CCR – Impromptu Series

Monday, July 24th 2023, 15:00

Sergio Andreu Sánchez

Ph.D. student, Department Genetics/Pediatrics,
University Medical Center Groningen

Phage display sequencing reveals that genetic, environmental, and intrinsic factors influence variation of human antibody epitope repertoire

The human antibody repertoire can be perceived as a journal that records an individual's current and past immune responses to thousands of antigens that they have been exposed to. Currently, we have little knowledge about genetic and environmental determinants shaping the human antibody repertoire and its relation with disease, especially in the context of immune response to the gut microbiome. To fill this knowledge gap, we applied the state-of-the-art phage immunoprecipitation sequencing (PhIP-Seq) technology to characterize serological antibody repertoires against 344,000 peptides derived from commensal gut microbes, pathogens and dietary antigens in a broadly phenotyped, population-based cohort (LifeLines-DEEP, n=1,443) and a patient cohort with inflammatory bowel disease (IBD) (1000IBD, n=497).

We demonstrated that the antibody repertoire is individual specific, consistent over time (4 years follow-up) and is similar within individuals who are co-housing. We identified co-occurring networks of antibody-bound peptides with phylogenetically distinct origins, including those from gut microbiome, but with highly conserved motifs which might highlight a role of residing microbiota in the development of immune diseases via bacterial mimicry. Genetic analyses showed multiple human genetic variants shaping the antibody repertoire of the population, mainly at HLA, IGHV and FUT2 regions. In addition, phenotypic factors including age, cell counts, sex, smoking behavior and allergies, were associated with 544 antibody-bound peptides. In patients with IBD, a total of 373 peptides appeared to be significantly enriched or depleted in IBD patients in comparison to population controls. These peptides mainly belonged to bacterial flagellins, were predominately enriched in patients with Crohn's disease and were able to accurately discriminate Crohn's disease patients from population controls.

Our results indicate that human antibody epitope repertoires are shaped by host genetics, commensal microbes and environmental exposures like co-housing and smoking. We further highlight the role of previously undescribed antigens in relation to diseases, suggesting the potential value of measuring antibody-bound peptides for disease diagnostics and understanding their pathophysiological implications.

Venue: Lecture Hall CCR, Borschkegasse 8a
Time: Monday, July 24, 2023. 15:00
Host: Thomas Vogl

CENTER FOR CANCER RESEARCH
MEDICAL UNIVERSITY OF VIENNA