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Alireza Heidari
a) Faculty of Chemistry, California South University, 14731 Comet St. Irvine, CA, USA
b) Bio-Spectroscopy Core Research Laboratory, California South University, 14731 Comet St. Irvine, CA, USA
c) Cancer Research Institute (CRI), California South University, 14731 Comet St. Irvine, CA, USA
d) American International Standards Institute, Irvine, CA, USA

Elena Locci
a) Faculty of Chemistry, California South University, 14731 Comet St. Irvine, CA, USA
b) Bio-Spectroscopy Core Research Laboratory, California South University, 14731 Comet St. Irvine, CA, USA
c) Cancer Research Institute (CRI), California South University, 14731 Comet St. Irvine, CA, USA

Silvia Raymond
a) Faculty of Chemistry, California South University, 14731 Comet St. Irvine, CA, USA
b) Bio-Spectroscopy Core Research Laboratory, California South University, 14731 Comet St. Irvine, CA, USA
c) Cancer Research Institute (CRI), California South University, Comet St. Irvine, CA, USA

Correspondence
Alireza Heidari
a) Faculty of Chemistry, California South University, 14731 Comet St. Irvine, CA, USA
b) Bio-Spectroscopy Core Research Laboratory, California South University, 14731 Comet St. Irvine, CA, USA
c) Cancer Research Institute (CRI), California South University, 14731 Comet St. Irvine, CA, USA
d) American International Standards Institute, Irvine, CA, USA

Emerging concepts for immune checkpoint blockade-based combination therapies

Alireza Heidari, Elena Locci and Silvia Raymond

Abstract
Aging is a condition in which the cell cycle is essentially irreversible and is caused by a variety of stressors such as obesity, radiation and chemotherapy. Aging cells that accumulate in the body during this period communicate with surrounding tissues through the production of pro-inflammatory proteins, called the SASP, and play a number of physiological and pathological roles. In the elderly, inflammatory agents of SASP increase various age-related diseases, including cancer; therefore, clarification of the SASP monitoring mechanism is essential for the development of new prevention and treatment strategies against age-related cancer. A group of Cancer Research Institute (CRI) of California South University researchers have hypothesized that the abnormal chromatin architecture observed in aging cells is related to SASP, and have begun analyzing chromatin interaction at the genome level and gene expression using next-generation sequencing techniques. They showed that the region containing the pericentromeric repetitive sequences called Human Satellite II (hSATII), which is genetically inactive in normal cells, has a significant state in aging cells; In addition, non-coding RNA expression (hSATII RNA) was significantly regulated during cellular aging. Further analysis showed that hSATII RNA regulated the expression of SASP-like inflammatory genes by disrupting chromatin interactions in some regions of the SASP gene through dysfunction of the CCCTC-binding factor (CTCF), which is important for maintaining genomic integrity. Small extracellular vehicles (EVs) secreted by cancer cells and stromal cells are dynamically involved in the development and progression of non-cellular tumors in the tumor microenvironment, and surprisingly more than the amount of hSATII RNA in small EVs caused by aging cells. Thus, our data suggest that hSATII RNA derived from aging stromal cells is transported to surrounding cells via small EVs and acts as an SASP-like inflammatory agent in the tumor microenvironment. In addition, the researchers found that hSATII RNA could be detected in cancer cells in surgical specimens of patients with primary colon cancer. Significantly, the population of hSATII-positive RNA cells was higher among cancer-associated fibroblasts than in fibroblasts in normal stromal tissues. These findings demonstrate the new role of hSATII RNA, which supports non-cellular tumor growth by secreting inflammatory agents similar to SASPs and small EVs. Understanding this molecular mechanism could facilitate new preventive and therapeutic development and provide solutions for future age-related injuries.

