Neddylation inhibition marks esophageal cancer cells for death

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Video Byte

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Abstract

Neddylation is the process by which the molecule NEDD8 is attached to cellular proteins. Elevated neddylation in the body has been linked to various cancers. Inhibiting this protein modification has therefore become a promising anticancer strategy. A new study describes how researchers used this anti-neddylation approach to kill esophageal cancer cells. The team treated lab-grown esophageal cancer cells with MLN4924, a known neddylation inhibitor. They found that MLN4924 indirectly led to the programmed cell death, or apoptosis, of the cancer cells. By reducing neddylation, MLN4924 actually promoted a cell survival mechanism known as autophagy. Autophagy keeps cells healthy and alive by clearing harmful debris. Interestingly, it also gave the researchers access to a “kill switch” for diverting from autophagy to apoptosis. That switch came in the form of the protein ATF3, which can be silenced to cause cell death. By combining MLN4924 with an ATF3 inhibitor, the team effectively programmed esophageal cancer cells to die. Manipulating this cellular circuitry could lead to effective ways of fighting against forms of esophageal cancer.