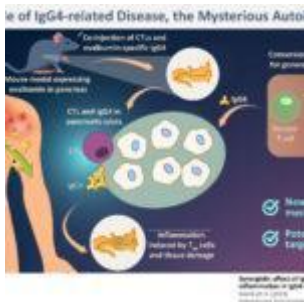


# Solving the puzzle of IgG4-related disease, the elusive autoimmune



Autoimmune diseases are a medical conundrum, where the very system designed to protect you, starts attacking your cells and/or organs. Often the cause for this spontaneous dysfunction is not clear. As a result treatment of these diseases is challenging.

IgG4-related disease (IgG4-RD), a recently discovered autoimmune disease, is characterised by the infiltration of lymphocytes including plasma cells that secrete IgG4 and cause irreversible tissue damage. Most patients with IgG4-RD, tend to have higher blood levels of IgG4 than healthy individuals. In addition to IgG4, cytotoxic T lymphocytes (CTLs) have been shown to play a key role in the disease mechanism. Specifically, an abundance of CTLs and IgG4 have been detected in tissue damaged pancreas of IgG4-RD patients.

In a new study published in *International Immunology*, a team of scientists lead by Prof. Masato Kubo, “planned to explore how IgG4 Abs contributes to the CTL-mediated pancreas tissue damage in IgG4-RD, and also to evaluate the pathogenic function of human IgG4 Abs using the mouse model that we have established.” The latter is especially important, as IgG4 is not naturally present in mice, meaning that there is a severe lack of adequate animal models to explore this disease.

Using murine models of IgG4-RD they were able to show that, IgG4 was not the causative factor of the autoimmune diseases. Specifically, they showed that injecting antigen-specific IgG4 that target antigens in the pancreases, did not cause IgG4-RD in the pancreas. However, when they injected IgG4 in combination with CTLs, they observed pancreatic tissue damage and inflammation. Suggesting that the combination of IgG4 and CTLs is responsible for IgG-RD. Further probing by the researchers, showed the T follicular helper ( $T_{FH}$ ) cells also contribute to pathology by secreting self-reactive Abs. Further, they showed that blocking  $T_{FH}$  cell development by targeting the JAK-STAT cellular signalling pathway, reduces pathology. Indicating a potential therapeutic intervention of IgG-RD. These proposed therapeutic targets need further exploration, but once developed, they have the potential to improve the lives of millions of patients with IgG4-RD worldwide.

Journal Article: Sasaki et al., 2019. [Synergistic effect of IgG4 antibody and CTLs causes tissue inflammation in IgG4-related disease.](#) *International Immunology*

*Article provided by Indrani Das, summarised by Cheleka Mpande*

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With a mission of "Creating science and technology for the

harmonious development of nature, human beings, and society”, TUS has undertaken a wide range of research from basic to applied science. TUS has embraced a multidisciplinary approach to research and undertaken intensive study in some of today’s most vital fields. TUS is a meritocracy where the best in science is recognized and nurtured. It is the only private university in Japan that has produced a Nobel Prize winner and the only private university in Asia to produce Nobel Prize winners within the natural sciences field.

### **About Professor Masato Kubo from Tokyo University of Science**

Dr Masato Kubo is a Professor at the Tokyo University of Science. A respected and senior researcher in his field, he has more than 226 publications to his credit. He is also the corresponding author of this study. His research interests include Immunology and Allergology. He is the team leader at the Laboratory for Cytokine Regulation, RIKEN Center for Integrative Medical Sciences.

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