

Bosch Institute Annual Scientific Meeting 2012

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Title	Platinum drugs applied to ovarian tumour models
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Ovarian cancer is the most common cause of gynaecological cancer deaths and the sixth most common cause of cancer-related deaths among Australian women. The disease remains an on-going challenge due to the development of drug resistance and also because the cancer is likely to have metastasized at the time of diagnosis. Chemotherapy based on platinum drugs is the primary treatment option for the disease after reductive surgery. Diverse strategies may be employed to overcome the mechanisms of resistance based on the multi-factorial nature of platinum resistance. Increasing the level of cellular accumulation of platinum, preventing the deactivation of platinum drugs, increasing the level of platinum–DNA binding and reducing the tolerance of platinum-DNA adducts can be engaged to overcome resistance.

Cisplatin is thought to cross the cell membrane by carrier-mediated transport and passive diffusion. One influx carrier for cisplatin is the copper transporter CTR1. Counterintuitively, cisplatin triggers the down-regulation of CTR1 through proteasomal degradation. A proteasome inhibitor, bortezomib, is found to prevent cisplatin-induced down-regulation of CTR1 so that in the presence of bortezomib, the cellular uptake of cisplatin and consequently the level of its binding with the DNA may be increased.

In this study synergism in activity from the sequenced combination of the three platinum drugs widely used in the clinic: cisplatin, carboplatin and oxaliplatin with bortezomib in the human ovarian A2780, A2780^{cisR} and A2780^{ZD0473R} cancer cell lines has been investigated.

The results show that in presence of bortezomib both cellular accumulation of platinum and the level of platinum–DNA binding are increased in line with the idea of protective role being played by bortezomib namely the prevention of CTR1 degradation.

† Underline presenting author

Would you like to be considered for a three-minute oral presentation?		NO
Are there any dietary preferences that we need to be informed of?	NO	