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# Scientists reveal link between cell metabolism and the spread of cancer

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Scientists at VIB and KU Leuven have discovered a crucial factor in the spread of cancer. A team led by professor Massimiliano Mazzone has demonstrated that the metabolism of macrophages, a particular type of white blood cell, can be attuned to prevent the spread of cancer. The key is in making these macrophages more prone to 'steal' sugar from the cells forming the tumor's blood vessels. As a result, these blood vessels will be structured more tightly, which can prevent cancer cells from spreading to other organs. These conclusions are published in the leading scientific journal *Cell Metabolism*.

Macrophages are types of white blood cells that attack foreign micro-organisms and remove harmful substances within the body. As a result, they are an essential part of our immune system. On top of their positive effect on pathogens, macrophages can also play a negative role in cancer biology. Indeed, tumors contain a lot of specific macrophages that play a decisive role in the formation of blood vessels. In tumors, these vessels traditionally have a chaotic and dysfunctional buildup. As a result, cancer cells are more likely to escape through the vessels, enter the bloodstream and invade other organs.

## Out-of-control vessel creation

While properties of macrophages have already been studied extensively, it remained unknown whether changing their metabolism would impact their functions. The team of prof. Mazzone and Dr. Mathias Wenes

investigated this by blocking a specific gene called REDD1 in the macrophages. This stimulated the cells' glycolysis, the process by which they convert sugar into energy.

Prof. Massimiliano Mazzone (VIB-KU Leuven): "The supply of glucose to a tumor has a negative effect, comparable to giving too much sugar to a child: it causes hyper-activation of many cellular compartments. More specifically, the cells that are forming the blood vessels are getting out of control by this glucose overload. They quickly give shape to a chaotic, irregular vessel network typical to cancer.

By changing the macrophages' metabolism, we actually set up a 'glucose competition' between the macrophages and the tumor's blood vessels. As a result, the macrophages can eat the glucose instead of the blood vessel cells. Because the latter are not overstimulated anymore, they are able to create vessels in a gentler way. This forms a structured and strong vessel barrier around the tumor, preventing cancer cells to escape to the bloodstream and invade distant organs."

## Impact on future therapies

Because of research's many aspects, prof. Mazzone joined forces with the lab of prof. Peter Carmeliet (VIB-KU Leuven), specialized in the formation of blood vessels, and with Bart Ghesquière (VIB-KU Leuven), a leading metabolism expert. Together, they also investigated the consequences of mTOR inhibitors, existing cancer drugs aimed at reducing the growth of tumors.

Prof. Massimiliano Mazzone (VIB-KU Leuven): "These mTOR inhibitors are only partially effective in patients. In mice, we found that these drugs can sometimes increase the spread of cancer because they hinder glycolysis in macrophages. That is why we are currently examining whether we could use our findings to predict people's

resistance to mTOR inhibitors."

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