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The Kakenhi Goddess at Long Last Smiled upon Me



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Looking up my history of receiving grants on the database of the Grants-in-Aid program, I found myself listed as having been selected as the representative of 15 grant-supported research projects. Virtually all of them had been on or after 1997. Twenty-five years had elapsed since the time I obtained a post of research associate in the medical department of Nagasaki University to the end of my research career upon appointment as president of the university in 2008. Going back to 1978 when, aspiring to do basic medical research, I knocked on the door of Prof. Nakao Ishida's lab in the graduate school of Tohoku University, I had been engaged in research for some 30 years. Amidst them, I had only benefited from the receipt of Grants-in-Aid for the last ten years or for far less than half of my overall research career.

Prof. Ishida's method of instruction in the graduate program allowed for a great degree of freedom and individuality in conducting our research. Under it, I was able to enjoy carrying out a variety of experiments in directions that my own interests took me. Starting with the structural elucidation of antibiotics, these investigations straddled a wide range of research domains, encompassing bacteriology, immunology and virology. At the time, Prof. Ishida's lab was a large one, having nearly 50 members. Able to secure plentiful external funding, the lab offered me an environment in which I was blessed not to have to worry about getting money for doing my research.

Earning my doctorate, I returned to my alma mater, Nagasaki University. After lying low for a year working as a ship's doctor, I was hired as a research associate in the bacteriology lab of the university's medical department. This is when my life of belt-tightening austerity began. To give one example, I reused over and over again disposable plastic items such as the chips for Pipettman® (devices for measuring small amounts of liquids) and petridishes for cell cultures. Other than its basic operating budget, the lab did not have any surplus research funding. Using an array of approaches, I applied every year for Grants-in-Aid, mainly under the Encouragement of Scientists and General Scientific Research categories, but to no avail. After having my research that amended conventional thinking on the parasitic hosts of the Epstein-Barr (EB) virus published in *Nature* in 1985 and having

returned to Japan from a stint in the US during which I successfully extracted new oncogenes through molecular cloning, I went after Grants-in-Aid with new gusto, but again to no avail. After all, I had compiled a dismal record of ten straight losses and no wins in my challenge to win a Grant-in-Aid. All I could do was console myself by thinking that I must have poor affinity with these grants.

It wasn't that I was just going through the motions during that time: I was devising and trying various approaches. Entering my forties, I came to the conclusion that the world had not yet recognized me as a full-fledged researcher. Not having shed my peculiar way of doing research since my graduate days, after becoming an independent researcher as a university faculty member, I took up various themes that my interest drew me to in the domain of virology, including the EB virus, HTLV (ATL virus), HIV and oncogenes. Though not great in number, I wrote what I considered to be impactful papers on these themes. They managed to evoke puzzlement in others as to what my specialization actually was. Therefore, I decided to perch myself upon one theme, and chose as my life's work *prions*—an infectious factor in a chain of infectious neurodegenerative disorders including scrapie in sheep and Creutzfeldt-Jakob disease in humans.

Dr. Stanley B. Prusiner in the US advocated a prion concept (hypothesis) in 1982. It was a pathogen comprising only one protein without nucleic acid (abnormal prion protein: structural isomer of normal protein). I felt that there was sufficient value in the research elucidating the nature of prion pathogens to make it my own life's work, which I embarked upon in earnest in 1990.

The wind finally caught my sails in 1996, when I published a paper in the April issue of *Nature* on the occurrence of cerebellar neurodegeneration in knockout mice with loss of normal prion protein, which were developed jointly with Dr. Tetsuo Noda of the Cancer Institute. Coincidentally, just before that it had been shown that humans could be infected via food with prion disease (BSE) of cattles, which was then rife in the UK. The outbreak of this new infectious disease caused uneasiness about food safety, thrusting society into a sort of panic. In the midst of it, our research revealed the functional loss of normal prion protein to be a component of prion disease pathology, receiving wide media coverage. Thereafter, my lot in applying for Grants-in-Aid took an about-face, with a string of successes that continued without gaps for over a decade. These grants coupled with other external funding allowed me to straightaway expand the breadth and scope of my research. Among these research initiatives, there were several that yielded and disseminated to the world major scientific results.

Looking back, it was after a long but thwarted romance with the goddess of Grants-in-Aid that, after a decade and a half of anguish and trial and error, she finally smiled upon me. I now see this period as having been instrumental in solidifying me as a researcher. Indeed, I was steeled by my experience with Grants-in-Aid.

In April 2007, I was hired as a senior program officer of the Research Center for Science Systems in the Japan Society for the Promotion of Science (JSPS). A major function of the Center is creating systems for selecting and distributing Grants-in-Aid. While desiring to participate in this process, I had another, more personal reason for accepting the position: I wanted to see what it was about the system that had caused me to be rejected ten times in a row for a grant. Now on the inside, I was very impressed with the tremendous energy expended in the grant-screening process and great effort taken to be fair and impartial in carrying it out. Each year, every some 100,000 applications are document reviewed by four or six specialists in the respective field, who screen and score the applications. They are also obligated to provide comments with regard to their scoring. When lopsidedness is found in the scoring results, a statistical process is even used to correct it. Those applications short-listed in the document review are then referred to a panel review, with applicants for large grants receiving hearings, before the final selections are made. I doubt whether there is another grant-selection system of the same large scale and high degree of fairness anywhere else in the world. In order to be selected under it, one is required to explain his research in a manner that would convince a majority of researchers in his field that his research is both meaningful and of high future potential. Now I could see: The reason I had suffered so many rejections in the past was that my manner of writing applications was immature, lacking the power to persuade a majority of my peers. My question had been answered.