Keywords: Cancer, cells, tissues, tumors, prevention, prognosis, diagnosis, imaging, screening, treatment, management

1. Introduction
Most cancer cells are killed when trying to metastasize, which is a very stressful process. Few immortals have the ability to overcome the mechanism of cell death due to stress. We find that cholesterol plays a key role in boosting this ability. These studies have shown that cancers caused by the hormone estrogen benefit from cholesterol derivatives that act like estrogen and cause cancer to grow. But there was a contradiction between estrogen-negative breast cancer and estrogen. These cancers are not estrogen dependent, but high cholesterol is still associated with worse diseases, suggesting that different mechanisms may be involved. In the current study, using cancer cell lines and mouse models, Cancer Research Institute (CRI) of California South University researchers found that the migration of cancer cells in response to stress swallowed cholesterol, but if it did not lead to death, it would make the patient stronger and increase his resistance to fructose. A natural process in which cells are exposed to stress. These stress-resistant cancer cells then proliferate and metastasize easily. This process appears to be used not only by ER-negative cancer cells, but also by other types of tumors, including melanoma and the identified mechanisms can be targeted by treatment. Opening this pathway has highlighted new approaches that may be useful in treating advanced diseases.

Contemporary therapies are evolving, and the important point is that these findings once again show why lowering cholesterol, whether with medication or diet modification, is a good idea for better health [1–200].

2. Results and Discussion

Immunotherapy helps strengthen the body's immune system to fight cancer cells. Immune checkpoints regulate the immune system, which are very important in preventing the body from attacking healthy cells. Some cancers bypass these checkpoints and allow the cancer cells to continue to spread from the bite detected by the immune system. Blocking an Immune Checkpoint (ICB) is a new treatment that can basically release the brakes on the immune system and help the body fight the disease again. ICB treatments are effective for some types of cancer, but they do not work for every patient. For example, only about 4 percent of patients with colorectal cancer, the second leading cause of cancer death in the United States, respond to ICB treatment. Recent research has focused on ways to increase the potency of ICB therapies by combining them with chemotherapeutic agents such as computation. Although computation is strong, it is also unstable, has little solubility in water, and can have serious side effects on healthy cells. Using the nanotechnology delivery method, the researchers increased the ability of computation to integrate with ICB therapies and made them more effective against invasive tumors. This nano therapy platform was able to increase the effectiveness of ICB treatment to eradicate a large proportion of colorectal cancer tumors in the early stages, while simultaneously activating the body's immune system and preventing tumor recurrence. Our research team linked computation to sphingomyelin, a natural fat found on the cell surface. Combining these two molecules into one nanoparticle improves treatment efficiency and reduces systemic toxicity. The nanotechnology-based drug delivery method also improved drug uptake in the rodent model, where penetration into the tumor is improved by efficient release of chemotherapy drug into the tumor.

3. Conclusions

The researchers tested the device on 90 people who had been screened for lung cancer and had remarkable results; The device detected almost 90% of cancer cases, however, researchers hope that better screening and diagnosis technologies can detect more cases of lung cancer earlier, which could greatly speed up patients' recovery. These results suggest that Delphi lung cancer screening technology can reduce lung cancer mortality by providing a high-performance, eligible trial to qualified individuals. We have already started enrolling 1,700 patients for testing and clinical evidence to finalize the commercialization of lung screening. Blood tests are much easier and more common than low-dose CT scans (LDCTs). Allows them to be tested at shorter intervals. It makes perfect sense to use artificial intelligence technology to identify tumor cells, and this is not the first time this feature has been used to diagnose cancer, and other systems have been able to diagnose colon cancer and breast cancer.

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Spectroscopy, Infrared Photo dissociation Spectroscopy, Infrared Correlation Table Spectroscopy, Near–Infrared Spectroscopy (NIRS), Mid–Infrared Spectroscopy (MIRS), Nuclear Resonance Vibrational Spectroscopy, Thermal Infrared Spectroscopy and Photothermal Infrared Spectroscopy Comparative Study on Malignant and Benign Human Cancer Cells and Tissues under Synchrotron Radiation with the Passage of Time", Glob Imaging Insights 2018;3(2):1-14.

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