When a cell's 'fingerprint' can be a weapon against cancer

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Centrosome amplification is a hallmark of cancer cells and therefore a promising target for cancer therapy. To circumvent the technical difficulties of profiling centrosome amplification in patient samples, we used the expression of 20 genes known to promote centrosome amplification (CA20) to estimate its relative prevalence across nearly 10,000 human tumours of over 30 cancer types. We found that those genes are indeed highly active in tumours and associated with cancer genome alterations and poor prognosis in different cancer types. By integrating these data with drug screenings in human cancer cell lines, we identify candidate drugs for selectively targeting cancer cells through centrosome amplification. Credit: Bernardo de Almeida, iMM.

A research team led by Nuno Barbosa Morais, group leader at Instituto de Medicina Molecular João Lobo Antunes (iMM) in Lisbon, computationally analysed the expression of marker genes that are

associated with a "fingerprint" of cancer cells in thousands of tumors and revealed its therapeutic potential in the fight against cancer. The study published today in *PLoS Computational Biology* shows the types of tumors in which these genes are most active and identifies drugs that can selectively eliminate cells that carry that label.

The centrosome is an organelle present in all animal cells that is fundamental in several cellular processes, such as division, migration and communication between cells. For more than a century, researchers have believed that the abnormal increase in the number of these structures could induce cancer, and since then, the increase in the number of centrosomes is seen as one of the hallmarks of cancer cells. The technical difficulties in characterising this abnormality in patient samples have prevented its clinical potential or research on a large scale.

The team led by Nuno Barbosa Morais at iMM have now studied the expression of genes that cause this increase and analysed its incidence in thousands of tumors of different types of cancer and in normal tissue samples from the same patients. "The results revealed that this signature is present only in tumor samples, and is more prevalent in aggressive forms of cancer," explains Nuno Barbosa Morais, adding, "More importantly, a higher expression of these genes is associated with a lower survival rate in different types of cancer. "

Using drug sensitivity studies, the scientists also identified selective compounds for cells with this abnormality that could be targeted specifically against cancer cells, leaving healthy cells unaffected. "Additionally, the samples that we have analysed are now characterised at the levels of their DNA sequence and the expression of thousands of genes. This means that the integration of this data allows us to better understand the causes and molecular consequences of this increase of centrosomes in our cells," explains Bernardo de Almeida, the first author of this study.

"The next steps are to translate the expression data of the genes that cause this 'fingerprint' into support information for clinical decision. We also intend to validate the efficacy of the drugs identified by our computational approach as having greater therapeutic potential. These are studies that will naturally involve collaborations with colleagues who are specialists in clinical oncology and pharmacology," says Nuno Barbosa Morais, group leader and supervisor of the study.

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