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Gefitinib resistant lung cancer stem cell associated bulky-ball-like nucleolus as p53 molecular cage is resolved in soft-X-ray tomography

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The enlarged distinct nucleolus matrix assembly is observed in most cancer stem cells (CSCs); however, the detail structure of the recent discovered bulky-ball-like nucleolus and its underlying mechanism is largely unknown. Here we show that matrix metalloproteinase-7 (MMP-7) mediates shedding of surface receptor MUC-1 SEA domain releasing the MUC-1 C-ter and insulating tumor suppressor p53 in the bulky-ball-like nucleolus compartment in gefitinib-resistant lung CSCs. MUC-1 C-ter mediating nucleolus trafficking of p53, attributes to the CSC chemo-resistant phenotype. The nucleolus colocalizations of p53, MUC-1 C-ter, MMP-7 and nucleolin were observed in the gefitinib-resistant EGFR^{L858R/T790M} CSC colonies. Salinomycin, an anti-CSC agent, disrupted the nucleolus by inducing nucleoplasm translocation of p53 and sensitized CSC to chemotherapy drug. It is the first time to reveal the detail architecture of the bulky-ball-like nucleolus in soft-X-ray tomography. Thus, this

study highlights the nucleolus as a potential therapeutic target for anti-CSCs to resolve the chemotherapy-resistance dilemma.

Keywords – nucleolus, shedding, cancer stem cell(CSC), chemoresistance, MUC-1

References:

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