Changes in cellular degradation hubs can lead to cancer

March 17 2020

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Cancer cells grow and divide in an uncontrolled manner. A new study from Uppsala University now shows how alterations in a cell's degradation hubs, called lysosomes, can cause abnormal cell growth. The

results are published today in the scientific journal *Nature Communications*.

Normal cells have several control mechanisms that prevent them from growing uncontrollably. During the last few years, it has become increasingly clear that these regulatory processes are taking place on the surface of lysosomes, which are small membrane-encapsulated vesicles that function as degradation centers of all cells. A cell can have hundreds of lysosomes that are organized into complex networks. Cancer cells frequently have alterations in the organization of their lysosome networks, although it remains unclear to what degree this contributes to tumor progression.

In the present study, scientists from Uppsala University and Weill Cornell Medicine, U.S., have found that the amount of lysosomes in a lysosomal network affects cellular growth through the activation of a protein called mTOR.

"We saw that when the number of lysosomes increased, mTOR molecules on the lysosomal surface became hyperactivated. Since mTOR is a central stimulator of cellular growth, this leads to increased growth," says Anders Mutvei, researcher at the Department of Immunology, Genetics and Pathology, Uppsala University, who led the study together with John Blenis at Weill Cornell Medicine.

The scientists also identified another protein, Rap1, that regulates both the number of lysosomes present in the lysosomal network, and its organization.

"Although this study is in an early phase, it demonstrates that lysosomes play a central role in cellular growth control. We need more knowledge about how changes in a lysosomal network contribute to cancer, which is something we are about to test in models of human cancers," says

Anders Mutvei.

More information: Rap1-GTPases control mTORC1 activity by coordinating lysosome organization with amino acid availability (2020) *Nature Communications*, DOI: 10.1038/s41467-020-15156-5

Provided by Uppsala University