Cell endogenous activities of fukutin and FKRP coexist with TMEM5.

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Abstract
Dystroglycanopathies are a group of muscular dystrophies that are caused by abnormal glycosylation of dystroglycan; currently 18 causative genes are known. Functions of the dystroglycanopathy genes fukutin, fukutin-related protein (FKRP), and transmembrane protein 5 (TMEM5) were most recently identified; fukutin and FKRP are ribitol-phosphate transferases and TMEM5 is a ribitol xylosyltransferase. In this study, we show that fukutin, FKRP, and TMEM5 form a complex while maintaining each of their enzyme activities. Immunoprecipitation and immunofluorescence experiments demonstrated protein interactions between these 3 proteins. A protein complex consisting of endogenous fukutin and FKRP, and exogenously expressed TMEM5 exerts activities of each enzyme. Our data showed for the first time that endogenous fukutin and FKRP enzyme activities coexist with TMEM5 enzyme activity, and suggest the possibility that formation of this enzyme complex may contribute to specific and prompt biosynthesis of glycans that are required for dystroglycan function.

KEYWORDS: FKRP; Fukutin; O-mannosyl glycan; Protein complex; TMEM5; α-Dystroglycan

PMID: 29477842 DOI: 10.1016/j.bbrc.2018.02.162