The presence of Dex significantly inhibited the expression of this DC marker in all cultures.

Conclusion This study demonstrates that synovial tissue macrophages have the capacity to differentiate into either functional osteoclasts or mature dendritic cells depending on the presence or absence of specific humoral factors.

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THU0039 LOCAL IL-17 GENE THERAPY ACCELERATES COLLAGEN ARTHRITIS WITH SEVERE BONE EROSION AND RANK LIGAND AND RANK EXPRESSION IN SYNOVIAL INFILTRATE AND AT BONE EROSION SITES

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Background

Objectives To examine the effects of local IL-17 application in the knee joint of type II collagen immunised mice on the induction of bone erosion.

Methods Collagen induced arthritis (CIA) was induced in male DBA-1 mice by immunising intradermally at the base of the tail with suboptimal dose of bovine type II collagen. On day 21, mice were given a booster injection (i.p.) of the same dose of type II dissolved in PBS. Just before expected onset, mice were intraarticularly (i.a.) injected into the right knee joint with 10^7 pfu of either an IL-17 expressing (AdIL-17) or control (AdControl) recombinant human type 5 adenovirus vector. Five days after the i.a. injection of the viral vector, arthritis was monitored visually and joint pathology was examined by histology. Formation of osteoclast-like cells was determined by tartrate-resistant acid phosphatase (TRAP) staining. In addition, RANKL and RANK protein expression was evaluated by specific immunohistochemistry.

Results Local IL-17 over-expression in the knee joint of type II collagen immunised mice promotes synovial inflammation. Five days after viral injection of AdIL-17, histologic analysis showed aggravation of bone erosion in the patella and femur/tibia region compared with the control vector group. Induction of bone destruction by IL-17 was accompanied with marked TRAP activity in the bone marrow and at bone erosion sites, indicating that IL-17 accelerates the formation of osteoclast-like cells. Interestingly, local IL-17 promotes local protein expression of RANKL and its receptor RANK in the synovial infiltrate and at bone erosion sites compared with the control vector group.

Conclusion These data shows that local IL-17 gene therapy during onset of collagen arthritis promotes osteoclastic bone erosion accompanied with accelerated expression of local RANKL and its receptor RANK. These findings suggest IL-17 to be a potent stimulator of osteoclastogenesis during arthritis.

THU0040 ANAEMIA OF CHRONIC DISEASE (ACD) IN A RODENT MODEL IS SIMILAR TO HUMAN ACD AND CAN BE ALLEVIATED BY ARANESP TREATMENT

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Background We previously reported that ARANESP™ alleviates ACD in a rodent model of peptidoglycan-polysaccharide polymer (PG-APS) mediated inflammation. We report here the further characterisation of this model and the effects of ARANESP™ treatment on ACD.

Objectives

Methods Immunisation of Lewis rats with PG-APS induces chronic systemic inflammation characterised by relapsing arthritis and hepatic granulomas. Associated with the inflammation is acute, severe anaemia followed by chronic, moderately severe anaemia. As previously established, a 30 μg/kg dose of ARANESP™ every 2 weeks starting day 36 normalised peripheral blood (PB) haemoglobin levels by day 64.

Results Acutely anaemic rats had greatly enhanced mean PB reticulocyte counts and greatly reduced mean RBC counts. Mean PB reticulocyte and RBC counts normalised during chronic anaemia, but RBC remained hypochromic and microcytic. Individual anaemic rats had transient increases in serum erythropoietin (EPO) concentrations. However, there was no significant difference in mean EPO concentrations compared to controls, which suggests EPO production was blunted. Histology of day 36 and day 112 anaemic rat spleen sections revealed greatly enhanced iron retention by splenic macrophages. In contrast, bone marrow (BM) macrophages were nearly devoid of iron. Serum iron concentratioans were significantly reduced by day 7 and remained low throughout the study. Interestingly, ARANESP™ treated rats showed decreased iron retention in macrophages and increased serum iron starting day 98. To identify which cytokines may contribute to the chronic anaemia of this model, peritoneal exudate cells (PEC) were isolated and challenged with PG-APS *in vitro*. Unstimulated PEC produced little or no cytokines. PG-APS challenged PEC from anaemic rats produced IL-1α, TNF-α, and IFN-γ. PG-APS challenged PEC from ARANESP™ treated anaemic rats trended towards reduced levels of these cytokines relative to anaemic PEC cultures.

Conclusion In summary, we have shown this ACD model is similar to human ACD. Importantly, ARANESP™ treatment alleviates ACD in this model, thus indicating its potential therapeutic utility for human ACD.

THU0041 DISTINCT EFFECTS OF TNFALPHA BLOCKADE FROM TNFALPHA AND LTALPHA BLOCKADE IN A PRIMATE MODEL OF SUBCUTANEOUS ABSCESS FORMATION

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Background TNFα exerts both physiologic and pathologic effects in response to infection conferring the benefit of host defense against infection at the risk of eliciting severe pathology if the response is excessive or inappropriate.

Objectives To examine whether the currently used anti-TNF therapy would affect the innate response to infections in an animal model of subcutaneous abscess formation.