A novel target for treatment of Parkinson's disease

Our team have identified a male-specific factor that may underlie the sex-based bias of Parkinson's and influence development of disease in men.

This factor represents a unique target for developing therapeutics to reduce symptoms and potentially stem the progression of Parkinson's disease in male patients.

Summary

Parkinson's disease is a chronic, debilitating neurological condition, altering co-ordination and movement. It results from progressive degeneration of cells in part of the brain, the substantia nigra. These nigral cells produce dopamine, which is needed for smooth, controlled movements. The loss of these cells and resulting decreased dopamine levels causes many of the symptoms of Parkinson's disease.

The cause of Parkinson's disease is unknown, likely a combination of environmental and genetic factors. A strong risk factor is being male, with more men than women diagnosed (nearly 2:1); disease severity can also be greater in males, and these sex-based differences are also observed in animal models of Parkinson's disease. Hence, a male-specific factor may contribute to Parkinson's disease.

The Hudson Institute team has found a male-only gene called SRY (located on the Y chromosome) may underlie the sex-based bias in Parkinson's disease, and influence development of disease in men. They have found levels of SRY are abnormally high in multiple models of Parkinson's disease. In proof-of-concept studies, reducing SRY levels using antisense oligonucleotides mitigates dopamine cell loss and motor symptoms in rodent models of disease, suggesting SRY is a novel target for treatment of Parkinson's disease.

New approaches to treatment

There is no cure for Parkinson's disease, and the treatments currently available focus on reduction of symptoms. This includes supportive treatments such as physiotherapy, dopamine-regulating medication, and surgery. These treatments do not change disease progression. There are no therapeutics currently on the market that halt or reverse the brain cell death associated with Parkinson's disease.

By targeting SRY, our teams aims to reduce or halt nigral cell death and therefore reduce or prevent the worsening of motor symptoms in male patients.

Development pathway and capabilities

The team have identified SRY as a target for treatment of Parkinson's disease, and demonstrated proof-of-concept using antisense oligonucleotides specific for SRY. The laboratory has access to "gold standard" research models for appropriate testing. Alongside continuation of the antisense oligonucleotide program, they seek to explore opportunities for investment or collaboration to identify or develop a small molecule inhibitor to reduce SRY levels.

The team have developed a range of in vitro cell-based assays for the assessment of SRY modulation, as well as in vivo rodent models of toxin-induced Parkinson's disease representing both acute and chronic disease.

Team

Driving this project are Professor Vincent Harley and Dr Joohyung Lee. This partnership combines Professor Harley's internationally-recognised expertise in SRY (co-discovered role of SRY in the brain) with Dr Lee's extensive experience in Parkinson's disease research (expert in preclinical models demonstrating the link between SRY and Parkinson's disease).

IP position

Hudson Institute holds a patent application progressing in National Phase in the USA, Australia and China, covering SRY ASOs and their use in treatment of neurological diseases (WO/2016/164977A1).

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