



aGvHD, cGvHD

Educational theme | The role of the microbiome in graft-versus-host disease

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Graft-versus-host disease (GvHD) remains the most prominent cause of mortality post-allogeneic hematopoietic cell transplantation (allo-HSCT). Both biological and human studies have provided evidence that changes in the gut microbiota are associated with a higher risk of GvHD, however, the underlying cause of this relationship is still not fully understood. Currently, investigators hypothesize that, given the clear link between gut microbiota and the development of GvHD, manipulating it may offer a promising avenue for preventing or treating this condition. The GvHD Hub will focus on providing educational content around the microbiome and its relation to GvHD.

Here are some highlights of content the GvHD Hub has previously covered on the microbiome:

Marcel van den Brink | EBMT 2019 | Microbiome changes in allogeneic hematopoietic SCT

Marcel van den Brink, from [Memorial Sloan Kettering Cancer Center, New York, US](#) spoke to the GvHD Hub about the role of the intestinal microbiome in the risk for GvHD after allo-HSCT). Dr van den Brink discussed a multicenter study where weekly stool samples were collected from four centers in Japan, Germany and the US. The investigators noticed a dramatic change in the composition of flora, specifically a loss of diversity. The pattern identified indicated that when the diversity of flora was lost, specifically 14 days after allo-HSCT there was a greater risk of lethal GvHD.

Gut microbiota dynamics in relation to the development of aGvHD in pediatric patients following allogeneic hematopoietic cell transplantation

[Elena Biagi from the University of Bologna, Italy](#), and colleagues, published findings in the journal [BMC Medical Genomics](#) on a study exploring the gut microbiota trajectory in 36 pediatric HSCT recipients in relation to aGvHD onset.¹

[Dr. Biagi](#) and her team presented a longitudinal observation of microbiota dynamics in pediatric patients undergoing HSCT for a variety of hematological diseases. Despite the complexity of the study in terms of possible confounding variables (i.e. chemotherapy, antibiotics, proton-pump inhibitors, and hospitalization), it was possible to detect a signature which would predict the development of aGvHD in the gut microbiota composition of patients before HSCT.

How can we better utilize FMT in patients undergoing stem cell transplantation?

At the 24th Congress of the European Hematology Association (EHA), Florent Malard from Saint-Antoine Hospital, Paris, FR, talks about how we can better utilize fecal microbiota transplantation (FMT) in patients undergoing stem cell transplantation.

FMT has been used successfully to treat *Clostridium difficile enteritis* but the safety and efficacy of FMT in immunocompromised GvHD patients requires further studies

Can microbiome markers predict acute GvHD after allo-HSCT?

At the [44th Annual Meeting of the European Society for Blood and Marrow Transplantation \(EBMT\)](#), [Raffaella Greco](#) from [IRCCS San Raffaele Scientific Institute, Hematology, and Bone Marrow Transplantation Unit](#), Milan, Italy, entitled “Microbiome markers are early predictors of acute GvHD in allogeneic hematopoietic stem cell transplant recipients”. Recent studies have shown that longitudinal analysis of microbiome profile allows early identification of patients at risk for major transplant-related complications such as acute graft-versus-host disease (aGvHD). Thus, the study group retrospectively analyzed the role of intestinal microbiota in the setting of aGvHD in 100 consecutive adult patients, who previously underwent allogeneic HSCT between October 2014 and March 2016.

The role of intestinal microbiota in graft-versus-host disease

At the [24th European Hematology Association \(EHA\) Congress](#) in Amsterdam, Professor [Ernst Holler](#) from the University Medical Center, Regensburg, Germany, gave an educational talk on Saturday 15 June, entitled “Microbiota and graft-versus-host disease: a double-edged sword”. He spoke about current approaches in microbiota research and how the view of researchers has changed on the pathophysiology of hematopoietic stem cell transplantation (HSCT)-related complications in recent years.[i]

Elevated intestinal epithelial tight junction permeability leads to systemic graft-versus-host disease propagation

On 1 February 2019, [Sam C. Nalle](#) from the [Department of Pathology, The University of Chicago, Chicago, Illinois, USA](#), and colleagues [published their analysis](#) in *The Journal of Clinical Investigation*, on the impact of dysregulated intestinal permeability on the subsequent graft-versus-host disease (GvHD) propagation phase. Myosin light chain kinase (MLCK210), a serine/threonine-specific protein kinase that phosphorylates a specific myosin light chain, namely the regulatory light chain of myosin II, is also known as a key regulator of tight junction permeability. The study group hypothesized that MLCK210-dependent alterations in barrier function may drive GvHD propagation.

Highlights from the 1st EBMT GvHD Summit 2019

The [1st EBMT GvHD Summit](#) took place in Warsaw from 16–18 May 2019 at the Radisson Blu Sobieski Hotel. The aim of the Congress was to present the latest scientific developments in biology, prophylaxis, and treatment of graft-versus-host disease (GvHD) through dynamic discussions and cutting-edge presentations by experts in the field.

The final session of the day began with [Marcel van den Brink](#)'s presentation on the emerging role of the microbiome, concluding that changes in intestinal flora are associated with overall survival, lethal GvHD, bacteremia, sepsis, engraftment, and relapse in patients receiving allogeneic transplantation. He further added that antibiotics, certain drugs, diet, and conditioning regimens can affect flora changes, as well as enterococcus domination, is associated with GvHD. Ernst Holler then addressed the topic of microbiome and antibiotics, providing insights into how to overcome the negative impact of antibiotics and protect the intestinal microbiota.

Watch out for more content surrounding microbiome on the GvHD Hub, or via our social channels on [Facebook](#), [Twitter](#), and [LinkedIn](#).

References

1. Holler E. Microbiota and graft-versus-host disease: a double-edged sword. 24th European Hematology Association (EHA) Congress. 2019 June 15. Amsterdam.

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