



# PRESS RELEASE

Geneva | 16 May 2024

## At the right time for tumours

By examining the immune modulations of tumours during the day, scientists from the University of Geneva and the LMU Munich are demonstrating their impact on the diagnosis and management of patients.

The currently most promising anti-tumour treatments are immunotherapies, which aim to boost the action of the patients' immune system to fight cancer. However, while these treatments are highly effective in some cases, their success is sometimes disappointing. How can this variability be explained? In previous studies, a team from the University of Geneva (UNIGE) and Munich's Ludwig-Maximilian University (LMU) discovered the importance of the rhythmicity of the immune system for tumour growth. The same scientists have now demonstrated that the immune profile of tumours varies considerably depending on when during the day biopsies are performed. These variations over time might lead to misdiagnosis and the prescription of inappropriate treatments. In addition, certain therapeutic targets previously neglected could prove key in the fight against the disease. These results, published in the journal *Cell*, could have major implications for the organisation of clinical care and research into new drugs.

In 2022, the research team led by Christoph Scheiermann, full professor in the Department of Pathology and Immunology and at the Centre for Inflammation Research at the UNIGE Faculty of Medicine and the University of Munich, observed an unexpected phenomenon: the growth and severity of tumours are linked to the circadian rhythm of immune cells. «But to use these results in a clinical context, we needed to understand their details in a model closer to reality», stresses Christoph Scheiermann.

To do so, the scientists injected a group of mice with melanoma tumour cells, then harvested the resulting tumour at different times of the day, two weeks later. Depending on the time of day, and therefore on the immune activation of the animal, the quantity of immune cells, but also the type of cells and their characteristics, varied considerably. This could have important implications in clinical settings. «In hospital, patients undergo a biopsy to identify the tumour and its immune characteristics,» explains Christoph Scheiermann. «Treatments, and in particular immunotherapies, are then decided on the basis of this examination. Now, depending on the time of the biopsy, the number of infiltrated immune cells may be very high - and the tumour classified as 'hot' - or very low ('cold'), even though it is the same tumour. Taking the biopsy at the wrong time can therefore lead to a wrong diagnosis.»

### A closer look at the timing of immunotherapies

To get as close as possible to clinical reality, the scientists administered two approved and widely used treatments to their groups of mice:



©UNIGE

Christoph Scheiermann

High resolution pictures

CAR-T cells (that are custom-designed to recognise and target proteins specific to the tumour cells they will fight) and immune checkpoint blockades, which suppress the immune system's natural brakes in order to increase its activation against tumours.

«Administered at the wrong time, these treatments had no effect. At the right time, tumour burden could be significantly reduced», explains Christoph Scheiermann. «The number of immune cells present or not present in the tumour is a factor, but so are their characteristics and the resulting behaviour». Indeed, depending on the modulation of the molecular elements used to generate these treatments, the time at which they are administered becomes crucial. At the right time, the cells to be fought are immediately recognised. At the wrong time, the target molecules show lower expression, and the drug will have no effect.

### **Adapting schedules and treatments**

These studies, carried out in mice, are corroborated by an examination of the survival rates of patients following immunotherapies. Morning treatment — at the peak of immune activation in humans — is systematically associated with a better survival rate. Studies are planned to assess the impact on patients of changing their examination and treatment times. Other projects will look at potential drug targets that have so far been underestimated.

In addition, these discoveries about immune rhythms have even wider implications: from the point of view of personalised medicine, on the one hand, to adapt therapeutic approaches to the temporal profile of patients (between 10 and 20% of people have a biological rhythm that is out of sync with the general population), and in the context of other pathologies, notably autoimmune diseases.

## contact

### **Christoph Scheiermann**

Full Professor

Department of Pathology and Immunology

Geneva Centre for Inflammation Research (GCIR)

Translational Research Centre in Oncohaematology (CROH)

Faculty of Medicine UNIGE

Institute of Genetics and Genomics in Geneva (iGE3)

+41 22 379 57 47

Christoph.Scheiermann@unige.ch

**DOI: [10.1016/j.cell.2024.04.015](https://doi.org/10.1016/j.cell.2024.04.015)**

**UNIVERSITÉ DE GENÈVE**  
**Communication Department**

24 rue du Général-Dufour  
CH-1211 Geneva 4

Tel. +41 22 379 77 17

[media@unige.ch](mailto:media@unige.ch)

[www.unige.ch](http://www.unige.ch)