

PRESS RELEASE

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Identification of a Promising Immunotherapy Target for Incurable Leukaemia

Blocking Galectin-9 found to boost immune responses against Chronic Lymphocytic Leukaemia

In a new study published in the prestigious journal “Nature Communications”, researchers from the Luxembourg Institute of Health (LIH), in collaboration with the [German Cancer Research Center \(Deutsche Krebsforschungszentrum - DKFZ\)](#), investigated the immune system of patients suffering from Chronic Lymphocytic Leukaemia (CLL) and discovered several mechanisms that weaken their natural defences against the tumour. Importantly, the international group of scientists identified the protein galectin-9 as a key molecule that impairs the function of T cells, central players in the body's own cancer defence system.

The development of treatments aiming to reactivate a patient's immune system against tumours, also known as immunotherapies, has led to complete remissions from previously incurable malignancies, revolutionising the field of cancer treatment. Unfortunately, a significant amount of patients do not respond to these treatments, often because their T cells have lost the ability to fight infections and cancer, a dysfunctional immune state scientists refer to as “exhaustion”. This is also the case for CLL, the most common type of adult blood cancer in Europe, which remains incurable despite major therapeutic advances.

In their search for effective immune-based treatments, immuno-oncology experts from the [Tumour Stroma Interactions \(TSI\) group](#) at the Department of Cancer Research (DoCR) of the LIH, led by Dr Jérôme Paggetti and Dr Etienne Moussay, mapped the immune system of CLL patients at single-cell resolution. The study was based on an unprecedented collection of biopsies from the lymph nodes, blood, and bone marrow of CLL patients, obtained via a large network of international clinical and research institutions.

Using state-of-the-art technologies and comparing the cellular biology of CLL patients with healthy individuals, the team discovered that key T cell populations necessary to fight tumours were missing, while molecules that block T cell function accumulated, helping explain why immune treatments often fail in CLL patients. Among the molecules identified, galectin-9 emerged as a particularly promising treatment target, as it is released in large amounts by leukemic cells and attaches to TIM-3, a T cell receptor that acts like a brake on the immune system, preventing them from attacking the tumour.

In a promising step, TSI researchers showed that blocking galectin-9 boosts the immune response and slows tumour growth in a preclinical model, effectively ‘waking up’ the exhausted T cells. Importantly, this approach could be extended to other cancers, since galectin-9 is also overexpressed in many tumour types, underscoring its broader therapeutic applications. The study also uncovered additional molecules that remain to be tested, offering opportunities to develop further treatments, alone or in combination with immune-based therapies, to improve their efficacy and extend their benefits to patients.

“Elevated levels of galectin-9 are also linked with poorer prognoses in kidney and brain tumours, highlighting the broader translational therapeutic relevance of our findings”, says Dr Etienne Moussay, co-leader of the TSI research group.

“We hope that our work will lay the foundation for the development of new immunotherapies targeting galectin-9, thus also benefiting patients for whom existing immunotherapies are ineffective”, concludes Dr Jérôme Paggetti, co-leader of the TSI and Deputy Head of the DoCR.

Funding and collaborations

This study was supported by multiple international and national grants, including grants from FNRS-Télévie, the Luxembourg National Research Fund (FNR), the Fondation Cancer and the Plooschter Projet. It was carried out in collaboration with the German Cancer Research Center (Germany), the University of Heidelberg (Germany), the Heidelberg University Hospital (Germany), the European Molecular Biology Laboratory (Germany), RareCyte (USA), the University of Würzburg (Germany), and the Institut d’Investigacions Biomèdiques August Pi i Sunyer (Spain).

About the Luxembourg Institute of Health (LIH)

The Luxembourg Institute of Health (LIH) is a public biomedical research organisation focused on precision health and invested in becoming a leading reference in Europe for the translation of scientific excellence into meaningful benefits for patients.

The LIH places the patient at the heart of all its activities, driven by a collective obligation towards society to use knowledge and technology arising from research on patient derived data to have a direct impact on people’s health. Its dedicated teams of multidisciplinary researchers strive for excellence, generating relevant knowledge linked to immune related diseases and cancer.

The institute embraces collaborations, disruptive technology and process innovation as unique opportunities to improve the application of diagnostics and therapeutics with the long-term goal of preventing disease.

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