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Commentary

Commentary to "Carrimycin, a first in-class anti-cancer agent, targets selenoprotein H to induce nucleolar oxidative stress and inhibit ribosomal biogenesis"☆

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On January 2, 2023, *Cancer Pathogenesis and Therapy (CPT)* published an online article entitled "Carrimycin as an anticancer candidate inhibits tumors by targeting selenoprotein H in the nucleus of tumor cells to induce nuclear oxidative stress and inhibit ribosome biosynthesis," authored by Yu LC et al.[1] from the National Cancer Institute of the National Institutes of Health. Yu LC et al.[1] discovered that isovalerylspiramycin I (ISP I)—the key active ingredient of carrimycin[2]—directly inhibits selenoprotein H (SELH) expression. As the sole antioxidant enzyme in the nucleolus, SELH serves key regulatory roles in relation to numerous oxidants produced during rapid rRNA synthesis. Such synthesis often occurs during the intense protein production of high cellular activity associated with rapid cancer cell growth, acute inflammation, and host-cell infection by viruses. Thus, SELH affects not only the stability and homeostasis of the internal reactive oxygen species (ROS) environment but also ribosome biogenesis in tumor cells. Inhibition of SELH by ISP I leads to cell cycle arrest and tumor cell apoptosis, ultimately inhibiting tumor growth and metastasis without significantly impacting on normal cellular functions.[3] By revealing a link between the disruption of ROS homeostasis, induced by carrimycin-mediated SELH inhibition, and ribosome biogenesis dysregulation in tumor cells, Yu LC et al.[1] direct our attention beyond traditional perceptions about the purely bactericidal and anti-inflammatory roles of antibiotics toward a new paradigm for cancer treatment. Furthermore, illuminating the mechanism of ISP I may provide clues to the maintenance of a stable ribosomal environment and pathological state characterized by a high protein-synthesis burden. Such insights could pertain to the disruption and dysregulation of oxidative stress response in the nucleolus of host cells under acute viral infection and acute inflammatory disease, respectively, which also may involve similar mechanisms of SELH. Accordingly, this study points the way to future exploration of pathological states under viral infection and inflammatory stress. Additional advanced experimental work on the antiviral effects of carrimycin is underway worldwide.[4]

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Conflicts of interest

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