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What exactly is it that makes Parkinson's disease *Parkinson's disease* … particularly when it is compared to similar diseases? While this is the question behind much of Parkinson's science, the Parkinson's Disease Foundation (PDF) is particularly excited about the way it is being approached in the scientific studies of Vikram Khurana, M.D., Ph.D., Instructor in Neurology at Harvard Medical School and Massachusetts General Hospital in Boston, MA.

Dr. Khurana — who is conducting his research in the laboratories of Susan Lindquist, Ph.D., and Rudolf Jaenisch, M.D., at the Whitehead Institute — is supported by the Clinician-Scientist Development Award that is jointly funded and sponsored by PDF and the American Academy of Neurology Foundation (AANF). The award was created three years ago to encourage young clinicians to pursue research or a combined clinical-and-research career in Parkinson's. Dr. Khurana will focus his award upon the task of designing an ambitious plan to "re-think the fundamental aspects of Parkinson's."

Dr. Khurana notes that a significant portion of Parkinson's research focuses on the hallmark of the disease — the build-up of a protein known as alpha-synuclein in dopamine-producing neurons in the brain. He believes that we should broaden our approach. Why? Because a similar build-up of alpha-synuclein occurs in other types of cells and in diseases other than PD.

Classic Parkinson's, along with two other Parkinson's syndromes, Dementia with Lewy Bodies (DLB) and Multiple System Atrophy (MSA) — are all marked by the accumulation of alpha-synuclein in cells in the body. In classic Parkinson's, neurons in an area of the brain called the substantia nigra are most vulnerable to alpha-synuclein's accumulation, causing the motor symptoms of Parkinson's. Alpha-synuclein can also damage neurons in the cortex, resulting in dementia. In DLB, it is these cortical neurons that are more affected than dopamine neurons. So people with DLB often experience dementia earlier on in life than those with PD. What determines the vulnerability of the different cell types in a given individual remains unknown — but synuclein is the common link.

Dr. Khurana is conducting a multi-faceted research plan to better understand why Parkinson's progresses the way it does … and how its underlying mechanisms differentiate it from other Parkinson's syndromes.

His plan begins with an intensive investigation of simple yeast cells and complex human stem cells. Research has established that the ways in which alpha-synuclein damages neurons is remarkably similar to how it damages yeast cells. So yeast cells will provide clues as to how alpha-synuclein accumulation causes cell damage. Dr. Khurana will use these clues to inform his studies in induced pluripotent stem cells (iPS cells) and make predictions about disease indicators in cells from people with classic PD, DLB and MSA.

Dr. Khurana hopes that through the study of Parkinson's disease and other Parkinson's syndromes that result from accumulations of alpha-synuclein, we can further understand the exact role of alpha-synuclein in each disease. He believes that by getting back to these basics, and understanding just what it is that makes Parkinson's *Parkinson's,* we can shed light on the course of the disease and in turn imagine new therapeutic advances "not only for the *motor* symptoms of Parkinson's, but also for its *non-motor* symptoms."

Dr. Khurana is the second recipient of the PDF-AANF Clinician-Scientist Development Award, which will be funded over the next three years in the amount of $240,000.