**Zinc Importer ZIP2 and the Dendritic Cell Response to *Histoplasma Capsulatum* Infection**

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Zinc influences multiple processes in the innate and adaptive immune systems. For example, during murine dendritic cell (DC) stimulation with LPS, decreased intracellular zinc potentiates upregulation of activation markers such as class II major histocompatibility complex (MHCII) and CD86. However, during DC activation following exposure to the fungus *Histoplasma capsulatum* (*Hc*), upregulation of zinc storage, zinc exporter, and zinc importer genes, including ZIP2, has been observed, making the role of zinc homeostasis in *Hc*-induced DC activation less clear.

Through the use of murine bone marrow derived dendritic cells (BMDCs), this project aimed to define the function of zinc importer ZIP2 in the DC response to *Hc* infection. Upregulation of ZIP2 may be a critical component in the DC activation process during *Hc* infection; therefore, we predicted silencing ZIP2 would alter activation patterns in DCs exposed to *Hc*.

BMDCs transfected with ZIP2 siRNA were incubated for 24 hours with heat-killed *Hc* in a BMDC:*Hc* ratio of 1:2, live *Hc* in a BMDC:*Hc* ratio of 2:1, or LPS (1μg/mL). Flow cytometry with monoclonal antibodies specific for CD40, CD80, MHCII, and CD11c was performed to assess the effects of ZIP2 silencing on DC activation. Expression of these activation markers in ZIP2 silenced BMDCs was evaluated against control BMDCs transfected with scramble RNA.

When exposed to heat-killed *Hc*, CD40 high, CD80 high, and MHCII high cell populations increased by 21.1%, 19.6%, and 40.6% respectively in ZIP2 silenced BMDCs compared to scramble RNA controls. In ZIP2 silenced BMDCs exposed to live *Hc*, CD40 high, CD80 high, and MHCII high populations increased by 12.7%, 16.7%, and 24.4% over controls. Decreased mean cell surface expression of the integrin CD11c was also observed in ZIP2 silenced BMDCs under live and heat-killed *Hc* conditions, another indicator of increased activation. ZIP2 silencing in BMDCs exposed to LPS resulted in less substantial shifts in the expression of these activation markers.

Silencing ZIP2 altered BMDC activation marker expression 24 hours after *Hc* exposure in patterns consistent with increased activation, indicating that at this specific timepoint in *Hc* infection, ZIP2 upregulation and increased zinc import may serve to temper BMDC activation.

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