Targeting of lineage-specific antigens: A new strategy to fight Acute Myeloid Leukemia

Florence Borot, PhD, Associate Research Scientist in the Department of Medicine, Columbia University Medical Center

Despite improvements in the supportive care and bone marrow transplantation, the principles of treatment for acute myeloid leukemia (AML) patients remain unchanged. The emergence/development of targeted immunotherapy have opened new possibilities, demonstrating tremendous success for patients with lymphoblastic leukemia. However, until today, no clinical study with CAR-T cells has shown success beyond CD19-targeted CAR-Ts, due to lack of unique targetable cell surface antigens. Indeed, the success of CD19 therapy is due to the fact that B cell aplasia can be treated with immunoglobulin supplements.

Nevertheless this approach has not been successful in other hematological malignancies due to lack of unique targetable cell surface antigens. In order for an antigen to be an ideal candidate for a CAR-T therapy, it should be unique to cancer cells and not expressed on normal cells and should be indispensable for cancer cell survival.
Because no such antigen has been found for any cancer, we have designed a novel approach combining the targeting of a lineage specific antigen expressed by cancer cells with the transplantation of stem cells lacking that lineage specific antigen. As a proof of concept, we have developed this approach using the myeloid lineage marker CD33 and are currently extending this new approach to others cancers.