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PRESS RELEASE

THE INTESTINAL FLORA AS A COMPLEMENT TO IMMUNOTHERAPY IN ONCOLOGY

The vital role of the intestinal flora in successful immunotherapy has just been revealed in a study published in the journal *Science*. Intestinal bacteria have been identified that can improve the therapeutic response to this drug and reduce a side-effect, “inflammatory colitis,” regularly encountered with this treatment.

This research implies that the efficacy of immunotherapy in oncology might in future be dictated by the composition of the patient’s intestinal flora. The researchers hope to develop a test for predicting the response to these treatments by analysing the intestinal flora. They also hope to offer those patients who need it the opportunity to reconstitute a flora which will restore the anti-tumour effect of the immunotherapy.

This research was conducted jointly by French researchers from Gustave Roussy, Inserm, Institut Pasteur Lille and Institut Pasteur Paris, the AP-HP (Paris Public Hospitals) and Paris-Sud University, in collaboration with a team from the French National Institute for Agricultural Research (INRA), and was mainly funded by ARC Foundation for Cancer Research.

“Certain bacteria naturally present in the intestinal flora are becoming the pillars of success for an immunotherapy used in clinical oncology,” comments Prof. Laurence Zitvogel, Director of the Tumour Immunology and Immunotherapy Laboratory (Inserm / Gustave Roussy / Paris-Sud University), and last author of the publication.

The role of two types of bacteria from the intestinal flora in the alleviation of these side-effects and in increasing the efficacy of an immunotherapy based on a monoclonal antibody against CTLA4 (ipilimumab) has just been demonstrated by Prof. Laurence Zitvogel’s team, with assistance from teams led by Dr Mathias Chamailard, Institut Pasteur Lille, Dr Ivo Gomperts Boneca, Institut Pasteur Paris, and Dr Patricia Lepage, INRA.

The researchers showed that when the intestinal flora lacked the two bacterial types identified, either in germ-free mice or after treatment with broad-spectrum antibiotics, the drug was no longer effective against the tumour. Colonisation of the intestinal flora by one or other of these bacterial types is necessary and sufficient to restore the effect of the monoclonal antibody and improve the symptomatology of inflammatory colitis in these mice.

The relevance of these findings was also successfully tested in humans. The teams led by Prof. Caroline Robert, Head of the Dermatology Department in Gustave Roussy, and by Prof. Franck Carbonnel, Head of the Gastroenterology Department at Bicêtre Hospital, AP-HP, began a clinical trial in order to demonstrate the relevance of these findings in patients with melanoma.

Analysis of the intestinal flora of patients with metastatic melanoma following treatment with ipilimumab thus showed the importance of these immunogenic bacteria in sensitivity to the treatment and in tumour reduction. These results suggest that it is of interest to consider immunogenic bacteria as an adjuvant treatment for cancer.

“Concurrently with our work, an American team came to the same conclusions regarding the role of other bacteria in the efficacy of the anti-PD1 antibody nivolumab,” adds Prof. Laurence Zitvogel, who points out that this work shows that the microbiota dictates the therapeutic response, opening up interesting possibilities for treatment. We could thus offer patients with a relatively unfavourable intestinal flora a compensatory bacterial composition, whether by prebiotic treatment, by immunogenic bacteria from the intestinal flora, or by faecal transplant. However, there is a current lack of regulatory certainty in France regarding the transformation of intestinal flora into drugs that might become agents for adjuvant therapy in oncology with the help of legislators and regulatory agencies.

// About immunotherapy

Immunotherapies have enabled a revolution in cancer treatment. Not only do they make it possible to reduce the size of tumours, they also, for the first time, make it possible to prolong the survival of patients, or even cure them of metastatic or locally advanced cancer. These new immunotherapies, using monoclonal antibodies (anti-CTA4 or anti-PD1), make it possible to awaken the patient’s immune system. However, 20% of patients undergoing anti-CTLA4 treatment experience auto-immune side-effects such as “inflammatory colitis.”

// About the intestinal flora

The intestinal flora, or intestinal microbiota, is composed of 100,000 billion bacteria. These colonise the intestine from birth, and are involved in the maturation of the immune defences. Every individual has his/her own unique microbiota. The composition of this flora is dictated by genetic, nutritional and environmental factors. Certain bacteria can promote the occurrence of diseases; conversely, others have a protective effect.

Source:

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Anticancer immunotherapy by CTLA4 blockade relies on the gut microbiota

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/ About Gustave Roussy

Gustave Roussy, the leading cancer control centre in Europe, is a hub of world-class expertise in cancer control entirely dedicated to patients. It brings together 3,000 professionals with roles in care, research and teaching. – www.gustaveroussy.fr – www.gustaveroussy.fr/manifeste-innovationcancer

/ About Inserm+

Created in 1964, the French National Health and Medical Research Institute (Inserm) is a public scientific and technical research establishment, under the joint supervision of the French Ministry of Education, Higher Education and Research and the French Ministry of Social Affairs, Health and Women's Rights. Its researchers are devoted to the study of all diseases, from the commonest to the rarest, through their research work in biology, medicine and population health.

With a budget of €989 million in 2014, Inserm supports nearly 300 laboratories distributed throughout France. Together the teams comprise nearly 15,000 researchers, engineers, technicians, managers, clinician-researchers, post-doctoral fellows, etc.

/ About Institut Pasteur

Institut Pasteur, a recognised private non-profit foundation created by Louis Pasteur in 1887, is today an internationally renowned biomedical research centre, at the heart of a network of 33 institutes with a presence on all five continents. To carry out its role of disease prevention and control, in France and around the world, Institut Pasteur develops its activities in four areas: scientific and medical research; public health and health surveillance; teaching; and economic development and technology transfer. – www.pasteur.fr

In addition to these roles in public education and training of health professionals, Institut Pasteur Lille has been a recognised private non-profit foundation since 1898, and devotes its research efforts to diseases related to ageing, such as cancer. – www.pasteur-lille.fr

/ About AP-HP

AP-HP is an internationally renowned university hospital system with a European dimension. Its 39 hospitals receive 7 million patients a year, in clinics, emergency departments, and through planned admissions or home hospitalisation. It provides public health service for all, on a 24-hour basis, which for AP-HP is a matter of both duty and pride. AP-HP is the biggest employer in Ile de France: It employs 95,000 staff – physicians, researchers, allied medical staff, administrative staff and other workers. <http://www.aphp.fr>

/ About Paris-Sud University

Paris-Sud University is a major player in the Paris-Saclay Community of Universities and Institutions.

Multidisciplinary in nature, with a strong emphasis on science and health, the excellence of its research has been distinguished by many international awards. Paris-Sud University is one of the most prestigious universities in Europe for research, is ranked among the top institutes of higher education in France, and 41st in the world according to the 2015 Shanghai ranking.

Paris-Sud University brings together more than 70 internationally recognised laboratories, hosts 30,000 students including 2,500 doctoral students, has 2,500 lecturer-researchers and researchers, and 2,700 engineering, technical and administrative staff. – www.u-psud.fr

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