For the people, by the people

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As a clinician, it is somewhat awkward to talk about one's own research career. Since advancements of molecular biology, which created an environment where scientists without medical background can conduct research with serious medical implications, we have entered an era in which patient care and research are two completely separate disciplines of medicine. Investigation in medical science used to be conducted by clinicians who confront clinical problems in their practice. As a matter of fact, at the time I graduated from my medical school, we were still advised to receive clinical training, even if one intended to pursue basic science in medicine. Currently, the majority of medical research is conducted by non-MD scientists. It is generally believed that, in the rapid paced society, attending medical school, let alone clinical training, could be "a waste of time." Even in Japan where MDs still occupy a relatively high percentage among researchers in medicine, very few clinicians play a significant role in the leading sciences. At famous academic universities in Japan, where achievements in research are considered to be the main selection criteria for chairmanship/professorship, clinicians are becoming an endangered species among chairmen and professors. Therefore, I can only conclude that I have been extremely lucky to secure sufficient funding to carry out my projects despite of my persistence to being a clinician throughout my life.

I have been practicing medicine both in Japan and the US. More accurately, I thus far practiced medicine 80% in the US and 20% in Japan. As a matter of fact, before I moved my research base to Niigata from California in 1996, I conducted my research project entirely in the US. Accordingly, my first encounter to research funding systems was those of public research grants in the US. There are three main public organizations for scientific research funding in the US, namely, NIH, VA and NSF. In the past, scientists who had attained this "triple crown" were regarded as the top researchers in their fields. As the NSF had halted its support for medical research at the time I was active in the US, it was considered a badge of honor as a researcher to have received the

“double crown” of the NIH R01 and the VA Merit Review. I was extremely fortunate to have had this honor bestowed upon me across a period of many years.

I originally moved to the US to receive clinical training. Naturally, I stayed as a faculty member of University of California to practice and teach clinical medicine. Therefore, research had always been a “side job” for me. I could work on my research project far into the night, only after having taken care of patients with interns, residents, and fellows. Nevertheless, the US government consistently funded my research recognizing the importance of the projects I proposed. This fact not only made me realize that I was extremely fortunate, but also that the US possesses an inherent strength within its society. The field of my research is the one which is now known as magnetic resonance imaging, or MRI. To think that the word MRI did not even exist back then makes me realize just how much time has passed.

The reason I moved my research base to Japan in 1996 was to develop higher field MRI technology. The ultimate goal of my research is to elucidate how the brain works. I have been chasing functionality of water molecular dynamics in its relationship to consciousness since the age of 23. Since the target is human brain function, one eventually has to study humans directly, although molecular and animal studies are also necessary. This implies that one must rely on the clinical practice of neurological patients and non-invasive methods in the investigation of brain functionality. When my laboratory started our investigation with electroencephalography (EEG), my engineering colleagues teased me by saying “how the computer works cannot be understood by your placing electrodes on the outside of the chassis.” However, once we successfully developed functional MRI (fMRI), everybody jumped on the technique. To achieve the next step of sophistication, it was necessary to develop a higher field MRI for use in humans.

Developing new devices and technologies require a tremendous amount of money. Although the level of funding we required was commonplace in physics or engineering, it was unprecedented in the field of medicine. It cost100 million yen to obtain results equivalent to those that a DNA researcher could attain for 1 million yen. This was due to the fact that the components required cost tens of millions each. Although one could argue that our project was a sound investment if one realizes that firing a single missile would see 1 billion yen go up in smoke, doing so would be of no help at all in our case. Despite these circumstances, however, the research support provided by the Ministry of Education, Science and Culture (currently the Ministry of Education, Culture, Sports, Science and Technology) was outstanding. Firstly, in fiscal year of 1997, I was selected to be a leader of the first Center of Excellence (COE) Program. Again, I can only

conclude that I was extremely lucky. I am so grateful that my senior scientists recognized the importance of my proposed research project. My research was subsequently funded by Grants-in-aid for Scientific Research (Kakenhi) on numerous occasions, including Specially Promoted Research, Scientific Research (S), Scientific Research (A), and so on.

