1. No.
   2019G014

2. Title
   Translational approach toward clinical application of immune modulators via action on alpha7nAChR

3. Period
   2019-2021

4. Summary

The promotion of mouse CD4+ T cell proliferation and differentiation into (regulatory T cells) Tregs by the α7nAChR agonist GTS-21 indicates that GTS-21 helps collect sufficient numbers of Tregs or chimeric antigen receptor T cells for adoptive immunotherapy and cancer treatments. In 2019, we investigated the effects of GTS-21 on gene expression of the α7nAChR subunit (*CHRNA7*) and mutated dup α7 subunit (*CHRFAM7A*) in human T cell line CCRF-CEM and MOLT-3 cells and normal human peripheral blood CD4+ T cells using real-time PCR. GTS-21 down-regulated *CHRNA7* expression but did not affect cell proliferation. *CHRFAM7A* expression was not modulated by GTS-21. In 2020, the effects of GTS-21 on cell proliferation and Tregs differentiation were studied in human $CD4^+$ T cells activated with Dynabeads (Human T-Activator CD3/CD28). GTS-21 promoted stably the proliferation of $CD4^+$ T cells, but the cell count on Day 7 was not statistically significantly higher than that of the control. GTS-21 upregulated the differentiation into Tregs. In 2021, we investigated the effects of GTS-21 on the proliferation in Dynabeads-activated human $CD4^+$ T cells cultured for 9 days. GTS-21 promoted proliferation and the cell number increased 5-fold on Day 9. Expression of α7nAChR on the surface of human $CD4^+$ T cell membranes was detected throughout the 9-day experimental period using a specific monoclonal antibody against the α7nAChR protein and immunofluorescence. These findings suggest that GTS-21 is useful for collecting large numbers of CD4+ T cells in adoptive immunotherapy.