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On the original aspiration of researching neurodegenerative diseases—an interview with Prof. Jeffrey Kordower

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Abstract

The article is an interview with Prof. Jeffrey Kordower, the Founding Director of the ASU-Banner Neurodegenerative Disease Research Center at Arizona State University, conducted by Min Zhu of the Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, on behalf of *Aging Pathobiology and Therapeutics*.

Jeffrey Kordower, PhD

Jeffrey Kordower is the founding director of the ASU-Banner Neurodegenerative Disease Research Center and endowed chair as The Charlene and J. Orin Edson Distinguished Director at the Biodesign Institute at ASU. He has been a pioneer in the field of neural transplantation techniques and his pathbreaking investigations into the underpinnings of the neurodegenerative disease have made him a leader in the field. Kordower's interests include the study of gene and stem cell therapies, and disease pathogenesis including the morphological and molecular changes during neurodegeneration, learning and memory, and aging. He comes to ASU from the Rush University Medical Center in Chicago, where he was a faculty member for more than 30 years. (https://search.asu.edu/profile/3942692)

Min Zhu: Prof. Kordower, could you please tell us why did you choose to study neurodegenerative diseases?
Jeffrey Kordower: Well, first of all, let me thank you for the opportunity to conduct this interview with you. I'm going to enjoy it and I hope everyone enjoys the interview as well.
I really didn't choose neurodegenerative diseases, they actually chose me. When I was a graduate student, I was at the Society for Neuroscience conference, a conference with about thirty thousand attendees. I was walking around with my friend and colleague. We stumbled into a room where they were talking about brain cell transplantation, which I thought was very interesting, and there was a professor there named Don Gash who was doing transplants of vasopressin-containing cells into rats who couldn't make vasopressin and then they cured their diabetes insipidus symptoms, so they were able to drink and urinate normally. Since I was doing vasopressin analgesia at the time, I thought that was a terrific match, so I went up to him and told him I'd like to join his lab. I interviewed and I got the job, then about six months later, I walk into his office and say, "Don, I'm here, let's go do vasopressin transplants", and he says, "no, our lab is now Parkinson's disease lab, and you're the monkey guy". It was that situation that led me to study nerve degenerative diseases, and I couldn't be happier because it's thrilling to serve a community of people who desperately need science to improve their lives. So, it was a lucky shift, but one that I'm always grateful for because my lab and my life would have been very different if Don Gash's group hadn't switched the set-

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ting to Parkinson's disease, and that's how I got interested in neurodegenerative research.

Min Zhu: It can be difficult for a researcher to change the main topic of their research. I know that you had been studying on fetal transplantation for many years and then you shifted your research to Parkinson's disease (PD). What do you think was the most difficult thing about changing your research topics?

Jeffrey Kordower: The research focus didn't change because I'm still doing stem cell transplants while we don't do fetal transplants for a variety of reasons, one of which is that getting a large number of fetal tissues is difficult, especially since the way abortions take place, we used to do suction abortions so we could dissect the fetuses but now it's medical abortions, which are much more difficult. But now, thanks to the discovery of stem cells, we can drive the production of fetal cells from blood, which is what we do currently: we collect blood from humans and then treat it with substances that convert the blood cells back into embryonic stem cells, and then we treat them coming forward for Parkinson's disease to make him dopamine stem cells, and so we've been studying stem cells for the last five to ten years now. We are able to get them to act just like fetal cells, they survive beautifully in the brains of animals, and they innovate, and it's really the innovation that's critical. They restore function in lesioned animals, and because of all of this, and because they're also very safe, we're now planning our first clinical trial in which we'll be grafting stem cells induced pluripotent stem cells into patients with Parkinson's disease, and we're starting with a specific group of patients who have a mutation called parkin because those Parkinson's patients have pure dopamine cell loss, and so we think that they're the best population to test our initial trials.

Min Zhu: Currently your research is still focused on treatments for Parkinson's disease, so except for the stem cell therapies you mentioned before, can you share with us the new findings of your team in PD treatment in the past 5 years?

