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Differential expression of osteoblast related genes in mesenchymal progenitor cells induced by serum of patients with active crohn's disease with and without osteoporosis

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Introduction:

Crohn's disease (CD) is associated with a higher prevalence of osteoporosis, a complication that is increasingly recognized as a significant source of morbidity also in these patients (pts.). Predicting those individuals at high risk remains controversial, yet disease activity is thought to be one of the main contributing factors. We used primary human mesenchymal progenitor cells directed to the osteoblastic phenotype to investigate the effect of serum of seven pts. during the active phase in CD on expression of osteoblast related genes. Four of the investigated pts. had osteoporosis or osteopenia (CD-opo), three showed no obvious bone disease (CD-con).

Materials and Methods:

Mesenchymal progenitor cells obtained from a healthy patient were grown up to confluence in DMEM supplied with 10% FCS, glutamine, penicillin/streptomycin. Cells were seeded at 105/ml in 6 well plates. Supplementation was switched to 1% human serum (healthy

proband). When reaching confluence, cells were stimulated with 10 mM β -glycerolphosphate and 10 μ M ascorbic acid and human serum was changed to eight different CD sera (four CD-opo, three CD-con, one healthy control). After 3 and 14 days cell were harvested and mRNA was isolated using TRIZOL. Marker expression was determined with real-time PCR and beta-actin was used for normalization.

Results:

A clear difference in gene expression profile between sera from CD pts. and from the healthy proband was detectable. Sera from CD-opo pts. induced RANKL gene expression 100 fold compared to healthy proband and 50 fold compared to CD-con. Osterix and RUNX 2 expression increased 2 to 10 fold, respectively, by serum from all CD pts., whereas no difference was seen for alkaline phosphatase and interleukin 6. Collagen and osteocalcin gene expression seemed to be influenced without reaching significant effects.

Discussion and Conclusion:

Serum from pts. with CD induced RANKL gene expression reflecting activation of bone resorption. This induction was largest in CD-opo pts. suggesting RANKL as one of the main contributing factors in this condition. Osteoblastic transcription factors osterix and RUNX2 were also induced by inflammatory activity but did not differentiate between CD-opo and CD-con. No effect on late osteoblast differentiation markers was detectable. Our results suggest that factors in the serum of pts. with active CD lead to bone disease mediated by mesenchymal progenitor cells.

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