Biochemical and Biophysical Research Communications xxx (2016) 1–6

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Gallus gallus orthologous to human alpha-dystroglycanopathies candidate genes: Gene expression and characterization during chicken embryogenesis

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ARTICLE INFO

Article history:
Received 22 July 2016
Accepted 4 August 2016
Available online xxx

Keywords:
POMT1
Dystroglycanopathies
Chicken
Walker-Warburg syndrome

ABSTRACT

Alpha-dystroglycanopathies are a heterogenic group of human rare diseases that have in common defects of α-dystroglycan O-glycosylation. These congenital disorders share common features as muscular dystrophy, malformations on central nervous system and more rarely altered ocular development, as well as mutations on a set of candidate genes involved on those syndromes. Severity of the syndromes is variable, appearing Walker-Warburg as the most severe where mutations at protein O-mannosyl transferases POMT1 and POMT2 genes are frequently described. When studying the lack of MmPomt1 in mouse embryonic development, as a murine model of Walker-Warburg syndrome, MmPomt1 null phenotype was lethal because Reitchert's membrane fails during embryonic development. Here, we report gene expression from *Gallus gallus* orthologous genes to human candidates on alpha-dystroglycanopathies *POMT1*, *POMT2*, *POMGnT1*, *FKTN*, *FKRP* and *LARGE*, making special emphasis in expression and localization of GgPomt1. Results obtained by quantitative RT-PCR, western-blot and immunochemistry revealed close gene expression patterns among human and chicken at key tissues affected during development when suffering an alpha-dystroglycanopathy, leading us to stand chicken as a useful animal model for molecular characterization of glycosyltransferases involved in the O-glycosylation of α-Dystroglycan and its role in embryonic development.

1. Introduction

O-Mannosylation of proteins is a post-translational modification that is performed in the endoplasmic reticulum and is catalysed by a family of highly conserved proteins known as o-mannosyl transferases. Those proteins are responsible of the transfer of mannose from doliquil-P-mannose to serine and threonine residues of target proteins. Further elongation of the glycan occurs in the Golgi apparatus by the successive transfer of additional sugar residues from nucleotide-activated sugar donors [1]. One of the main targets of mannosylation is α-dystroglycan (α-DG), which is a key component of muscle cell and neurons membrane being part of the glycoprotein complex binding to dystrophin [2]. Dystroglycan is a single gene product (DAG1) that is processed into two subunits: β-dystroglycan that is a transmembrane protein that interacts with dystrophin in the cytoplasm, and α-dystroglycan, which is a soluble secreted glycoprotein that interacts with both β-dystroglycan and multiple components of the extracellular matrix. O-glycosylation of α-dystroglycan is essential for binding to extracellular matrix components. Over the last decade, a variety of enzymes and proteins have been implicated in the O-mannosylation pathway that,

Abbreviations: CMD, Congenital muscular dystrophy; DG, dystroglycan; DGC, Dystrophin-binding glycoprotein complex; FCMD, Fukuyama's Disease; Gg, *Gallus gallus*; Hs, *Homo sapiens*; LGMD, Limb-Girdle Muscular Dystrophy; MEB, Muscle-Eye-Brain Disease; Mm, *Mus musculus*; OMIM, Online Mendelian Inheritance in Man; ORF, open reading frame; RT-PCR, reverse transcription-polymerase chain reaction; WWS, Walker Warburg Syndrome.

