



Drug-Drug Interaction and Therapeutic Mechanism of Doxetaxel towards Clinical Breast Cancer Patients

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SUMMARY. Docetaxel is a drug approved by the Food and Drug Administration to treat locally advanced or metastatic breast cancer. Drug-drug interaction between irinotecan and docetaxel was determined, and metabolomics-based analysis of serum was employed to elucidate the therapeutic mechanism of docetaxel towards breast cancers. Docetaxel 100 μ M inhibited about 20% activity of human liver microsomes (HLMs)-catalyzed SN-38 (active metabolite of irinotecan) glucuronidation ($p < 0.001$). Compared with healthy volunteers, the level of tryptophan in serum of patients with breast cancers increased significantly ($p < 0.01$). The treatment with docetaxel can significantly prevent the elevation of tryptophan in breast cancer patients ($p < 0.01$). In conclusion, metabolomics has been successfully applied to indicate irinotecan-docetaxel interaction, and the potential therapeutic mechanism of docetaxel towards breast cancers.

RESUMEN. Docetaxel es un medicamento aprobado por la Administración de Alimentos y Medicamentos para tratar el cáncer de mama localmente avanzado o metastásico. Se determinó la interacción fármaco-fármaco entre irinotecán y docetaxel, y se empleó el análisis metabolómico de suero para dilucidar el mecanismo terapéutico de docetaxel en cánceres de mama. Docetaxel 100 μ M inhibió aproximadamente el 20% de actividad de microsomas de hígado humano (HLM) que catalizada la glucuronidación de SN-38 (metabolito activo de irinotecán, $p < 0,001$). En comparación con voluntarios sanos, el nivel de triptófano en el suero de los pacientes con cánceres de mama aumentó significativamente ($p < 0,01$). El tratamiento con docetaxel puede prevenir significativamente la elevación de triptófano en pacientes con cáncer de mama ($p < 0,01$). En conclusión, la metabolómica se ha aplicado con éxito para indicar la interacción irinotecán-docetaxel, y el potencial mecanismo terapéutico de docetaxel en los cánceres de mama.

KEY WORDS: docetaxel, drug-drug interaction, irinotecan, *in vitro*, metabolomics.

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