

Dissecting side-by-side *Trypanosoma cruzi*-specific and cardiac-specific B cell responses in Chagas disease

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Background

Chagas disease, caused by *Trypanosoma cruzi* parasites, is the most frequent cause of infectious cardiomyopathy in the world and the highest-impact parasitic disease in the Americas. No vaccines are available, and current medicines are toxic and limited. Historically a neglected tropical disease of the Americas, it is now spreading globally. Chagas heart disease (CHD) is an inflammatory cardiomyopathy that develops in approximately one-third of infected people. The reasons why some infected individuals develop cardiomyopathy while others remain asymptomatic for life remain largely unknown. In response to *T. cruzi* infection, and driven by poorly understood triggers, the immune system produces both antibodies against the parasite and against the host's heart tissues.

Methods

We used magnetic enrichment and novel B-cell tetramers combined with mouse models of bioluminescent *T. cruzi* infection to track, by flow cytometry and side-by-side, the development of *T. cruzi*-specific and cardiac-specific B-cell responses in spleen and heart.

Results

We observed a striking accumulation of plasma cell/plasmablast B cell subsets in the heart of *T. cruzi*-infected mice during early chronic infection. While *T. cruzi*-specific B cells gave rise to robust germinal centre responses in the spleen, cardiac-specific B-cell responses were primarily extrafollicular.

Conclusions

Our data suggest that activation of *T. cruzi*-specific and autoreactive cardiac-specific B cell responses are driven by drastically different mechanisms. Future work with our newly developed tools will allow us to identify the main drivers of pathogen vs autoreactive cardiac-specific B cell responses, as well as exploring the role of different B-cell subsets in the pathogenesis of CHD.