Voice Series: Interview with Prof. Kwang Soo Kim, Harvard Medical School

Published Online: January 13 2021

Phei Er Saw
Executive Editor of BIOI

Foreword

Prof. Kwang-Soo Kim, has over 30 years’ experience investigating the molecular and developmental neurobiology of the midbrain dopamine neuronal system in health and disease, focusing on elucidating the transcriptional mechanisms underlying the development and maintenance of dopamine neurons. Prof. Kim’s lab focuses on the biological study of brain cells that rely on the brain chemical dopamine to communicate. Major brain disorders such as Parkinson’s disease (PD), attention deficit hyperactive disorder (ADHD), and schizophrenia are related to abnormalities affecting these dopamine secreting cells.

PD is one of the most common neurodegenerative disorders, affecting 6–10 million patients worldwide. At present, all available treatments are only symptomatic and there is no treatment that can slow down or stop the disease’s progress. Based on basic transcriptional studies of midbrain dopamine neurons, Prof. Kim identified the orphan nuclear receptor Nurr1 as a potential drug target of PD and has been working to develop neuroprotective and mechanism-based therapeutics. In addition, since relocating to McLean Hospital/Harvard Medical School two decades ago, Prof. Kim has been investigating cell replacement therapy for PD. Recently, Prof. Kim and his collaborators’ breakthrough in personalized PD treatment was highlighted in a press release. In a recent issue of the New England Journal of Medicine, Prof. Kim published a Brief Report of the reprogramming of a patient’s own skin cells to replace brain cells that are progressively lost during PD, establishing the technical feasibility of the approach [1]. In this interview, we learn first-hand of Prof. Kim’s exciting new discoveries in PD treatments using a patient’s own cells.

BIO Integration: Thank you Prof. Kim for being so gracious in accepting the invitation of BIOI to being interviewed. First of all, congratulations on your exciting report “World’s First Personalized Treatment for Parkinson Disease”. This has indeed sparked hope that we can dream of the impossible and work hard to achieve it. Could you please tell us a little bit of background how this whole idea started?

KS Kim: As you kindly introduced, I started my research on dopaminergic neurons as a junior faculty in 1989 (hard to believe that it is already more than 30 years ago). I learned that age-dependent loss of these neurons is the major cause of PD. Since the loss of a single cell type (dopamine neurons) causes PD, I became interested in the possibility of cell replacement therapy. So, I started this line of research in 1999 when I relocated to my present laboratory. In 2006, Professor Yamanaka in Japan published an exciting study showing that somatic cells can be reprogrammed all the way back to early embryo-like stem cells, so-called induced pluripotent stem cells (iPSCs), for which he was awarded the Nobel Prize in 2012. Since then, my stem cell research focused on personalized cell therapy for PD using iPSCs because it will allow us to use a patient’s own cells without the need to use immunosuppression.

BIO Integration: What was your major concern during the progress of this research? Did you encounter any major stumbling blocks along the way? How did you overcome these problems?

KS Kim: For any type of “first-in-human” trial, the most critical issue is whether it is absolutely safe. This is also the major issue when applying for FDA approval. In the case of iPSC-based cell therapy, the biggest concern is how you can eliminate any undifferentiated iPSC because they can form teratoma. Fortunately, we established a chemical method that eliminates undifferentiated iPSCs with great efficiency (>99.99%).

BIO Integration: Would you say that you have found the “magic bullet” of personalized PD therapy? What are the obstacles that you might face down the road?

KS Kim: I don’t think so. This is just an “n of 1” study and we cannot say that this study proved either safety or efficacy. However, this study established proof-of-concept and it is worthwhile for us to pursue further clinical trials. There are also many aspects of personalized cell therapy that need improvement and more extensive and creative studies are needed to make it feasible and affordable for many patients.

BIO Integration: From your CV, we understood that you came from molecular biology background. When did you...
KS Kim: This is a great question. I majored in Microbiology for my undergraduate degree and studied Microbial Genetics for my Master’s and PhD. I then studied molecular mechanisms of gene regulation in yeast during my postdoc training at the Massachusetts Institute of Technology. When I decided to move to the Department of Neuroscience at Cornell Medical School, many of my postdoctoral friends questioned my sanity for accepting an offer in the neuroscience field! I was able to survive this transition because my expertise in molecular biology helped me study and understand the regulatory mechanisms of dopamine neurons at the molecular levels. In order to use stem cells to generate functional dopamine neurons for cell replacement therapy I decided to start stem cell research by applying the molecular information gained from the study of dopamine neurons. Thus, I made a few stupid/brave (?) jumps in my career, but it allowed me to study a challenging disease and address exciting questions.

BIO Integration: Did you envision that your PD therapy could also be used in other neurological diseases as well?

KS Kim: It is too early to answer that question. However, once our personalized PD cell therapy becomes well established and helps many patients, I believe that the approach could be applied to other neurological diseases. As you know, many aspects of personalized cell therapy are common in many diseases, including the generation and selection of clinical grade iPSC lines and complete elimination of any remaining undifferentiated iPSCs, etc.

BIO Integration: What advice do you have for the young generation of scientists today?

KS Kim: For young students and scientists, I would like to emphasize that you first must like what you are doing. More specifically, scientists or researchers are those who ask questions (“re-search”), propose hypotheses, and then prove or disprove them through experiments. You really need to learn to enjoy all these processes. Of course, these processes are challenging and often frustrating. Still, it is crucial that you enjoy them. For me, I am fascinated by the possibility to speculate about invisible life processes and then visualize them through experiments. I am willing to pay to keep this kind of job (if I am rich enough). In reality, we get paid by having this kind of job. Isn’t it amazing? I am so grateful that I am a scientist.

BIO Integration: Do you have any advice for BIO Integration as a new journal?

KS Kim: There are already too many journals. For BIO Integration to become a very useful and important journal, it is critical to pursue unique and creative approaches. Also, as the name already indicates, it is critical to become a platform for multidisciplinary approaches to solve sophisticated issues of BIO sciences and their applications.

Reference