possibility that Gal4E might be promiscuous towards other NDP-sugars and derivatives thereof. In this study, we identified a novel Gal4E displaying an unprecedented specificity on guanosine diphosphate (GDP) sugars. Indeed, a detailed biochemical investigation performed on Gal4E from Pyrococcus horikoshii (phGal4E_1) revealed that it is a GDP-sugar 4-epimerase. In addition, we confirmed that it accepts a variety of other NDP-sugars including L-sugars moieties, such as GDP-L-Gal/Glc as well as their 6-deoxysugars counterparts GDP-L-fucose and GDP-L-quinovose, respectively.

FIGURES

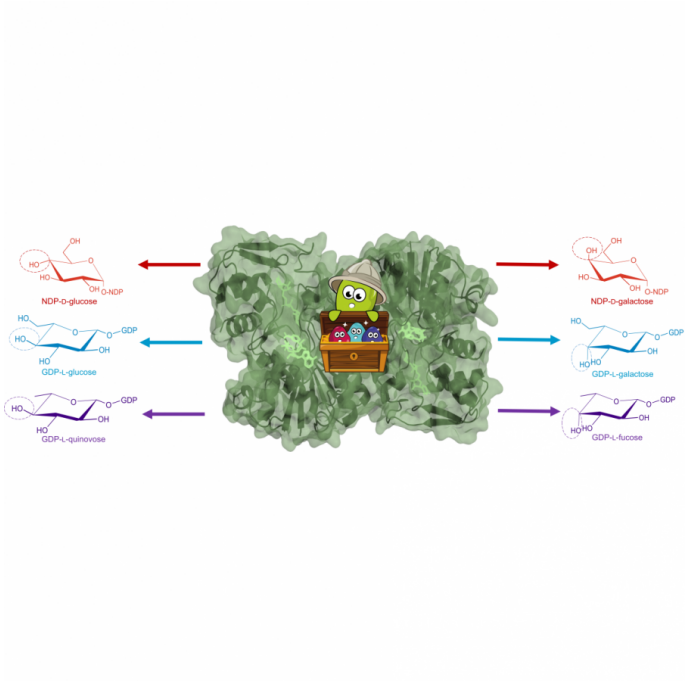

FIGURE 1

PhGal4E_1 Archaeal epimerase

Promiscuity of phGal4E_1 towards different NDP-sugars including L-sugar and deoxy-sugar moieties

FIGURE 2

KEYWORDS

Promiscuity | Epimerases | NDP-sugar | Enzyme discovery

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