STING-rich Ciliated Cells Protect the Fallopian Tube From Early Transformation in the Development of Ovarian Cancer

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High-grade serous ovarian cancer (HGSOC) remains the fifth leading cause of cancer death among women. It has recently been demonstrated that stimulator-of-interferon genes (STING) is highly expressed in the fallopian tube epithelium (FTE), with its highest expression concentrated in ciliated cells; however, STING's expression is lost in HGSOC. It remains unknown at which stage along HGSOC's development STING is lost. Given STING's well-studied role as a sensor of genomic stress and the fact that in HGSOC, tumorigenesis is driven by the genomic stress of monthly ovulation, I hypothesized that loss of STING-expressing cells may permit the accumulation of genomic stress. I then assessed the tumor- suppressive role of STING through accumulation of DNA damage markers, p53 activity, and cell survival. I demonstrate that loss of STING activity is a driver of early-stage disease by permitting the accumulation of genomic instability. Despite evidence that STING-deficient cells acquire equal or higher DNA damage when challenged with an ovulation memetic, these cells are able to evade apoptosis resulting in unabated cell growth. This study also demonstrates that STING is lost in humans in the earliest known precursor lesions of the fallopian tube, p53 signatures, indicating that this event is an early and prevalent feature in the development of FTE-derived HGSOC. Taken together, these data indicate that loss of STING may permit a fertile ground for a pro-proliferative and mutagenic microenvironment in the fallopian tube, driving malignancy.