Bacteriophages and Gut Bacteria's Effect on Parkinson's Disease

Wendy Xiong[1], Christine Zang[1], Yumei Xiong[2] // [1]Henry M. Gunn High School, [2]Amgen

INTRODUCTION

Parkinson's disease (PD) is the second most common age-related neurodegenerative disease characterized by stiff movements, tremors, and sometimes even dementia and emotional changes. It is generally accepted that a major indication of PD is the presence of Lewy bodies in neuronal cells that are created through alpha-synuclein protein misfolding. However, one recent study by George and Victor Tetz from the Human Microbiology Institute has challenged the default answer by suggesting that bacteriophages in the gut may have a major role in the development of PD. We explored his hypothesis through our research.

BACKGROUND INFORMATION

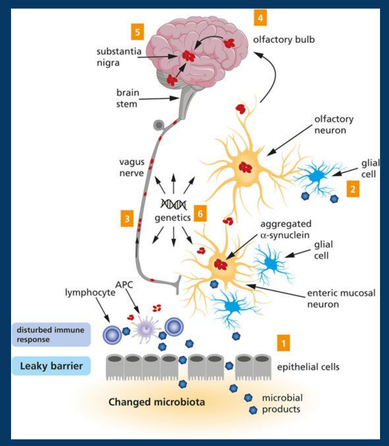

Figure 1: Pathogenesis of PD according to Braak's Theory (Rietdijk et al).

New studies have tackled the idea of the vagus nerve, gut microbiome, and most recently, bacteriophages as a part of the onset of PD. Several studies done by Dr. Braak have revealed a new hypothesis: alpha-synuclein protein misfolding and aggregation begins in the nervous system of the gastrointestinal tract and those aggregates migrate to the central nervous system.

We concluded that the three factors listed below are universally accepted as contributors to PD.

01	Alpha-synuclein misfolding	• Protein misfolding occurs during onset of Parkinson's disease. • The proteins aggregate and are major components in Lewy bodies
02	Lewy Body Hallmark	• Most Parkinson's patients have Lewy bodies in their brain • The Lewy bodies disrupt neuronal function in dopamine-producing neurons
03	Substantia Nigra	• This brain part plays an important role in and movement (reduced in PD patients) • These cells make dopamine neurotransmitter

RESEARCH METHODOLOGIES

- Analyzation of previously published research papers and scientific articles to confirm the reliability of ideas or theories and for background information.
- Interviews with professors & researchers specializing in PD, bacteriophage, and gut microbiome research

DATA AND FINDINGS

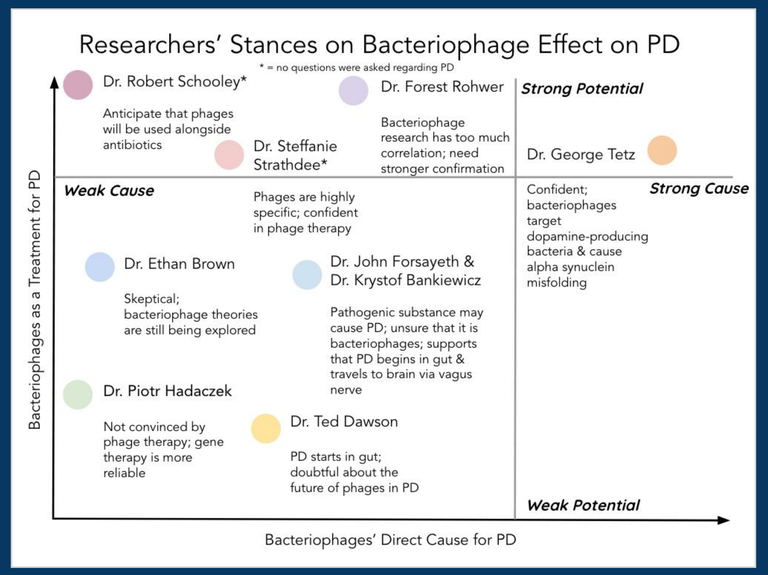

Figure 2: Data organizer to represent the opinions of interviewed researchers.

We transcribed and selected main ideas from each interview and identified how strongly each researcher supported or rejected the potential role of bacteriophages in the development of PD.

CONCLUSIONS AND ANALYSIS

While we were relatively confident in the Tetz research in the beginning, after we interviewed various researchers, we are skeptical about the reliability of the role bacteriophages in PD. We realized that we had not paid attention to the difference between correlation and causation. Because of the lack of certainty and significant evidence, we propose two different paths the onset of PD can take based on our results:

Proposal 1: Dr. Tetz's research is correct.
Lytic/temperate phage interaction with eukaryotic cells → Increased intestinal permeability → Phages cause changes in gut microbiome → Increased intestinal inflammation → Alpha-synuclein protein misfolding → Travel out of "leaky gut"through vagus nerve to brain → Aggregate into Lewy bodies → Loss of dopamine-producing neurons in substantia nigra → Compromise movement in patients

Proposal 2: Dr. Tetz's theory is invalid (no involvement of bacteriophages).
Environmental factors (e.g. toxins) → Alpha-synuclein protein misfolding → Aggregate into Lewy bodies → Loss of dopamine producing neurons in substantia nigra

continued

After careful consideration of documents, research papers, and interview content, we believe that even though there is potential in Dr. Tetz's findings, it is still too early to tell whether this data can be trusted and implemented in future tests and treatments. We have found that it is relatively probable that bacteriophages play a role, and we hope that future research can be conducted to clarify this question.

IMPLICATIONS AND NEXT STEPS

Many researchers we interviewed were skeptical of the relationship between bacteriophages and PD presented by Dr. Tetz, and we believe that while there is potential for the idea that Parkinson's disease is related to phages, it is still a very novel theory that is just beginning to be explored. If proven true, this discovery can lead to steady advancements in PD research. However, we must be wary of ambitious discoveries, for many may not turn out to be as promising as they seem. Our finding encourages future research to consider using more advanced technologies and methods to target the phages that may trigger the development of PD.

We hope the Parkinson's community will continue to research with larger sample sizes, try to fully understand the gut-brain axes, and conduct deeper research of the relationship between PD and bacteriophages. Personally, we wish to take part in Parkinson's research and participate in labs and continue to do document analysis to follow up with newer findings. We hope that even after we finish our project, we will continue to immerse ourselves in PD research and discover along with leading researchers.

ACKNOWLEDGEMENTS / REFERENCES

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