

## Trends in Academic Research

Miyuki Azuma

Professor, Graduate School of Medical and Dental Sciences,  
Tokyo Medical and Dental University

Member of Science Council of Japan, 23rd Term

Research Theme Implemented in FY2016:

Mechanisms of Immune Regulation in the Oral Cavity  
(Grant-in-Aid for Scientific Research (A))



When I look back on my career, it occurs to me that my research has been supported by the Grants-in-Aid for Scientific Research (Kakenhi) program for more than thirty years, ever since I completed my graduate studies in dentistry, which enabled me to apply for a grant myself—first as a clinical doctor in oral surgery, and then for the second half of that period as a researcher in basic immunology. To put it another way, it would be fair to say that I have hardly received any funding from any source *other than* Kakenhi grants. In particular, the generous funding available from Grants-in-Aid for Scientific Research (S) and for Scientific Research on Priority Areas provided vital support in 2000 when I launched my own research laboratory as the university's first professor in a new field as part of the new priority which gave more importance to graduate-level programs. This support made it possible to launch the research lab that exists today, to recruit graduate students, and to provide them with a research environment that lacks nothing (setting aside the super-small size of the lab itself for now), as well as making it possible to achieve satisfactory research results. I am deeply grateful to the Kakenhi program for all of these reasons.

My interest in immunology was initially sparked by a desire to use the power of the immune system, the body's own defenses, to defeat cancer. At that time, the main strategy in cancer immunology research focused on trying to proliferate and boost the activity of cytotoxic "killer" T cells. Researchers successfully cloned IL-2, which promotes the proliferation of these cytotoxic T cells, and it became possible to use genetically modified IL-2 in the laboratory. This breakthrough gave a massive boost to research on Lymphokine-Activated Killer cells (LAK), which are induced by IL-2, and for a while researchers in the field presented their latest papers to crowds that

overflowed into the corridors at academic conferences in Japan and around the world. Unfortunately, it was not possible to replicate the same results with LAKs in clinical trials as had been obtained in vitro, and the initial high hopes for this line of research faded away. The major lesson learned was that killer cells without antigen specificity do not reach the site of the cancer. The focus shifted toward a new approach based on inducing killer T cells with tumor antigen specificity. Identifying cancer antigen peptides and the use of dendritic cells became the mainstream of research in the field. I became aware that some molecules then thought to be adhesion molecules were able to exert strong regulatory control over the abilities of killer T cells, and since my first research on CD28-B7 molecules at the DNAX laboratory in the United States I have now spent nearly 30 years working on co-stimulatory molecules. When I first presented my findings at an academic conference immediately after returning to Japan, few people were interested in these molecules, and I remember giving my paper at a sparsely attended final session on the third day of the conference. The following year, however, workshops and symposia were organized and I was able to present my results to much wider audiences. This brought home to me for the first time from my own experience the truth that trends exist in academic research. In recent years, the manual of cancer therapy is changing again, and today researchers are focusing their attention on immune checkpoint inhibition therapy targeting negative co-stimulatory molecules like CTLA-4 and PD-1. It has become clear that in attempting to use immunity to cure cancer, eliminating negative factors from the cancer environment was more essential than increasing the activity of killer cells. In the field of immunology, researchers are now looking at various regulatory cells and regulatory molecules, including regulatory T cells. Trends exist both in the topics of individual research and within the academic field as a whole. Of course researchers whose work sparks trends deserve our praise; but a trend cannot take place unless large numbers of colleagues and competitors are also working on similar research. For a researcher, is it a good thing to follow trends? In today's world of information overload, it may sometimes be necessary to follow a trend in order to get funding. But to return to Kakenhi's fundamental aim of providing funding for research "based on the free ideas of the researcher," it is also important to provide support for researchers who are not afraid to step aside from the trends and work steadily on completing research in the areas that truly interest them.

Until March this year, I had the opportunity to take part in the selection and evaluation of the Kakenhi screening committee members, and was also involved in the ongoing reforms of the Kakenhi system as a program officer at the Japan Society for the Promotion of Science's Research Center for Science Systems. This was a valuable experience for me, allowing me to consider funding from a new perspective. Until then, I had always been a recipient of funding. Reforming the screening system is a key part of the Kakenhi 2018 reforms. But even if an ideal system is put in place, these reforms will not succeed without fair and appropriate screening and fair and appropriate peer review and collegial screening by members of the screening committee. One concern in the past has been the lack of time given to researchers who are appointed to evaluate written applications as screening committee members. Faced with a huge volume of application materials sent to them at the end of the fiscal year, the pressure of time meant that many committee members struggled just to complete their evaluations in time. In the future committee members will be called on to review proposals in an even wider sphere of fields, and this will require even higher levels of competency and expertise. Also, in the overall screening and two-stage written screening, each member's evaluations will be visible to other committee members. This will require more responsible judgments from committee members. Screening committee members perform a hugely important task. My hope is that screening and evaluation for Kakenhi grants will continue to be carried out without being unduly influenced by the latest trends.