CHRD 2021: Abstract & Poster Submission Form

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Research Category:

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

What was your role in the project?

- ☑ Design
- ☐ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Presenter Status:

- ○ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ◉ Non-Trainee

Title

Tafazzin deficiency impairs mitochondrial metabolism and function of lipopolysaccharide activated B lymphocytes in mice

Background

Barth Syndrome (BTHS) is a rare X-linked genetic disease of young boys. BTHS boys are susceptible to severe infections, in part due to neutropenia, but the exact mechanism is unknown. BTHS is caused by mutation in the TAFAZZIN gene which codes for the mitochondrial enzyme Tafazzin. Tafazzin is a cardiolipin remodeling enzyme required for optimal mitochondrial function. B lymphocytes are responsible for humoral immunity and play a key role in the immune response. Optimal mitochondrial function is required to support B cell activity during activation.

Objective

We examined how deficiency of tafazzin alters the metabolic activity of B cells and their response to activation by lipopolysaccharide in mice.

Methods

B cells were isolated from 3-month-old wild type or tafazzin knockdown mice and incubated for up to 72 h with lipopolysaccharide and cell proliferation, expression of cell surface markers, secretion of antibodies and chemokines, proteasome and immunoproteasome activities, and metabolic function determined. In addition, proteomic analysis was performed to identify altered levels of proteins involved in survival, immunogenic, proteasomal and mitochondrial processes.

Results

Compared to wild type lipopolysaccharide activated B cells, lipopolysaccharide activated tafazzin knockdown B cells exhibited significantly reduced proliferation, lowered expression of cluster of differentiation 86 and cluster of differentiation 69 surface markers, reduced secretion of immunoglobulin M antibody, reduced secretion of keratinocytes-derived chemokine and macrophage-inflammatory protein-2, reduced proteasome and immunoproteasome activities, and reduced mitochondrial respiration and glycolysis. Proteomic analysis revealed significant alterations in key protein targets that regulate cell survival, immunogenicity, proteasomal processing and mitochondrial function consistent with the findings of the above functional studies.

Conclusion

The results indicate that the cardiolipin transacylase enzyme tafazzin plays a key role in regulating mouse B cell function and metabolic activity during activation through modulation of mitochondrial function.

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- For each author, please click "**[+] Add Item**" and provide the author's information

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