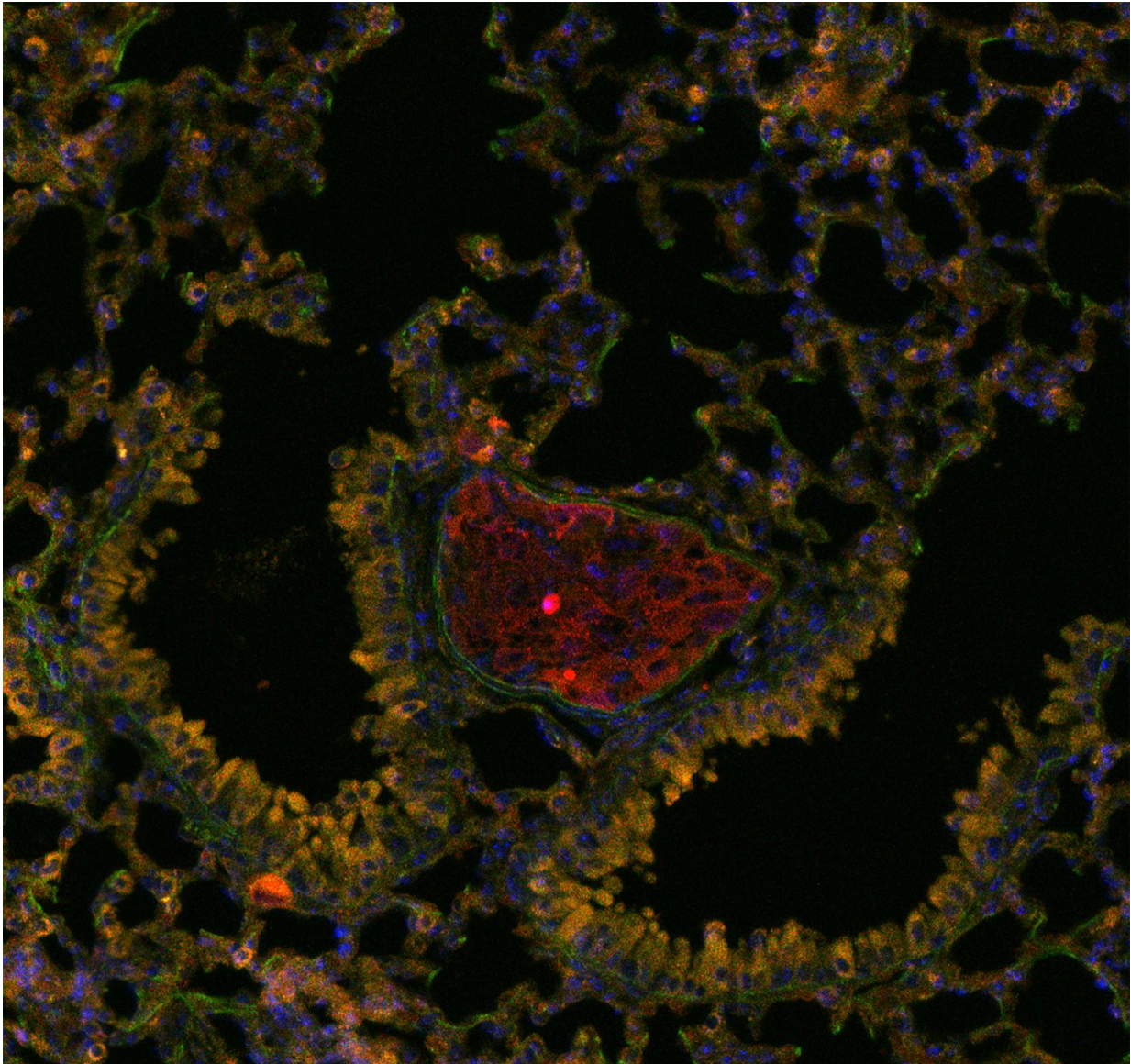


Tighten the grip on metastasis

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Breast cancer metastatic cells (red) nesting in a pre-metastatic niche at the lungs.
Credit: Héctor Peinado, Spanish National Cancer Research Centre (CNIO)