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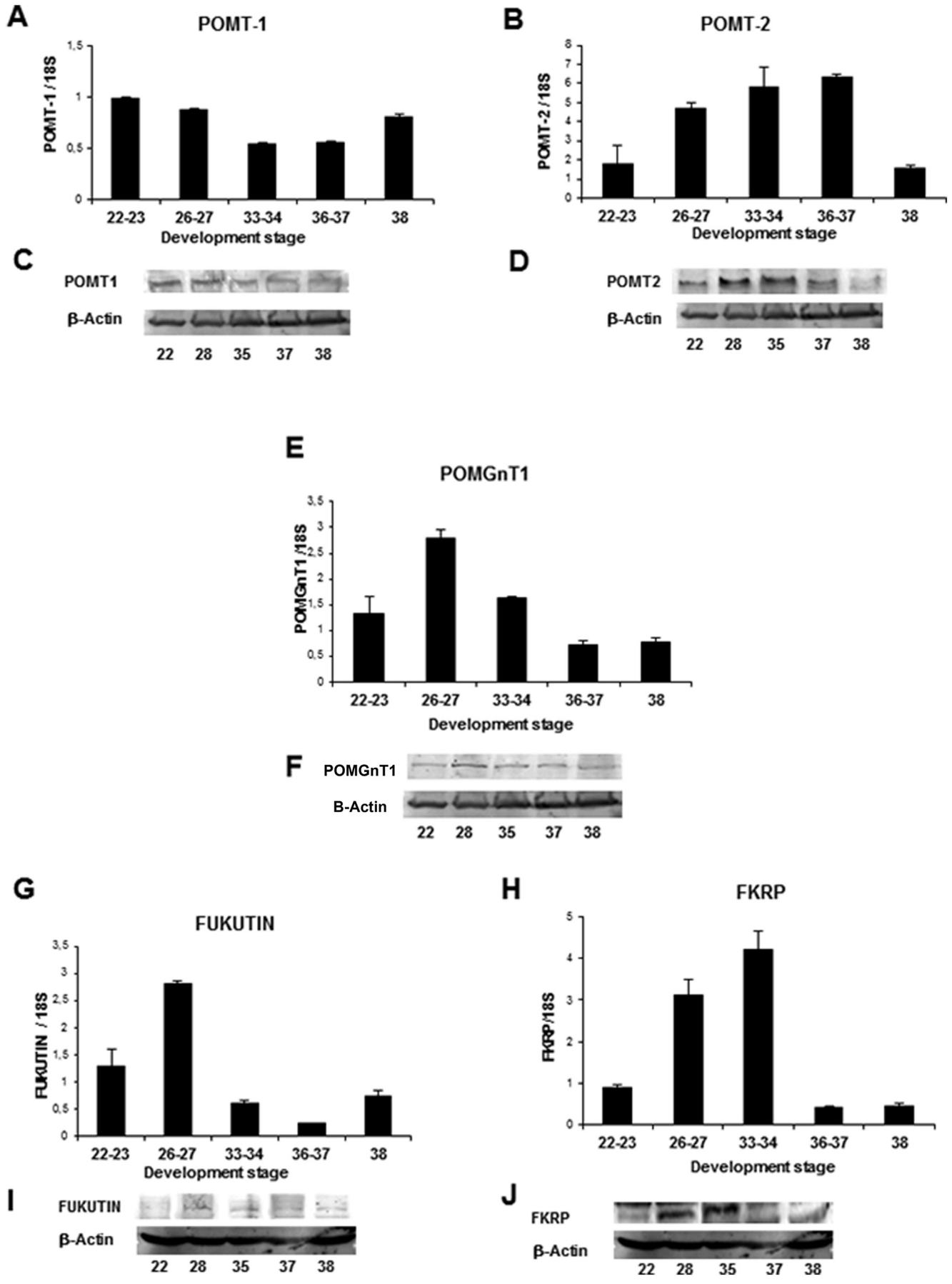
http://dx.doi.org/10.1016/j.bbrc.2016.08.027
0006-291X/



Please cite this article in press as: A. Izquierdo-Lahuerta, et al., *Gallus gallus* orthologous to human alpha-dystroglycanopathies candidate genes: Gene expression and characterization during chicken embryogenesis, Biochemical and Biophysical Research Communications (2016), http://dx.doi.org/10.1016/j.bbrc.2016.08.027