Deciphering the biological mechanisms involved in the regulation of the anti-tumor response after allogeneic hematopoietic stem cell transplantation (allo-HSCT) by azithromycin (AZM).

Initiated in 2018 by Anne Bergeron, head of the Pulmonology Division at the University Hospitals of Geneva (HUG)[1], and researchers David Michonneau and Nicolas Vallet from the HIPI "Human Immunology, Pathophysiology, Immunotherapy" Lab at the Saint-Louis Research Institute (IRSL)[2], this project benefited from financial support of CRYOSTEM[3] for access to samples (cryopreserved cells in DMSO, cell pellets and plasma) and patient consents.

Our research focuses on understanding the immunological mechanisms behind complications following allo-HSCT: acute or chronic Graft versus Host Disease (GvHD) and relapse.

ALLOZITHRO clinical trial highlighted the association between AZM intake and relapse, without preventing GvHD, and paved the way to better understanding of relapse mechanisms after allogeneic HSCT.

Coordinated by Anne Bergeron, ALLOZITHRO was a randomized, placebo-controlled, double-blind, multicenter clinical trial designed to evaluate the effect of an antibiotic, azithromycin (AZM), on the prevention of respiratory function decline after allo-HSCT.
This trial was stopped prematurely due to an increased risk of relapse (hazard ratio=1.7) in the AZM arm, with no impact on the incidence of GvHD.

The aim of the AZIMUT project[4] was therefore to use the prospective CRYOSTEM collection to identify the biological mechanisms involved in the increased risk of relapse after allo-HSCT in patients treated with AZM.

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[1] Pulmonology Division at the University Hospitals of Geneva (HUG)
[2] HIPI - “Human Immunology, Pathophysiology, Immunotherapy”
[3] Visit CRYOSTEM’s website
[4] Read the AZIMUT project final report (French)

About the CRYOSTEM's prospective collection.

CRYOSTEM is a national cohort of high strategic value for human immunology research in the field of bone marrow transplantation. The CRYOSTEM network provides the scientific community with 3 types of samples derived from blood samples collected at different stages of the transplant kinetics: viable cells in DMSO, dry pellets and plasma. All cohort samples and associated data are managed by a dedicated database software program, MBioLims CRYOSTEM, shared by all CRYOSTEM centers. This unique organization provides a high degree of homogeneity in sampling practices, allowing researchers to address a wide range of scientific questions using high quality and reliable samples.

"The expertise and logistical resources provided by CRYOSTEM make our work a lot easier when setting up a research project in humans in which we have to provide the regulatory and legal elements."

A second major advantage of CRYOSTEM is to simplify the access to a multicentric collection of biological resources that meets all the regulatory standards issued by the *Commission Nationale de l'Informatique et des Libertés* (CNIL), the *Comités de Protection des Personnes* (CPP) and the legal requirements, with access to patient consents and information notes for the use of data in our research programs. CRYOSTEM also has a dedicated patient information page on its website, with the latest advances in research projects using the biological resources from the collection.

Perspective after the AZIMUT project: Proposing microbiota-targeted therapy as a new clinical practice to prevent relapse after allograft transplantation.

Today, we are starting a new research project proposing an alternative approach to fecal microbiota transplantation, which specifically targets microbial species to improve the immune response as part of anti-tumor therapy. In the field of microbiota, current clinical practice favors fecal transplantation, an approach that remains unspecific. Following our recent work with Nicolas Vallet[5], we have filed a patent to propose a highly targeted therapeutic approach that takes into account the gut microbial composition and the presence of bacterial species associated with relapse events. Our initial results are very encouraging and pave the way to research deciphering the role of the microbiota in other pathologies such as myeloid hemopathies and myelodysplastic syndromes.

[5] Link on publication