



<b>Title</b>	<b>Development of murine model of autoimmune thyroiditis induced with homologous mouse thyroid peroxidase</b>
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### **EM-03 Transforming growth factor-beta1 gene polymorphisms and bone turnover, bone mineral density and fracture risk in southern Chinese women**

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Genetic contributions play an important role in determining bone mineral density (BMD) and bone turnover. Transforming growth factor-beta (TGF-beta) is abundant in bone and has been implicated as an important regulator of both bone formation and resorption. A T→C polymorphism in exon 1 of the TGF-beta1 gene, which results in the substitution of proline for leucine, has recently been suggested to be associated with higher BMD. In the present study, we analyzed the relationship between TGF-beta1 polymorphism and BMD in southern Chinese women. The TC polymorphic site of TGF-beta1 gene at nucleotide position 29 was analyzed in 366 healthy southern Chinese women by direct sequencing. BMD at lumbar spine and hip region, biochemical markers of bone turnover and PTH level were measured. Among the postmenopausal women (n=239), the prevalence of fragility fractures was significantly higher in individuals with TC genotype (p<0.05). Serum alkaline phosphatase and osteocalcin as well as urine N-telopeptide excretion were significantly higher in women with TC than TT or CC genotypes (all p<0.05). Women with TC genotype had lower BMD at total hip, femoral neck and trochanteric region. However, after adjusting for age, height, weight and years since menopause, the BMD at both the hip and spine did not differ among the three genotypes. With respect to the premenopausal women (n=127), no difference was seen in the BMD at the hip or spine among the three groups. In conclusion, we observed an association between TGF-beta1 gene polymorphism and bone turnover as well as fragility fractures in postmenopausal southern Chinese women.

### **EM-04 Development of a murine model of autoimmune thyroiditis induced with homologous mouse thyroid peroxidase**

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Autoimmune Thyroid Disease (AITD) is a common condition affecting mostly female subjects. Thyroid peroxidase (TPO) is a well-characterized autoantigen in AITD. Autoantibodies and autoreactive T lymphocytes to TPO are believed to play a major role in the pathogenesis of lymphocytic thyroiditis. To understand the pathogenic mechanisms of AITD and the role of TPO, we have established a mouse model of lymphocytic thyroiditis by immunizing C57Bl/6(H-2<sup>b</sup>), CBA (H-2<sup>k</sup>) and C57Bl/6×CBA F1 mice with recombinant mTPO (rmTPO) ectodomain comprising amino acid residue 1-837 produced in E.coli. Mice were immunized with 30mg purified ectodomain in complete Freund's adjuvant. Antibodies against rmTPO were detected in the serum of all mice from week 3 onwards. Draining lymph node cells from rmTPO-immunized animals showed dose dependent proliferation to TPO stimulation. Mice sacrificed at day 50 revealed variable degree of thyroiditis with infiltration of mononuclear cells and destruction of thyroid follicles. C57Bl/6 and the F1 mice, in comparison to CBA mice, showed greater degree of thyroiditis and subnormal serum T4 levels. The degree of histological features of thyroiditis corresponded to the biochemical abnormalities of these animals but not to the anti-TPO antibody response. Immunotyping of the thyroid cellular infiltrates showed predominantly CD4<sup>+</sup> T cells and B220<sup>+</sup> B cells but scanty CD8<sup>+</sup> T cells. None of the control mice injected with the purified fusion partner developed anti-TPO antibodies and thyroiditis. Significant weight gain was exhibited in the mTPO-immunized animals, with the degree of hypothyroidism correlated strongly with the amount of weight gain, giving additional supportive evidence of thyroid dysfunction. In conclusion, a genuine mouse model of AITD induced with rmTPO was established which possessed all features of lymphocytic thyroiditis. This model will enable the study and understanding of the autoimmune process of AITD and may assist in the development of new strategies for modulating the pathogenic immune response involved in this disease.