the information concerning characteristics of this antibody by use of synthetic chromogenic substrate assay for factor VIII and factor IX. Combined use of these assays further suggested that this antibody was directed against FXI.

【Conclusion】 In the present study we revealed that a high titer of autoantibodies which bind against FXI existed in the patient's plasma and led to complicated laboratory results.

P2-26

Strong TCR stimulation promotes the demethylation of Foxp3 CNS2 in regulatory T cells induced in vitro

（免疫学）
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Foxp3 is the master transcriptional regulator of regulatory T cells（Tregs）, and the stabilization of Foxp3 expression is regulated by the demethylation of conserved non-coding sequence 2（CNS2）in the Foxp3 locus. Recent studies have shown that TCR stimulation is required for the demethylation of Foxp3 CNS2 during Treg development. However, the relationship between the strength of TCR stimulation and the demethylation of Foxp3 CNS2 remains unclear. To address this issue, we compared the frequency of demethylation of the Foxp3 CNS2 among in vitro-induced Tregs（iTreg）that had received a range of TCR stimulation during their development. We found that the frequency of demethylation of the Foxp3 CNS2 was increased with increased TCR stimulation strength, whereas CD28 stimulation had only a limited effect. Mechanistically, the binding of Tet2, a member of the TET family of enzymes involved in DNA demethylation, on the Foxp3 CNS2 was increased by strong TCR stimulation. Furthermore, compared with iTreg induced by weak TCR stimulation, iTreg induced by strong TCR stimulation maintained Foxp3 expression both in vitro and in vivo. These data indicate that the strength of TCR stimulation is a key factor for induction of the demethylation of Foxp3 CNS2 and the generation of stable Tregs.

P2-27

Calmodulin-like skin protein suppresses hydrogen peroxide- or ultraviolet-induced increase in senescence associated beta-galactosidase in keratinocytes

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Calmodulin-like skin protein（CLSP）is a secreted peptide that is restrictedly produced in skin keratinocytes and some related epithelial cells. It has been previously shown that CLSP is recruited via blood stream into the central nervous system where it likely exerts neuroprotective effect against toxicity related to Alzheimer's disease（AD）by binding to the heterotrimeric humanin receptor and activates intracellular survival signaling. However, it remains to be elucidated whether secreted CLSP has some biological activities outside the central nervous system. In the current study, using hydrogen peroxide（H_2O_2）- and ultraviolet（UV）-induced senescence models of primarily cultured skin keratinocytes, we have addressed to the question as to whether CLSP is involved in senescence of skin keratinocytes. We first found that CLSP expression was potentiated by the treatment with H_2O_2 and the exposure to UV in keratinocytes. Furthermore, the co-incubation with recombinant CLSP reduces Senescence-associated beta-galactosidase-positivity in keratinocytes that is induced by the treatment with H_2O_2 and the exposure to UV. These results suggest that CLSP may function as a senescence-suppressing factor for keratinocytes.