Even when the objective of the research at hand is the analysis of cerebral function, technological innovations in non-invasive imaging methods can be directly applied to clinical practice. Much of the technology now used in the 3T (Tesla) MRI model, which has become the primary clinical apparatus of its type around the world, and the 7T (Tesla) MRI, which is widely used as an ultra-high field MRI device, was developed in Japan by our team. However, few people are aware of this fact. Machines and technologies only see the light of day once these new devices and applications have been marketed and disseminated to the public by vendors. At the time we commenced our research, Japanese MRI vendors lacked the capability required to develop high-field MRI devices, and, hence, we ultimately embarked on a joint research project with GE. As a US company, GE could not emphasize the fact that its products were developed primarily at a Japanese university, and likewise, the Japanese government could not proactively promote a US company. Although globalization is now complete and internationalization is proclaimed as a virtue across all walks of life, there is still a gap between principle and practice. Despite this, as an old-school academic physician, whose objective is to contribute to clinical practice, seeing something I developed being utilized in clinical medicine around the world is a true badge of honor, far greater than having several hundred papers published.

Most elements in the relationship between water molecules and consciousness, which has comprised my life's work, and the fundamental "Vortex Theory of the Brain" on which this is based, have now been proven. Nevertheless, these principles are not yet widely understood in the current scientific world, which is dominated by linear neuroscience. Conversely, however, the relationship between excretion of β-amyloid through glymphatic fluid flow and Alzheimer disease (AD), which was proposed as part of this research, is becoming the global standard in AD investigation. We also successfully developed a drug to stimulate aquaporin-4, the water channel in the brain that plays a primary role in regulating this process. Conducting clinical trials of this drug as a means of preventing and treating AD looks set to become the final research topic of my career, having passed 65 years of age and being shunted into the role of Professor Emeritus. Although there is the opinion that collaboration with a pharmaceutical company would be quicker than Kakenhi, considering the principles

involved, it would certainly be desirable to complete the project with public funding. As was the case in MRI development, joint research projects with corporations, which place priority on monetary gain, inevitably lead to conflict of interest. If not careful, a certain well-known US university may actually work to hinder a researcher's progress rather than helping, while taking most of the credit, as occurred when I was developing MRI technology.

Kakenhi is an investment in academia. Just as economic investment has become extremely difficult in an increasingly complex global society, the task of determining how to make effective investment in academia is a daunting one. Nevertheless, conducting healthy investment is an issue of critical importance for the survival of Japan, which prides itself as a scientific nation. In a globalized world, only countries that successfully adapt their operating methods to match this increasing complexity, such as the US, will survive. This is a world led by people who, rather than trying to solve visible problems, appropriately identify the order parameters that have the greatest impact on the system as a whole. Unless the policy regarding Kakenhi is overseen by leaders who possess a clear and overarching vision for the future that is not swayed by temporary trends, the effective structural reform of Kakenhi will not be achieved. Upon returning to Japan, I found that, just as in the US, the Japanese scientific community is full of people with a future vision. I have been able to lead my career because of them. However, from around the start of the 21st century the Japanese scientific community has gradually begun to crumble. It may simply be illusion due to my aging eyes. But looking at Japan's current scientific policies, I cannot take an optimistic outlook. It seems to me as though everyone is chasing short-term profits. I have raised my voice in distress at these circumstances on several occasions. Nevertheless, time and time again my message has been drowned out by a chorus of jeers. Ominously, Japanese medical research is increasingly losing sight of the most important principle: above all do no harm. The "academic achievements" are advertently affecting not only medical science, but also clinical medicine. While everybody is preoccupied with who wins the "so-and-so prize", the beautiful country of Japan is beginning to lose sight of what is most important: the values that it has held dear over the years. The role of science is to help people. And the role of medicine is, naturally, to help patients. I believe that Japan's future hinges on how it can avoid the ignorance of the mob and find a sound leader capable of taking a holistic outlook.