Lack of oxygen in cancer cells leads to growth and metastasis

September 13 2012, by Garth Sundem

CD24 is a rational target in hypoxic cancers. Image: Flickr/emiliokuffer

(Medical Xpress)—It seems as if a tumor deprived of oxygen would shrink. However, numerous studies have shown that tumor hypoxia, in which portions of the tumor have significantly low oxygen concentrations, is in fact linked with more aggressive tumor behavior and poorer prognosis. It's as if rather than succumbing to gently hypoxic conditions, the lack of oxygen commonly created as a tumor outgrows its blood supply signals a tumor to grow and metastasize in search of new oxygen sources – for example, hypoxic bladder cancers are likely to metastasize to the lungs, which is frequently deadly.

A University of Colorado Cancer Center study recently published in the journal Cancer Research details a mechanism by which these hypoxic conditions create aggressive cancer, with possible treatment implications

for cancers including breast, ovarian, colorectal, pancreatic, prostate, bladder and other cancers.

"We've known that the protein HIF-1a is overexpressed in hypoxic tumors. And we've known that the cancer stem cell marker CD24 is overexpressed in many tumors. This study shows a link between the two – the HIF-1a of hypoxia creates the overexpression of CD24. And it's this CD24 that creates a tumor's aggressive characteristics of growth and metastasis," says Dan Theodorescu, MD, PhD, director of the University of Colorado Cancer Center and the paper's senior author.

Outgrowing the blood supply leads to tumor hypoxia, which leads to overexpression of HIF-1a, which signals the production of CD24, which makes tumors grow and metastasize. In addition to aggression, CD24 has also been shown to confer resistance to chemotherapy, allowing this small population of cells to regrow the tumor once chemotherapy ends, leading to relapse and disease progression.

"Now imagine we target CD24," Theodorescu says. "Either by removing a cell's ability to make CD24 or by killing cells marked by this protein, it's likely we could disarm this most dangerous population of cells."

Theodorescu and colleagues showed this by adjusting levels of HIF-1a and CD24 in cancer cell samples and animal models. With HIF-1a low and yet CD24 artificially high, cells retained the ability to grow and metastasize. With CD24 low and yet HIF-1a artificially high, cell survival and proliferation decreased.

"It seems CD24 overexpression in hypoxic cells drives growth and metastasis in these hypoxic tumors," Theodorescu says. "Now we have a rational target: CD24 for these hypoxic tumors."

More information: cancerres.aacrjournals.org/con …

CAN-11-3666.abstract

Provided by University of Colorado Denver