HPV-E6 enriches CD71(+) population which promote radio-resistance in cervical cancer cells

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Abstract

Subpopulation of cells has been suggested to reside in tumors that possess the ability to initiate tumor cell growth and contribute to resistance of cancer therapy. Using flow cytometry and specific cell surface marker, we identified CD71(+) subpopulation possessed cancer stem cell-like characteristics and more radio-resistant than CD71(-). The size of the CD71(+) population was initially examined by flow cytometry using cell surface marker CD71 and was found ranging from 7.4% to >90%. ME180 and C33A have a CD71(+) population of 96.7% and 7.4% respectively and were chosen for the isolation of CD71(+) cells. Anchorage independent soft agar assay revealed enhanced transforming ability in CD71(+) subpopulation cells. Greater resistance to γ-irradiation were also observed in CD71(+) cells and the fraction of cells expressing CD71 was enriched after irradiation treatment. Furthermore, higher mRNA expressions of certain "stemness" genes, including Oct-4, Nanog, ABCG2 and Bmi-1, were detected in CD71(+) than CD71(-) cells isolated from cervical cancer cell lines and primary cervical cancer cells. In addition, we found that abundant CD71(+) population was detected in HPV-positive cervical cancer cell lines and ectopic expression of HPV-E6 protein in HPV-negative cervical cancer cells (C33A) enriched CD71(+) population. These findings suggest that HPV-E6 enriches CD71(+) population which promote tumor progression and radio-resistance in cervical cancer cells. Targeting CD71 by siRNA or specific anti-CD71 antibody may provide new insight for the establishment of novel strategies and effective therapies for cervical cancer.