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The epithelial mesenchymal transition property is involved in cell-in-cell structure between lung cancer and natural killer cell line

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Lung cancer is among the most deadly cancers for both men and women. Immunotherapy is a breakthrough treatment in oncology that uses the body's own natural defense system to fight off cancer. Higher numbers of T cells, natural killer cells, and/or dendritic cells are associated with better patient survival. In particular, NK cell therapy has the advantages of safety, economy, and versatility. Several studies have been undertaken to increase the target and efficacy of NK cell therapy, such as antibody or CAR-T therapy. We observed that when NK cells co-cultured with lung cancer cell line A549, NK cells entered A549 to form a cell-in-cell (CIC) structure and immune cells die. Previous reports have suggested that CIC structures may be formed depending on the characteristics of immune cells, but we assumed that CIC-associated cancer cells may have different characteristics from those of other cancer cells. In order to prove this, CIC-engrafted cancer cells and non-CIC cancer cells were sorted at the same time and proliferation, NK killing effect, foci, soft agar, migration, and invasion assays were performed. As a result, a more malignant phenotype was observed in CIC-engrafted cancer cells. To confirm the reason, proteomics and transcriptomics analysis showed that the epithelial mesenchymal transition (EMT) property in CIC-engrafted cancer cells. EMT marker analysis and phalloidin staining validated these results. The population of CIC-engrafted cancer cells after sorting CIC-engrafted cancer cells repeatedly co-cultured with A549 at the 2nd, 3rd and 4th cycles showed no significant change. Therefore, the EMT properties of CIC-engrafted cancer cells seem to be a temporary phenomenon that occurs dynamically in the cancer environment, not permanently maintained. In order to increase the efficacy of NK cell therapy, it is necessary to consider the study of targeting CIC-engrafted cancer cells.

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