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Poster

## [P25-10] P25-10: Oncologic drugs (2)

Chair: Takuya Iwamoto, Japan

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## [P25-10-6] Prohibitin 1, potential predictive marker of oxaliplatin response of colorectal cancer cells

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### Background

Oxaliplatin (L-OHP) is a key drug used for the treatment of colorectal cancer (CRC). L-OHP and 5-Fluorouracil (5FU) based chemotherapy (FOLFOX) have yielded high response rates (~50%) and good overall survival. However, approximately half of patients who receive FOLFOX gain no benefit despite the incidence of side effects. Therefore, it is desired to find predictive markers for response to L-OHP. In this study, we aimed to identify a predictive marker of response to L-OHP in human CRC cells. By means of proteomic approaches using two-dimensional difference gel electrophoresis (2D-DIGE), we identified a candidate protein that expressed differently in various CRC cells depending on the sensitivity to L-OHP.

### Methods

IC<sub>50</sub> value for L-OHP measured by MTS assay identified varied sensitivity to this drug in various human CRC cell lines. We performed a differential proteomic analysis between CRC cell lines displaying higher and lower sensitivity to L-OHP using 2D-DIGE. Spots of proteins, which expression level correlated strongly with the sensitivity to L-OHP, had been identified by LC-MS/MS. For validation of identified proteins, we examined the expression of each protein by immunoblot analysis in 9 CRC cell lines. We depleted the candidate protein by siRNA and evaluated the change in IC<sub>50</sub> value for L-OHP. In addition, we measured association of the protein with sensitivity to other anti-cancer drugs.

### Results

Proteomics analysis was performed to compare between low and highly sensitive cell lines and identified 21 unique differentially expressed proteins. Among them, the protein expression of spot1536 in highly sensitive cells was 2 times higher than that in low sensitive cells (P=0.00025). Spot1536 was identified as a Prohibitin1 (PHB1). Protein expression of PHB1 was correlated with IC<sub>50</sub> value for L-OHP by immunoblot (R<sup>2</sup>=0.6537, P<0.01). Knockdown of PHB1 by siRNA decreased the sensitivity to L-OHP in human CRC cell lines.

### Conclusions

This study found that PHB1 was highly expressed in high sensitive CRC cell lines and that PHB1 expression level was strongly correlated with the response to L-OHP. Therefore, PHB1 is considered a potential biomarker predictive of response to L-OHP for CRC.