Neutrophil Adhesion and Migration: Another Role of the Glucose-6-Phosphate Transporter

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Commentary

Glycogen storage disease type Ib (GSD-Ib) is caused by a deficiency in a glucose-6-phosphate transporter (G6PT) that belongs to the solute-carrier family of proteins involved in the transport of sugars and other molecules across cellular membranes. G6PT is localized to the endoplasmic reticulum (ER) and is responsible for the transport of glucose-6-phosphate (G6P) from the cytoplasm into the ER lumen, where it is hydrolyzed by the G6Pase-α (G6Pase-α) or the G6Pase-β to generate glucose-6-phosphate and ADP, respectively. The G6PT/G6Pase-α complex has been shown to be involved in the regulation of cellular energy metabolism and glucose homeostasis in the ER of neutrophils and the ER lumen serves as a critical site in protein maturation and its biochemical environment in the regulation of protein glycosylation [11].

Recent studies have shown that G6PT deficiency in neutrophils from GSD-Ib patients results in impaired glucose metabolism, impaired neutrophil energy homeostasis, and neutrophil dysfunction [12]. However, while G-CSF treatment increases both the frequency and the absolute neutrophil counts in the peripheral bloodstream [9], G-CSF cannot rescue impairment in neutrophil adhesion and migration. We also provided evidence showing that the decrease in the expression of CD11a and CD11b on neutrophils is associated with a major defect in protein glycosylation [10].

G-CSF is widely used to treat neutropenia patients including GSD-Ib and G6Pase-β deficiency [14, 15]. We have shown that G-CSF cannot correct impaired energy homeostasis in G6PT-deficient neutrophils in human GSD-Ib patients [5]. We recently showed that this growth factor also fails to rescue impaired neutrophil recruitment in G6pt-/- mice [9], highlighting the limitations of G-CSF in treating patients exhibiting neutrophil dysfunction. Understanding the functional roles of G6PT and/or G6Pase-β in neutrophils would facilitate the development of novel therapeutic approaches to address neutrophil dysfunction.

References


