A Method for Treating Autoimmune Disease Exacerbated by Host Immune Response to Commensal Bacteria

Targeting disease-associated bacteria via small molecule or biologics approaches to reduce or eliminate the harmful species.

Technology

This invention describes a novel contribution of a commensal bacteria species to the pathogenesis of Systemic Lupus Erythematosus (SLE) and, in particular, to lupus nephritis (LN), a severe and debilitating kidney complication. This approach provides new ways of treatment for this serious autoimmune disease. Several antibodies are associated with SLE pathogenesis. Bacteria were shown to be able to cause inflammatory disease such as ulcers by H. pylori. Therefore, NYU researcher Gregg Silverman investigated whether Lupus patients have antibodies that recognize specific bacteria.

Comparison of fecal samples from SLE patients in different disease stages revealed that individuals with high-disease activity have lower diversity of bacterial species in their gut compared to low-disease activity patients and healthy people. Comparisons of bacterial taxa from SLE patients, as well as known data from renal disease patients suggested that the species Ruminococcus gnavus is elevated in both. Moreover, serum from SLE patients had higher IgG anti-R. gnavus activity than healthy individuals and high-disease activity patients had higher antigenicity than low disease activity.

- **PI has developed a set of monoclonal antibodies against R. gnavus lipoglycan for potential use as a therapeutic (either protein-based or vaccine) or diagnostic. LG is attached to the bacterial cell wall in this species and is thought to get secreted and interact with the immune system, leading to disease exacerbation.**
- **The Silverman group has found a strong correlation between R. gnavus blooms in LN patients and a gene expression pattern that has not been previously linked to this disease.**

Background

Systemic Lupus Erythematosus (SLE) is a severe autoimmune disease in which the body attacks healthy cells. Some SLE symptoms may include skin rashes, arthritis, nerve problems and inflammation of the heart and lungs. A common lupus complication is kidney disease, also known as lupus nephritis that can be life-threatening. Current therapies for SLE are mostly drugs that diminish the immune response, making the human body more prone to infections and have many side effects.

Technology ID

SIL02-05

Category

Life Sciences/Diagnostics
Life Sciences/Therapeutics/Kidney Disease

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Applications

- Diagnosing and stratifying SLE, lupus nephritis, and other autoimmune diseases.
  - These data can be used to stratify patients based on their gut microbiome and determine whether they are in the high-disease activity group (as symptoms are varied) and develop kidney problems.
- Targeting the disease-associated bacteria via antibacterial drugs to reduce or eliminate the harmful species.

Advantages

- Using antibacterial agents to reduce the amount of RG in the gut is a targeted approach that does not render the body exposed to opportunistic infections like many current SLE drugs.
- Targeting the specific disease causing protein product of that bacterial species by small molecule or biologics approaches provides an even more specific treatment with less side effects than contemporary medications.

Intellectual Property

- US application on method of treating autoimmune disease issued: https://image-ppubs.uspto.gov/dirsearch-public/print/downloadPdf/11241488
- Provisional application on anti-lipoglycan antibodies pending
- Provisional application on gene signatures associated with microbial blooms in SLE and LN patients pending

References

1. Gregg Silverman, MD, et al. , https://pubmed.ncbi.nlm.nih.gov/30782585/