

Cover letter

9/11/2016

To.

Editor in Chief

International Journal of Integrated Health and Science

Dear Sir,

Please find the submission of our manuscript,

**Morphological changes of cisplatin-resistant human breast cancer
MCF-7 cell line**

which we would like to submit for publication in the International Journal of Integrated Health Science. Herewith, we also attached *3 sets of manuscript (hard copy) and 1 CD (soft copy)*.

In this manuscript, we evaluated morphological changes of breast cancer cell line MCF-7 following the development acquired resistance towards cisplatin. The cisplatin resistant subline MCF-7/CisR was developed *in-vitro* by cultivating the parental cell line cisplatin sensitive MCF-7 with raising concentration of cisplatin (from 0.01 to 2.3 μM) for four months. The resistance was showed by the increase of IC_{50} by 9 folds on MCF-7/CisR compared to the initial IC_{50} value of MCF-7. The change on cisplatin cytotoxic potency on the resistant cell line was accompanied by the morphological modification, including the enlargement of cell size, the increase of nucleus and cytoplasm ratio, and the increase of the number of microvesicular and cytoplasmic granules. This result has supported the underlying mechanism of cisplatin resistance, including the ability of the cells to decrease intracellular cisplatin concentration and to repair DNA damage effects.

Author and co-author have agreed with the contents of the manuscript and there is no financial interest to report. We certify that the manuscript submitted is an original work and is not under review at any other publication. We thank you for considering our manuscript for publication in the International Journal of Integrated Health Science and look forward to hearing from you at your earliest convenience.

Sincerely yours,

(DR. Nanda Ayu Puspita, dr, M.Kes)