Jeffrey Kordower: Using stem cell transplants to treat Parkinson's disease is only addressing the symptoms. What we want to do is to stop the progression of the disease. Parkinson's disease is caused by a misfolding of a naturally occurring protein called alpha-synuclein, and so we're using cellular antibodies to take pathological alpha-synuclein, have it bound to these antibodies, and have it cleared, so it doesn't spread around the brain and cause significant disability. So, this is a gene therapy approach that we're using to try to get at the very nidus of the pathology and prevent the Parkinson's disease brain from degenerating.

Min Zhu: You and your team have done a lot of work on PD research. Could you please tell me about your research priorities and your desired goals?

Jeffrey Kordower: We want to first continue the very successful studies, but I think where I want to start moving now is looking at aspects of cognition in neurodegenerative diseases, so looking at Parkinson's dementia, looking at Lewy body disease, and also looking at Alzheimer's models. Along with my colleague John Morrision, we have created of a novel rhesus monkey model of Alzheimer's disease. We first have to work on creating and validating these new models and then we're using experimental therapeutics to try and prevent the progression of the disease in these models and animals, and then hopefully we'll start clinical trials soon to see if we can stop the onset of dementia and cognitive decline in patients with neurodegenerative diseases because these are symptoms that really don't have any therapy at the moment.

Min Zhu: (Follow up) How many years do you think it will take us to transfer these therapies to humans?

Jeffrey Kordower: Certainly, stem cells and alpha-Synuclein reducing gene therapies are now in clinical trials for different companies, and I think our specific therapies will be in clinical trials within three to five years.

Min Zhu: If you were a new or a junior researcher to study neurodegenerative diseases, which specific areas would you like to study?

Jeffrey Kordower: Well, there are two more going back. I think that studying cognition diseases is quite important; I think that a young scientist would have many areas to work in, and there is a big window for non-incremental progress. When we study motor Parkinson's disease, we already have a variety of good therapies, so the potential for major improvement is limited. However, the potential for improvement in diseases of cognition is large, so that is one area I would focus on. There are also rare diseases that require intensive research, such as Huntington's disease, which is a genetic disorder that causes motor impairment and cognitive dysfunction, as well as multiple system atrophy, which is a rare disease that initially resembles Parkinson's but is much more aggressive and causes much more disability, and patients usually live between seven to nine years after diagnosis, whereas patients with Parkinson's disease live a normal lifespan. So, these are areas where young people have a great opportunity to make important contributions, and we welcome them to the club in the hope that we can all work together to treat and cure these diseases.

Min Zhu: Some people's research follows hot points and can result in achievements and honors quickly, while others focus on one point to study and it may take a long time to produce results. What do you think about this phenomenon?

Jeffrey Kordower: Well, you have to understand the practicality of science because everyone wants to make significant progress as soon as possible. I'm not sure what we look for, I don't really look for achievements or honors, I look to help people, and I believe that if you help people, the achievements and honors will follow. So, what I focus on is helping individuals with neurodegenerative diseases. I'm also starting to focus more on helping their caregivers, because the stress on caregivers is incredibly high, and it needs to be addressed so caregivers aren't so stressed when caring for their loved ones. Also, we need to train graduate

students as well as undergraduate students to get them into the field because I'm not going to be around forever. These are the three main missions of my center, the neurodegenerative disease research center, and that's the path that I've followed.

Min Zhu: Yes, it's important to help people, but not the achievements and honors. I watched your previous interviews and lectures, and it gave me the impression that you are a confident and sincere scientist. I believe that most young scientists, including myself, aspire to be like you. So, do you have any advice for young researchers?

Jeffrey Kordower: Sure, I think you should collaborate with experts who have demonstrated excellence in their field so that you may learn from their science. You should always be honest in your scientific approach so that you are confident in your findings. Because science is essentially self-correcting, if you make a mistake or fail to provide all of the data honestly, it will be found out and corrected by others, because that is how science works. So, if you want to be a confident scientist, ask excellent, important questions.

Additionally, cooperate and colleaborate with others to answer them in the best way possible, and then publish your findings as quickly and concisely as possible as well.

Min Zhu: Thank you, that's all the questions today. Thank you, Prof. Kordower. Thank you so much!

Jeffrey Kordower: All right, thank you!

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