Poster Session (Poster presentations categorized by each organ)

**P2 – 25 – 5**

**EFFICACY OF NAB-PACLITAXEL ON 5-FUOROURACIL (5FU) RESISTANT HUMAN GASTRIC CANCER CELL LINES**

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**Purpose:** 5-Fluorouracil (5FU)-based combination chemotherapy is widely used for the treatment of advanced gastric cancer in Japan. Thus, the development of effective chemotherapy for 5FU-resistant gastric cancer after 5FU-based chemotherapy is important. Nab-paclitaxel (Nab-PTX) is an albumin-bound, 130nm particle form of paclitaxel that exhibits a higher activity and lower toxicity than solvent-based paclitaxel. In the present study, the activity of Nab-PTX alone or in combination with 5FU was evaluated in four 5FU resistant cell lines.

**Method:** 5FU-resistant human gastric cancer cell lines were established from parent cells (MKN-45, MKN-74, NCI-N87, and KATO-III) by continuous exposure to 5FU for over a one-year period. The sensitivities of these cell lines to 5FU and Nab-PTX were evaluated using the WST-8 colorimetric assay. The effects of the combination of 5FU and Nab-PTX was evaluated by the combination index (CI) value. The gene expressions of secreted protein acidic and rich in cysteine (SPARC) was evaluated using a Whole Human Genome 44K oligo DNA microarray of Agilent Technologies.

**Results:** The IC\textsubscript{50} value of 5FU ranged from 2.35 to 36.7 µM, and its ratio (resistant/parent) ranged from 2.6 to 15.6. The IC\textsubscript{50} value of Nab-PTX ranged from 4.45 to 54.5 nM, and its ratio ranged from 1.0 to 1.2. Therefore, Nab-PTX showed no signs of cross-resistance to 5FU. The calculated CI value treated with 5FU and Nab-PTX was approximately 1; therefore, Nab-PTX additively inhibited the cell growth in combination with 5FU. Interestingly, the combination of 5FU and Nab-PTX had an additive activity in the 5FU-resistant cell lines. The relative expression of SPARC mRNA in the resistant cell lines to that in the parent ones ranged from 0.86 to 1.47, and SPARC expression might be weakly correlated with the acquisition of 5FU resistance.

**Conclusion:** Nab-PTX might be a promising agent for the treatment of 5FU-resistant human gastric cancer when used alone or in combination with 5FU.