BATF2, A BASIC LEUCINE ZIPPER TRANSCRIPTION FACTOR, IS REQUIRED TO CONTROL GUT PATHOLOGY DURING SCHISTOSOMIASIS

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Basic leucine zipper transcription factor ATF-like 2 (BATF2) belongs to a family of transcription factors critical in sterile and infectious inflammations. A role was first ascribed to this factor in the development of CD8+ dendritic cells, then a possible role was suggested as an inducer of type-1 inflammatory responses. More recently, this factor has been shown to inhibit immuno-pathological Th17 response during *Trypanosoma cruzi* infection through the suppression of IL-23. Given its tight association with immune polarization, this factor is increasingly suggested as a druggable target for host-directed therapies to combat infections. In the present report, a role during the most debilitating Human helminth infection, schistosomiasis, became envisageable when we noted that mice responded to the trapped eggs of the parasite by up-regulating the expression of BATF2 in the affected gut tissue.

To investigate such a possible role of BATF2 during experimental schistosomiasis, BATF2-deficient mice were used and characterized for host cellular, tissular, humoral, immunological and physiological parameters during steady state and infection with the parasitic helminth *Schistosoma mansoni* using histochemistry, flow cytometry and ELISA.

Cellularities, tissue integrity, baseline humoral responses and physiological features (weight, pain assessment) were unaffected in the absence of BATF2 under steady-state conditions. During experimental schistosomiasis, however, a severe wasting disease was apparent in BATF2-deficient mice as early as 8 weeks post-infection and culminated into premature death of all infected BATF2-deficient mice 12 weeks post-infection. Histological analyses revealed an aggravated level of intestinal fibrosis in BATF2-deficient mice when compared to littermate controls. Flow cytometric analyses combined with ELISA revealed a significant increase in CD8+ Dendritic cells, a considerable increase of pro-fibrotic Type 2, Type 17 and TGF-β-dominated responses paralleled by a reduction of Type 1 responses, consistent with the reported role of BATF2 in the mitigation of Type 17 responses and the promotion of type-1 responses.

Collectively, our data indicate that BATF2 is required by the host to control gut pathology during experimental schistosomiasis and newly propose this factor as a necessary regulator of gut pathology during schistosomiasis.