Blocking antioxidants in cancer cells reduces tumor growth in mice

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Many cancers have adapted to cope with high levels of immune system-produced free radicals, also referred to as reactive oxygen species, by overproducing antioxidant proteins. One of these proteins, superoxide dismutase 1 (SOD1), is overproduced in lung adenocarcinomas and has been implicated as a target for chemotherapy.

In this issue of the *Journal of Clinical Investigation*, Navdeep Chandel and colleagues from Northwestern University report the effects of a SOD1 pharmacological inhibitor on non-small-cell lung cancer (NSCLC) cells. The inhibitor, called ATN-224, stunted the growth of human NSCLC cells in culture and induced their death. The researchers also found that ATN-224 inhibited other antioxidant proteins, which caused high levels of hydrogen peroxide inside the cells. The ability of cancer cells to produce hydrogen peroxide was required for ATN-224-dependent effects, because hydrogen peroxide activated cell death pathways.

Furthermore, ATN-224 induced cancer cell death and reduced tumor sizes in a mouse model of lung adenocarcinoma. ATN-224 dependent effects in animals were improved when the inhibitor was used in combination with another drug that activates programmed cell death.

This study suggests inhibition of antioxidants may be a viable chemotherapeutic option.

More information: Targeting SOD1 reduces experimental non–small-

cell lung cancer, J Clin Invest. DOI: 10.1172/JCI71714