GVD and the UPR in transgenic pR5 mice that express human tau and in mice with an A_β-plaque pathology. pR5 mice and non-transgenic littermates were analyzed at 5 weeks (pR5: n=3, non-tg: n=3), 3-4 months (pR5: n=3, non-tg: n=3), 8.5 months (pR5: n=6, non-tg: n=3), 18.5 months (pR5: n=8, non-tg: n=6), 24 months (pR5: n=5, non-tg: n=5), and 28 months (pR5: n=4, non-tg: n=2) of age. Three APPSLxPS1mut mice with an A_β-plaque pathology were analyzed at 20 months of age. Neurons that developed an advanced stage of tau hyperphosphorylation and early tau fibrillary pathology in pR5 mice displayed inclusions with the morphology of GVD, but we rarely saw GVD in neurons with mature neurofibrillary tangles or early tau hyperphosphorylation. We confirmed the GVD nature of the granulovacuolar inclusions by immunolabeling with established GVD markers. In addition, the granulovacuolar inclusions in pR5 mice were labeled with markers of the activated UPR. We did not find neurons with GVD in mice with an A_β-plaque pathology and only exceptionally in very old non-transgenic mice. These findings show that human tau transgenic mice develop GVD and suggest that GVD and the activated UPR accompany neurofibrillary tangle formation in pR5 mice.

O-10

The role of antibody receptor TSH (TRAb) and goiter size in Graves' disease patients in Padang, West Sumatra, Indonesia

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Objectives: Graves' disease is an organ-specific autoimmune disease with several clinical manifestations such as hyperthyroidism, diffuse goitre, ophtalmopathy and dermopathy. Expression of thyroid stimulating hormone (TSH) receptor on the surface of thyroid cell plays pivotal role in regulation of thyroid hormone and thyroid gland growth. Thyroid overactivity in Graves' disease were caused by increasing of antibody receptor TSH (TRAb) from stimulation of Th2, thus increased thyroid hormone production, proliferation of thyroid gland, which later became goiter. Recent studies shown that goitre size may related with severity and prognosis of Graves' patients. Aim of this study was to investigated the correlation between antibody receptor TSH (TRAb) and goitre size in Graves' disease patients.

Methods: In this cross sectional study, we studied 30 patients with Graves' disease without any history of anti-thyroid medication. Serum were collected from patients to measure TSH receptor antibody using assay method. Goitre size were measured based on WHO classification (Grade I, II and III) and ultrasonography. Data analysis were using SPSS program version 20 (SPSS.Inc)

Results: Antibody receptor TSH (TRAb) was found increased in Graves' patients with mean serum TRAb 5.6±3.7 pg/ml. Size of goitre by using WHO Classification were mostly found in grade II and III (40% dan 36.7%) while thyroid volume found less than 10 gram. From our analysis, there is no significant differences occured between level of TRAb with goitre size (p>0.05).

Conclusion: There was no significant differences between antibody receptor TSH (TRAb) value and size of goitre in Graves' disease patients, nevertheless, further studies are required to compare the role of TRAb during and after treatment with thyroid enlargement.

Keywords: Graves' disease, TRAb, goitre size

O-11

Sca-1+Lin-CD117-Mesenchymal stem/stromal cells induce the generation of novel IRF8-controlled regulatory dendritic cells through notch-RBP-J signaling

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Mesenchymal stem/stromal cells (MSCs) can influence the destiny of hematopoietic stem/progenitor cells (HSCs) and exert broadly immunomodulatory effects on immune cells. However, how MSCs regulate the differentiation of regulatory dendritic cells (regDCs) from HSCs remains incompletely understood. In this study, we show that mouse bone marrow-derived Sca-1(+)Lin(-)CD117(-) MSCs can drive HSCs to differentiate into a novel IFN regulatory factor (IRF)8-controlled regDC population (Sca(+) BM- MSC-driven DC [sBM-DCs]) when cocultured without exogenous cytokines. The Notch pathway plays a critical role in the generation of the sBM-DCs by controlling IRF8 expression in an RBP-J-dependent way. We observed a high level of H3K27me3 methylation and a low level of H3K4me3 methylation at the Irf8 promoter during sBM-DC induction. Importantly, infusion of sBM- DCs could alleviate colitis in mice with inflammatory bowel disease by inhibiting lymphocyte proliferation and increasing the numbers of CD4(+)CD25(+) regulatory T cells. Thus, these data infer a possible mechanism for the development of regDCs and further support the role of MSCs in treating immune disorders.

O-12

The neuroprotective effect of a triazine derivative in an Alzheimer's rat model

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