

Genetically modified mice to visualize in vivo inflammation and metastasis

April 2 2012

One of the major routes of tumor cell dissemination to form metastasis at distant organs in the body is the lymphatic system. To study this process, still poorly understood, and to gain information on which tumors prefer this route for dissemination and how to block it, researchers of the Spanish National Cancer Research Center (CNIO), led by researcher Sagrario Ortega, have created transgenic mice in which, for the first time, the growth of the lymphatic vessels can be visualized in the whole animal, by a light-emitting reaction, as tumor progresses and forms metastasis. The technique is so sensitive that it allows monitoring those lymph nodes that are going to be invaded by tumor cells. The work is published today in the journal *PNAS (Proceedings of the National Academy of Sciences)*.

The normal [physiological function](#) of the lymphatic vessels is to collect fluid, molecules and cells from tissues and transport them to the blood stream. This system is essential for proper tissue drainage and its disfunction leads to fluid accumulation or lymphedema. The lymphatic system also participates in several diseases related to the immune response and inflammation and plays a very important role in the dissemination of tumor cells that, through the lymphatic vasculature reach first the [sentinel lymph nodes](#) and later distant organs to form metastasis.

The [mice](#) designed and created by the group of Sagrario Ortega, Head of the [Transgenic Mice](#) Unit of the CNIO, look completely normal at sight. But they carry additional genes that are expressed in the walls of the

lymphatic vessels, under the control of the regulatory signals of Vegfr3, the first marker of lymphatic vessels identified. One of these genes is the one encoding a protein called luciferase, responsible of the light emitted by fireflies.

In the insect, the luciferase catalyzes the oxidation of its natural substrate, the luciferin, in a light emitting chemical reaction. Therefore in these mice, the lymphatic vessels emit light when the animals are injected with the totally innocuous substance luciferin. This light emission is captured in the dark using highly sensitive cameras.

The other gene that is expressed in these mice is the green fluorescent protein (GFP) that allows visualization of lymphatic vessels at the cellular level.

"The generation and characterization of these mice has been a great effort but certainly worthwhile" says Inés Martínez-Corral, first author in the *PNAS* publication and for whom this work has been her Doctoral Thesis"

What makes these mice very useful for the study of cancer and metastasis is that, in them, the proliferation of the lymphatic vessels -technically lymphangiogenesis-, a process that in the adult only takes place in pathological situations such as inflammation and tumors, can be directly visualized in the whole animal without invasive histological techniques.

Tumor cells send signals that induce proliferation of lymphatic vessels, not only at the periphery of the tumor but also in the [lymph nodes](#) facilitating the dissemination of tumor cells and the formation of metastasis, by a mechanism that is still poorly understood.

A NEW STEP TOWARDS THE DEVELOPMENT

OF NEW THERAPIES

"These processes are detected in a very early stage in our mice, even before the lymph node invasion by [tumor cells](#), by an increase in light emission and without need of histological techniques. These mice provide a unique tool for the study of inflammation and metastasis and for the development of new anti-metastatic therapies", explains Ortega.

For some tumors, such as melanoma or breast, the [lymphatic system](#) plays an important role in metastatic spread. But, in general, the connection between formation of new [lymphatic vessels](#) from pre-existing ones and tumor dissemination is poorly understood. This is why this technique is especially useful.

The new transgenic mice are already being used for several groups at the CNIO in search for markers that identify tumors that spread mostly through the lymphatics and to investigate how to block this process pharmacologically. One of the first tumors that are being studied using these mice is melanoma, in collaboration with the group of Maria S. Soengas, Director of the Molecular Pathology Program of the CNIO.

Provided by Centro Nacional de Investigaciones Oncologicas (CNIO)

Citation: Genetically modified mice to visualize in vivo inflammation and metastasis (2012, April 2) retrieved 26 April 2024 from <https://medicalxpress.com/news/2012-04-genetically-mice-visualize-vivo-inflammation.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.