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Combating Obesity Through Gut Microbiome Targeted Bacteriophage Therapy

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Combating Obesity Through Gut Microbiome Targeted Phage Therapy

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Background

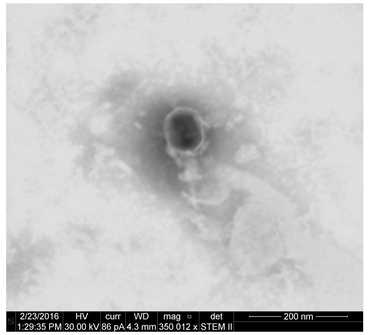
- Obesity is a serious health issue. In the U.S. two thirds of adults are overweight and half are obese. (Ogden, 2012)
- Previous research has shown a correlation between the gut microbiota and obesity.
- In 2013, by following Koch's postulates, researchers isolated Enterobacter cloacae str. B29 from a morbidly obese patient and demonstrated that it has the ability to cause obesity and chronic inflammation in its host (Fei & Zhao, 2013)

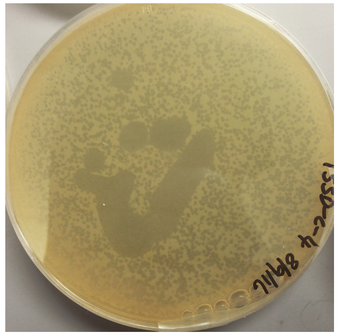
Hypothesis

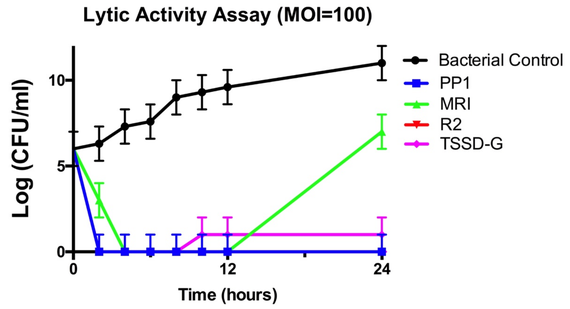
- Bacteriophages (phage) are viruses that infect bacteria by binding at specific and unique binding sites on the cell surface.
- Compared to broad-spectrum antibiotics, each phage only kills specific bacterium. Making it possible to only eradicate the pathogenic bacteria (like B29) in the gut while leaving the probiotics to flourish, thus treating obesity.

Results

Electron Microscopy and Lytic Activity Assay

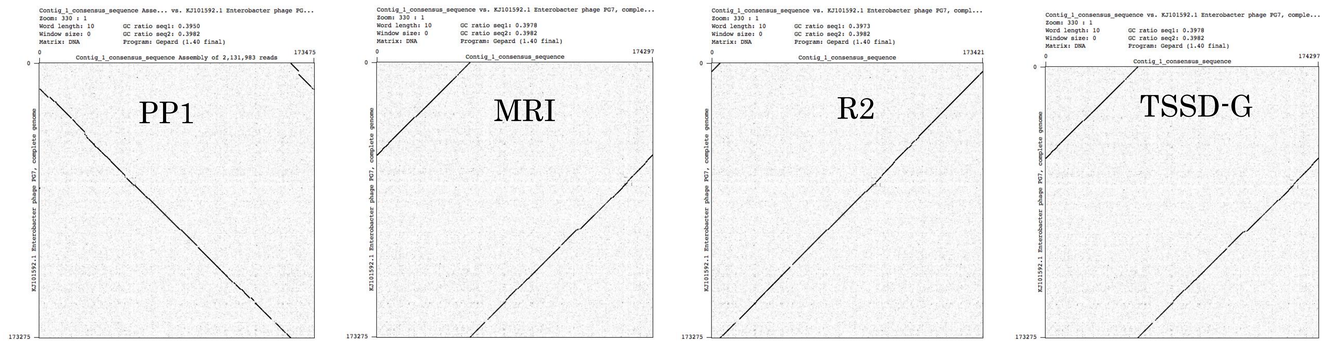






- Thirteen phages were isolated from local sewage plants in Salt Lake and Utah counties.
- Electron microscopy pictures revealed that most of them are in the myoviridae family.
- Lytic activity assays performed with an MOI of 100 showed that many of them are strongly lytic to E. cloacae B29, suggesting that they could be used to kill B29 bacteria in the gut.

DNA sequencing



- Phage genomic DNA was isolated and sequenced on the Illumina platform.
- Preliminary analyses by BLASTn search showed the phages to be 89% - 95% similar to myoviridae PG7, the most closely related phage in the database, indicating that each one is a novel, previously uncharacterized phage.
- Genomic dot-plots further strengthen this evidence and also reveal that the new phages are different from each other.

Summary

- We conclude that the phages we have isolated have promising potential to be used as a cocktail to eliminate E. cloacae B29 from the host's gut, to help alleviate obesity symptoms.
- We hope that we can pave the way to more studies on how phage therapy can treat other chronic illnesses.

Future Directions

- Finish genome assembly and annotation.
- Phage survivability test in conventional mouse models.
- Phage obesity treatment test in germ-free mouse models.

Work Cited

Fei N & Zhao L (2013) *An opportunistic pathogen isolated from the gut of an obese human causes obesity in germfree mice.* ISME J 7: 880-884.

Ogden CL, Carroll MD, Kit BK, Flegal KM. (2012) *Prevalence of obesity and trends in body mass index among US children and adolescents, 1999–2010. Journal of the American Medical Association.* 307(5):483–90.