New discovery may enhance chemotherapy's efficiency against leukaemia

December 13 2017

In patients with acute myeloid leukaemia, cancer cells resist the effects of chemotherapy, many times resulting in disease recurrence and ultimately death. Researchers from Instituto de Medicina Molecular (iMM) João Lobo Antunes have found a mechanism through which certain types of leukaemia resist chemotherapy, thus revealing novel molecular targets that may be used to improve the efficiency of this type of treatment.

The team, led by Sérgio Dias, had previously shown that leukemic cells activate certain molecular signals, namely a cell signalling pathway controlled by the Endothelial Vascular Growth Factor (VEGF), which allow cancer cells to survive despite chemotherapy.

The study, published in the journal *Cancer Research*, revealed that a metabolic alteration at the mitochondrial level derived from VEGF's action is involved in chemotherapy resistance. By creating an experimental model of leukaemia in mice whose cancer cells were resistant to chemotherapy, the team was able to characterize these cells' metabolic profile and observed certain modifications at the level of the mitochondria. Using drugs that specifically blocked VEGF's activation, it was possible to revert these mitochondrial modifications and render these cells vulnerable to chemotherapy.

"Our study contributes to an improved understanding of how cellular metabolism plays an important role in the acquisition of resistance to certain therapeutic agents," said Sérgio Dias. These newly discovered

molecular targets will allow the development of therapeutic strategies that may be explored as possible routes to eliminate leukemic cells' resistance to chemotherapy.

More information: Sandrina Nóbrega-Pereira et al, VEGFR-2-mediated reprogramming of mitochondrial metabolism regulates the sensitivity of acute myeloid leukemia to chemotherapy, *Cancer Research* (2017). DOI: 10.1158/0008-5472.CAN-17-1166

Provided by Instituto de Medicina Molecular