Metastasis is the major cause of cancer-related death and its appearance remains a phenomenon that is difficult to predict and manage. We now know that, prior to the arrival of the cancer cells, tumours prepare the ground in the organ that they will later colonise. These areas with ideal conditions for the onset of metastasis are called pre-metastatic niches and targeting them will help improve patient survival. These questions are the subject of a review paper published in *Nature Reviews* by an international group of experts in this field, including Héctor Peinado, head of the Microenvironment and Metastasis Group at the Spanish National Cancer Research Centre (CNIO).

There are certain areas and organs in the body where the onset of [metastasis](#) is more common. Lungs, bones, brain... What's more, each tumour has a predilection for colonising specific areas. The problem is that we are still unable to anticipate where metastasis occurs and when it does, it is often too late. However, Peinado and his colleagues have known for some years that the areas that are going to be affected by metastasis undergo changes before the arrival of the [tumour cells](#).

These areas are what David Lyden, Weill Cornell Medicine (USA), termed 'pre-metastatic niches' several years ago. In these niches, we can detect changes that will later allow the survival and growth of tumour cells. These changes are caused by soluble factors and extracellular vesicles secreted by the primary tumour. "Emerging evidence from our laboratory and others identified pre-metastatic niches in patients with various cancers. This is a paradigm shift in our understanding of metastasis that will be the cornerstone for developing strategies for the preventive treatment of metastasis, rather than treating metastasis after the fact."

Getting ahead of metastasis

Therefore, the challenge is - and this is the topic of the paper - to be able to identify the niches before metastasis occurs. "The three events that take place and that could serve to detect these niches are vascular leakiness, infiltration of immune cells (local inflammation) and remodelling of the organ," explains Peinado. These three processes facilitate the emergence of metastasis but can also serve as markers of future metastasis. "A better understanding of the biology underlying the inflammation and blood vessel dysfunction in pre-metastatic niches will allow us to identify therapies to block [metastatic progression](#)", says Haiying Zhang, the paper's co-author, also from Weill Cornell Medicine.

"The more we move forward in the early detection of metastasis, the higher the survival rates will be," said Peinado. This is, precisely, the crux of the matter, since most cancer patients succumb mainly to metastasis, while the treatment of the primary tumours is quite advanced. "If we can predict that a tumour is going to metastasize and detect where, and we can stop it in that time window, it will be easier to treat cancer," pointed out Peinado.

One of the things this review assesses is the development of molecular imaging techniques that can complement classic tests to analyse and detect the formation of these future metastatic niches. By using markers that indicate the formation of a niche, it would be possible to learn where a tumour is likely to metastasize.

The next step would be to prevent the metastasis. Once again, the study of these niches is providing information on how this can be achieved. Acting on changes in the blood vessels, blocking the signals that primary tumours send, or keeping these niches in a dormant state (as happens for years in some patients) are some of the strategies that are being explored in the laboratory. "Identifying strategies to restore immune function in pre-metastatic niches will also be crucial for the success of therapies aimed at preventing metastasis", added Irina Matei, also a co-author

from Weill Cornell Medicine.

"All this could contribute to prevention and therapy, but -Peinado says- although the concept is very interesting and has great potential, much work remains to be done to done to translate from bench to bedside". There are ongoing studies involving various tools and approaches such as the analysis of circulating vesicles (exosomes) in liquid biopsies with promising results to predict metastatic outcome and organotropism in the pre-clinical setting, but we will have to wait for it to reach the clinical phase.

More information: Héctor Peinado et al, Pre-metastatic niches: organ-specific homes for metastases, *Nature Reviews Cancer* (2017). [DOI: 10.1038/nrc.2017.6](https://doi.org/10.1038/nrc.2017.6)

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