

**Press information****Acting on the immune system even before cancer develops may be feasible**

The immune response is activated from a very early stage in the development of precancerous cells. Unfortunately, this response is simultaneously accompanied by the onset of mechanisms that block it, allowing cancer to develop. This is the first time that the immune response has been described in such detail in precancerous stages, here in lung cancer. This research conducted by the team led by Jérôme Galon, Inserm research director at the centre de recherche des cordeliers (Inserm/Université de Paris/Sorbonne Université) in Paris, shows that using immunotherapies at very early stages could potentially help prevent cancer. This research has been published in [Nature](#).

Our understanding of how the immune system works in the context of cancer is continually improving. Jérôme Galon and his Inserm team have made a significant contribution to such advances. After showing that cancer progression depends among other factors on the presence and functionality of T lymphocytes in the tumor microenvironment and the [Immunoscore](#), the researchers have proven that the immune response and its blocking mechanisms are triggered at very early, precancerous stages. This means that when a cancer develops, many components of immune surveillance but also the mechanisms designed to evade it have already been implemented.

At the moment, patients with precancerous lung lesions can be monitored and the lesions removed if doctors have the slightest suspicion that they are at risk of developing into cancer. But clinicians may be surprised to discover that it may already be possible at this stage to target the immune system in order to combat progression of these lesions. This is what the research by Jérôme Galon and his team has shown. The researchers had access to 122 lung biopsies from smokers at risk of cancer. They found all stages of precancerous to cancerous lesions in these biopsies. For each biopsy, they studied the immune system in the tumor microenvironment. They performed a genomic analysis of the cells present and looked at them using multispectral fluorescence, an imaging technique that uses specific antibodies to target different types of immune cell. This work enabled them to characterize the nature, quantity, and role of the various immune components in the tumor microenvironment at each precancerous and cancerous stage.

**The immune response takes place before cancer**

This made it possible for them to compare the development pathways of the cancer and the immune response. At the stage of low-grade dysplasia - an extremely early stage, when only a few morphological abnormalities, DNA repair defects, and greater ability to divide can be seen in the cells - the researchers observed activation of local immune cells and the arrival of naive T lymphocytes, i.e. T cells not trained to specifically destroy abnormal cells. At the stage of high-grade

dysplasia - where there is a higher level of morphological and molecular abnormalities - the researchers then observed mass recruitment of innate and adaptive immune cells, with the presence of B and T lymphocytes specific to abnormal cells and initiation of the immune memory response. But such activation is already accompanied at this stage by the triggering of blocking mechanisms called immune checkpoints and of immune suppressive cytokines, molecules that are also designed to block the immune response. This means that the functioning of the immune system is already altered before the cancer itself develops. This discovery in the context of lung cancer still requires confirmation in other types of cancer. Jérôme Galon is already working on doing so in colon cancer.

The researchers believe that this work will have major implications for the future of patient care. First, they highlight the importance of discovering immune biomarkers that will make it possible to better predict the risk of precancerous lesions developing into cancer. Second, using immunotherapies designed to inhibit the mechanisms that block the immune system, the much talked about immune checkpoints, could be of benefit to patients in the early stages of cancer prevention.

## Sources

### Immune evasion before tumor invasion in early lung squamous carcinogenesis

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