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Researchers discover mechanism of cell type-specific signaling in tumor development

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Mayo Clinic researchers have discovered the mechanisms behind two key checkpoints in cell growth and development — factors that may ultimately allow investigators to benchmark progression of tumor cells or stop them from further development. The findings appear in the current online issue of *Developmental Cell*.

The team led by Edward Leof, Ph.D., Mayo Clinic biochemist, demonstrated that p21-activated kinase 2 (PAK2), a key target for cancer growth and fibrotic tissue development, is activated in one type of tissue but not another. PAK2 is a downstream component of transforming growth factor beta (TGF-β) signaling in mesenchymal cells — those that make up connective tissues in the body, as well as blood and lymphatic vessels. However, TGF-β is unable to activate PAK2 in epithelial cells — those that make up external and internal linings, such as skin and the internal lining of many vessels.

"We decided to look at the factors that prevented PAK2 activation in epithelial cells," says Dr. Leof. "We found that a protein called Erbin, in cooperation with the NF2 tumor suppressor Merlin, controls the outcome."

Erbin, the researchers found, controls the tumor suppressor gene Merlin. When Merlin is absent or mutated, the result is schwannoma, a form of tumor involving Schwann cells which make up the myelin sheath that covers nerves. Merlin has also been shown to play a part in causing melanoma, mesothelioma and possibly colorectal cancers.

The researchers showed that in epithelial cells, which have high levels of Erbin, the formation of an Erbin/Merlin complex prevents PAK2 activity following growth factor stimulation. In the absence of Erbin (or Merlin), however, TGF-β stimulates PAK2 activity in some epithelia, overcoming a critical checkpoint in tumor progression.

The findings are important, says Dr. Leof, because they delineate a process by which tumors might be formed and allow future researchers to pinpoint steps where interventions could not just gauge disease progression, but halt tumor growth. There is even the prospect of intervening before a tumor begins to form.

Source: Mayo Clinic (news : web)