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Press information**A better evaluation of the body's ability to fight tumours**

Some individuals are better able to fight cancer for many years compared with others. This ability to fight tumours depends on the immune response, as observed for colorectal cancers by Jérôme Galon, Research Director at Inserm, and his team, the Laboratory of Integrative Cancer Immunology, at the Cordelier Research Centre (Inserm/UPMC/Paris Descartes University). The investigators show that the proportions of immune system cells in and around the tumour change with the stage of progression of the cancer, and demonstrate the importance of an increased concentration of some cell types to the survival of patients, namely, follicular T-helper cells (Tfh) and B lymphocytes. A better understanding of the dynamics of these cells will help to identify new strategies for developing targeted immunotherapies.

The results of this study are published in the 17 October issue of the journal [*Immunity*](#).

The immune system is able to fight some tumours before they can affect health. Once the tumour has been identified, immune system cells are mobilised to kill and eliminate the tumour cells. However, tumour cells can sometimes manage to survive the response of the immune cells, and become established. The tumour becomes malignant when it develops in an uncontrolled manner. The investigators at the Cordelier Research Centre (Inserm/UPMC/Paris Descartes University) study the manner in which the immune system fights tumours, in an effort to effectively unleash the body's intrinsic potential for fighting cancer.

Two factors indicate the body's potential for "fighting or defeating" a tumour: the intensity of the immune response, and the mechanisms adopted by tumours to escape recognition by the immune system. The complex interactions between tumours and their microenvironment were poorly known until now. In the present study, the investigators examined the spatiotemporal dynamics of 28 different types of immune system cells that infiltrate colorectal tumours. By combining the study of cellular interactions with bioinformatics, they observed that the proportions of immune system cells infiltrating tumours change with the stage of progression of the tumour.

The research team has demonstrated the importance of an increased concentration of some types of immune system cells to patient survival, i.e. **the T follicular-helper (Tfh) cells and B lymphocytes**. These results obtained for human tumours were also demonstrated in three mouse models of colon cancer.

The investigators also studied more specifically in patients the instability of the gene for the chemokine CXCL13, which modulates the infiltration of Tfh and B lymphocytes. CXCL13 and IL-21 have proven to be additional factors that promote the death of tumour cells: high levels of these molecules are correlated with patient survival.

These observations indicate that T, Tfh and B lymphocytes form a network of cells that communicate inside tumours. High levels of Tfh and B lymphocytes prevent tumour

progression and recurrence in colorectal cancer. As in patients, T, Tfh and B lymphocytes control tumour development in murine models of colon cancer.

“The immune response develops during cancer progression. The immune landscape that we describe in relation to colorectal tumours helps us to understand this development in order to intervene in the right place at the right time,” explains Jérôme Galon, Research Director at Inserm and last author of the study. *“The clinical outcome is highly variable among patients with the same stage cancer. Understanding why some individuals are able to defend themselves against cancer for many years is crucial in combating the disease,”* concludes the main author of the study.

Sources

[Spatiotemporal dynamics of intratumoral immune cells reveal the immune landscape in human cancer](#)

Gabriela Bindea, Bernhard Mlecnik, Marie Tosolini, Amos Kirilovsky, Maximilian Waldner, Anna C. Obenauf, Helen Angell, Tessa Fredriksen, Lucie Lafontaine, Anne Berger, Patrick Bruneval, Wolf Herman Fridman, Christoph Becker, Franck Pagès, Michael R. Speicher, Zlatko Trajanoski, Jérôme Galon

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Further information

The investigators have also developed a test, known as “Immunoscore,” which predicts the ability of an individual’s immune system to fight tumour cells. Using Immunoscore as part of routine prognostic evaluation may provide critical new information on prognosis, and facilitate clinical decision-making (including guidance for therapeutic decisions). In order to promote Immunoscore for routine use in hospitals, an international consortium directed by Jérôme Galon has been launched in association with the US Society for Immunotherapy of Cancer (SITC) and a large number of international institutions from 17 countries throughout the world.

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