Reactive oxygen's role in metastasis

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Researchers at the Burnham Institute for Medical Research have discovered that reactive oxygen species, such as superoxide and hydrogen peroxide, play a key role in forming invadopodia, cellular protrusions implicated in cancer cell migration and tumor metastasis. Sara Courtneidge, Ph.D., professor and director of the Tumor Microenvironment Program at Burnham's NCI-designated Cancer Center, and colleagues have found that inhibiting reactive oxygen reduces invadopodia formation and limits cancer cell invasion. The study was published on September 15 in the journal *Science Signaling*.

In a companion paper, published in the same issue of *Science Signaling*, Gary Bokoch, Ph.D., of The Scripps Research Institute, in collaboration with Dr. Courtneidge, found that the proteins Tks4 and Tks5, commonly expressed in cancer cells, are functionally related to p47phox, a protein found in phagocytes that is part of a complex that is instrumental in producing reactive oxygen to mount an immune response.

"Reactive oxygen has a complex cellular role," said Dr. Courtneidge. "Normal cells use reactive oxygen to signal, grow and move. Immune cells, such as neutrophils, produce reactive oxygen to destroy bacteria. Now we find that reactive oxygen is necessary for invadopodia formation, which allows cancer cells to become metastatic."

Invadopodia facilitate cancer cell migration by breaking down the extracellular matrix that normally keeps cells in place. In previous research, Dr. Courtneidge discovered that Tks5 is crucial for invadopodia formation. The structural similarities between Tks5 and

p47phox, which is part of the NADPH oxidase (Nox) system, led Dr. Courtneidge to consider the role reactive oxygen plays in invadopodia formation.

Using invadopodia-rich mouse fibrosarcoma cells, the Courtneidge laboratory tested a number of antioxidants and found both a marked reduction in invadopodia formation and invasive behavior. In addition, the team inhibited expression of Nox family enzymes with siRNA and had similar results, demonstrating that NADPH oxidases are involved in invadopodia formation. The scientists repeated these experiments with human melanoma, head and neck and breast cancer cell lines and also saw a marked reduction in invadopodia formation.

With the discovery of reactive oxygen's role in invadopodia formation, researchers have additional possibilities for drug intervention. Future research and drug development may focus on inhibiting NADPH oxidase activity and limiting invadopodia formation to prevent cancer cell migration.

Source: Burnham Institute (news : web)