The youth hormone DHEA in the treatment of liver cancer: die another way

Hepatocellular carcinoma (HCC) is a common form of malignant liver tumor and one of the leading causes of death all over the world.

As for other types of cancer, many drugs have been developed and tested with the aim of killing malignant cells by promoting a process of cell death (known as *apoptosis)*, and safeguarding healthy ones. Unfortunately, due to their plasticity, tumor cells often acquire the ability to repel drug-induced apoptosis and HCC cells make no exception. One good strategy may be to kill tumor cells by a mechanism of death other than apoptosis. The scientific community is in a constant race for finding new molecules to overcome this obstacle.

Dehydroepiandrosterone (DHEA) is a natural cholesterol-derived molecule and a precursor of sexual hormones. DHEA has been defined the “youth hormone” as its blood levels peak at 25 age and progressively decline at a rate of about 2% a year. Can you guess? The idea that DHEA’s decline could be the cause of various age-related disorders (e.g. diabetes, inflammation, cancer …) is becoming more and more convincing. Moreover, DHEA enforces the immune system and improves mood and memory. More importantly, DHEA is a safe molecule with few side effects: even sportsmen take it to build up bone and muscle strength!

Since little was known about the activity of DHEA as an anti-cancer molecule in HCC, our group investigated the possibility that it could kill hepatoma cells. We discovered that DHEA kills liver cancer by a death process known as programmed cell death type II (PCD II) or autophagic cell death, quite different from classical apoptosis. Going into detail, DHEA primes the massive activation of the protein p62, which is responsible for PCD II and the killing of about 50% tumor cells in only 24 hours. This effect seems to be very specific for HCC, since DHEA is able to destroy cervix carcinoma cells too, instead by triggering canonical apoptosis.

Our study sheds light on a new role for DHEA as an appealing adjuvant to use in combination with common chemotherapeutic drugs for the treatment of liver cancer. Indeed, DHEA may help to eliminate that percentage of tumor cells stubborn to perish from apoptosis by inducing a different way of dying.

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Dehydroepiandrosterone triggers autophagic cell death in human hepatoma cell line HepG2 via JNK-mediated p62/SQSTM1 expression.
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