中文題目：一種利尿酸衍生物氟化丁基利尿酸醯胺的抗癌作用與癌細胞內表現性低的穀胱甘肽 S-轉移酶 π1 有關

英文題目：The anti-cancer activity of an ethacrynic acid derivative Fluoro-butyl ethacrynamide is related to low expression of glutathione S-transferase π1 in cancer cells

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Background: Ethacrynic acid (EA), a once commonly used loop diuretic drug, is a glutathione S-transferaseπ1 (GSTπ1) inhibitor with weak antiproliferative ability in tumor cells. A novel EA derivative, Fluoro-butyl ethacrynamide (FBuEA), has recently been synthesized. This study is conducted to evaluate and characterize FBuEA's anti-cancer activity in cancer cell lines and the underlying molecular mechanism.

Materials and Methods: FBuEA was prepared from the precursor tosylate N-Boc-N-[4-(toluenesul- fonyloxy) butyl]ethacrynic amide. Human lung carcinoma cell lines A549, human erythroleukemia cell lines HEL and non-malignant human embryonic kidney cells 293T cell lines were seeded (5 x10^4 cells) into 24-well plates incubated in medium containing FBuEA with varying concentrations (0 to 20 μM) for 48hrs. Cell viability was assessed by trypan blue exclusion assay. To evaluate the relationship of FBuEA cytotoxicity and the expression of GST-π1, GST-π1 expression at mRNA level was semi-quantitatively assessed by RT- PCR. Total RNA were isolated from cell lines and cDNAs were synthesized. The cDNAs were then amplified for GST-π1 and GAPDH. Gel was photographed by digital gel image system (DigiGel, Taiwan) and the area under the curve of band peaks calculated and plotted. The pixel ratio of GST-π1 to GAPDH presented the relative amount of mRNA.

Results: After 48 hrs of exposure to FBuEA, inhibitory effect on proliferation was observed in HEL cells at low concentration (IC_{50} ~5 μM) compared to A549 and 293T cells. However, dose-dependent cytotoxicity was found in A549 and 293T cells at higher concentration of IC_{50}, ~14 μM and ~20 μM, respectively. In addition, the mRNA level of GST-π1 in HEL was lower than those in A549 and 293T cells.

Conclusion: FBuEA has a modest cytotoxicity against cancer cells and this effect is more significant in HEL cells with low expression of GST-π1.