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Autophagy in drug resistance of the multiple myeloma cell line RPMI8226 to doxorubicin

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ABSTRACT. We investigated the effect of autophagy on drug resistance of multiple myeloma (MM) to doxorubicin (DOX). A DOX-resistant MM cell line (RPMI8226/DOX) was developed by progressively increasing the DOX concentration gradient. The drug resistance index was determined using the MTT method. Transmission electron microscopy, anti-light chain 3-fluorescein isothiocyanate immunofluorescence, and Western blotting were used to detect autophagy of MM cells. Flow cytometry was applied to detect changes in apoptosis of RPMI8226/DOX cells (stained with annexin-V/propidium iodide) caused by inhibition by hydroxychloroquine and 3-methyladenine on autophagy. The drug resistance index of RPMI8226/DOX to DOX was 10.8, and autophagy/lysosomal was clearly observed in RPMI8226/DOX cells under transmission electron microscopy, while immunofluorescence showed granular immunofluorescence in cells. Western blot analysis showed that light chain 3-II protein expression level was higher in RPMI8226/DOX cells than in RPMI8226/S cells. The apoptosis test showed that hydroxychloroquine or 3-methyladenine partially reversed the drug resistance of RPMI8226/DOX cells by inhibiting autophagy.

Activation of autophagy in MM cells may explain the drug resistance of myeloma.

Key words: Autophagy; Doxorubicin; Drug resistance; Myeloma; RPMI8226

