A new miRNA-Modified coxsackievirus B3 inhibits triple negative breast cancer growth with improved safety profile in immunocompetent mice

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**Presenter:** Yi-Hui Su                      **Date/Time:**2023/09/07 15:10-16:00

**Commentator:** Pai-Sheng Chen **Location:** Room 601, Med College Building

**Background:**

Breast cancer, the most prevalent malignancy and the second leading cause of cancer-related death among women, exhibits distinct molecular subtypes. TNBC(ER-/PR-/HER-), the most aggressive subtype, constitutes around 15-20% of breast cancer cases and is associated with a bleak prognosis, high recurrence rates. Oncolytic viruses (OVs) are a class of viruses with the capacity to selectively infect and eliminate cancer cells, sparing normal tissues. They achieve this through two main mechanisms: direct killing of cancer cells via lytic virus infection and triggering an immune response against cancer by releasing various immune-stimulating agents. including pathogen-associated molecular patterns (PAMPs), danger-associated molecular patterns (DAMPs), cytokines, tumor-associated antigens (TAAs) and neoantigens. One of the main approaches to diminish off-target effects of RNA OVs is adding target sequences (TS) of microRNAs (miRNAs), which are highly expressed in normal tissues. but downregulated in cancer cells, into viral genome.

**Results:**

The authors engineered a modified CVB3 virus by inserting TS of specific miRNAs (miR-145 miR-143 and organ specific miR-1 miR-216 ). Both WT-CVB3 and miR-CVB3-1.1 effectively target tumor cells, triggering immune cell recruitment and inhibiting metastasis, notably in the lungs. However, WT-CVB3's tumor-suppressing ability is overshadowed by severe toxicity, causing lower survival rates than PBS treatment. miR-CVB3-1.1 offers a safer alternative, outperforming its predecessor, miR-CVB3, in terms of safety. It successfully infects and lyses TP53/RB1 mutant SCLC cells and various breast cancer cells, except MCF-7, attributed to MCF-7's low CAR expression and potent anti-viral IFNB1 production. These findings underscore miR-CVB3-1.1's safety and potential for tumor treatment, particularly in Balb/c animal models, showcasing its promise as a viable therapeutic option with enhanced safety and broad effectiveness.

**Conclusion:**

The miR-CVB3-1.1 is a promising candidate for clinical treatment of breast cancer, which highlights a promising avenue of using a genetic engineered miRNA-targeting CVB3 virus in cancer therapy.