The metabolism of prostate cancer cells of is a determining factor for the development of metastasis

• The expression of a central regulator of cell metabolism, PGC1A is associated with prostate cancer aggressiveness

• The research paves the way for the identification of patients at risk of developing metastatic disease

• The study, led by Dr. Arkaitz Carracedo, has been published in Nature Cell Biology

(Bilbao, xx May 2016). The metabolic regulator PGC1A dictates the metabolic program of prostate cancer cells, and its absence is associated with the development of metastasis, as demonstrated by a team of researchers from CIC bioGUNE (Spain) led by Arkaitz Carracedo (PhD in biology, Ikerbasque Research Professor and associate professor at the University of the Basque Country). Prostate cancer is among the most common tumor types worldwide. Despite its good prognosis, there is a group of patients who fail to respond to standard therapies and develop metastatic disease. Elucidating the connection between prostate cancer cell metabolism and disease aggressiveness represents an opportunity to identify patients at risk of relapse and metastasis. In words of Dr. Carracedo "defining high-risk patients is critical in order to develop customized therapies for more effective prostate cancer treatment". The research was recently published in Nature Cell Biology, one of the most prestigious international journals in the field of cell biology.

Cancer cells nourish differently than normal counterparts, mainly because they dedicate their metabolism to grow and multiply. This research stemmed from the need of identifying the metabolic requirements of prostate cancer, as a mean to unravel the necessary steps underlying disease progression. The

hypothesis of the group of Dr. Carracedo was based on the existence of master regulators that define the metabolic state of prostate cancer cells. After detailed analysis of twenty of these regulators, the research group identified PGC1A as the best candidate. Frequent alteration in patient specimens was indicative of the importance of this gene. "However, it was the use of mouse models which provided the ultimate proof: if we eliminate the gene PGC1A, prostate cancer metastasizes, whereas if we increase the dose of the gene in metastatic cells, their aggressiveness is reduced" Carracedo says. The team of CIC bioGUNE has demonstrated that PGC1A functions as a switch that turns off the metabolism associated with cancer cell growth. The results show that a genetic signature based on the activity of PGC1A discriminates patients with high risk from those with low risk of developing aggressive prostate cancer. According to Dr. Carracedo, "these results encourage us to translate the signature into a biomarker that can be used for the benefit of the patient, and we are taking the first steps in that direction".

This study sheds light on the importance of deciphering the molecular characteristics of each cancer to provide a personalized treatment strategy, dubbed as Precision Medicine. Precision medicine is included within the European Strategy for Smart Specialization or RIS3, the research mainframe for the coming years. Arkaitz Carracedo explains that "we need a name for every cancer, an identity card, in order to identify and exploit their weaknesses". "In the present study, we identified the metabolic requirements of aggressive prostate tumors, and we envision new modes of therapy based on these results", says the biologist.

The CIC bioGUNE team has worked closely with the Department of Urology at Basurto University Hospital, led by Dr. Miguel Unda, and the Basque Biobank for Research (BIOEF), in order to corroborate in prostate cancer tissue samples the results obtained from public datasets. "We have demonstrated the importance of PGC1A in aggressive prostate cancer; the next step is to identify

drugs that are more effective against cancer cells lacking this gene", explains Carracedo.

Biomedical research is, according to the head of the research "a collaborative effort in which researchers from different disciplines are essential". The main researchers involved from the Carracedo lab were Dr. Veronica Torrano and the PhD student Lorea Valcárcel. This project has been developed in collaboration with Dr. Roger Gomis, ICREA researcher at the Institute for Research in Biomedicine (IRB Barcelona) and an expert in metastasis, as well as with the expert in metabolism Dr. Jason Locasale, professor of Cancer Biology at Duke university (United States).

CIC bioGUNE, cutting-edge research in cell biology

The Centre for Cooperative Research in Biosciences, CIC bioGUNE, located in the Bizkaia Science and Technology Park, develops cutting-edge biomedical research at the interface between structural, molecular and cell biology. Its main objective is to generate knowledge around the molecular basis of disease, that can be translated into new diagnostic methods and advanced therapies. www.cicbiogune.es / @CICbioGUNE / www.facebook.com/pages/CIC-bioGUNE-Bilbao/184783114869478.

Institute for Reserach in Biomedicine (IRB Barcelona)

Founded in 2005 by the Government of Catalonia and the University of Barcelona, the Institute for Research in Biomedicine (IRB Barcelona) is “Severo Ochoa Centre of Excellence”, since 2011. The 22 groups and seven scientific platforms are devoted to basic and applied research with the common goal of conducting multidisciplinary projects that address important biomedical problems affecting our society, with special emphasis on cancer, metastasis, Alzheimer, diabetes and rare diseases. The institute is home to more than 400 employees from 36 countries. IRB Barcelona's ultimate objective is to translate research results to the clinic and has already established three biotechnology

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