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POSTER PRESENTATION

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Identification of an osteoclastogenic CD4+ T cell population producing IL-17 and TNF α

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Background

Crohn's disease is an inflammatory bowel disease (IBD) characterized by an augmentation of activated T cells and a severe osteopenia due to an increased activity of osteoclasts, the bone-resorbing cells. Osteoclasts result from differentiation of monocytes under the control of two cytokines, RANK-L and M-CSF, produced by bone-forming osteoblasts. Inflammatory cytokines produced by T cells have been shown to increase osteoclastogenesis, leading to osteopenia. The aim of this study is to identify CD4+ T cells implicated in osteolysis.

Material and methods

We used a murine model of IBD associated with severe osteopenia, the IL-10^{-/-} mouse to analyze the phenotype and function of bone marrow (BM) CD4+ T cells.

Results

We showed that CD4+ T cells isolated from the BM of IL-10^{-/-} mice with IBD induced in vitro the differentiation of osteoclasts. The analysis in BM of the Th subsets present among these CD4+ T cells revealed, in addition to Th1, a population producing both TNF- α and IL-17, cytokines known to increase osteoclastogenesis. Our results showed that sorted CD4+ IL-17+ TNF α + T cells increased the production of RANK-L by osteoblasts and induce the differentiation of osteoclasts in vitro. Furthermore, this population led to the recruitment of monocytes (pre-osteoclasts) in the BM in vivo participating thereby to the increased osteoclastogenesis. Altogether, the induction of RANK-L and monocyte recruitment by CD4+ IL-17+ TNF α + T cells may represent a possible mechanism of osteolysis in vivo. Lastly, we found the CD4+ IL-17+

TNF α + population in the blood of patients with Crohn's disease, but not in controls and experiments are in progress to confirm the osteoclastogenic role of this population in human.

Conclusion

Altogether, our results showed for the first time that CD4+ IL-17+ TNF α + cells represent an osteoclastogenic T cell subset present in vivo, and potentially responsible for osteopenia in mice and Crohn's patients.

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