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Profiling of Apoptotic Protein Expressions after Trabectedin Treatment in Human Prostate Cancer Cell Line PC-3 by Protein Array Technology

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Abstract : Microarrays have been developed for highly parallel enzyme-linked immunosorbent assay (ELISA) applications. The most common protein arrays are produced by using multiple monoclonal antibodies, since they are robust molecules which can be easily handled and immobilized by standard procedures without loss of activity. Protein expression profiling with protein array technology allows simultaneous analysis of the protein expression pattern of a large number of proteins. Trabectedin, a tetrahydroisoquinoline alkaloid derived from a Caribbean tunicate, Ecteinascidia turbinata, has been shown to have antitumor effects. Here, we used a novel proteomic approach to explore the mechanism of action of trabectedin in prostate cancer cell line PC-3 by apoptosis antibody microarray. XTT cell proliferation kit and Cell Death Detection Elisa Plus Kit (Roche) was used for measuring cytotoxicity and apoptosis. Human Apoptosis Protein Array (R&D Systems) which consists of 35 apoptosis related proteins was used to assess the omic protein expression pattern. Trabectedin induced cytotoxicity and apoptosis in prostate cancer cells in a time and concentration-dependent manner. The expression levels of the death receptor pathway molecules, TRAIL-R1/DR4, TRAIL R2/DR5, TNF R1/TNFRSF1A, FADD were significantly increased by 4.0-, 21.0-, 4.20- and 11.5-fold by trabectedin treatment in PC-3 cells. Moreover, mitochondrial pathway related pro-apoptotic proteins Bax, Bad, Cytochrome c, and Cleaved Caspase-3 expressions were induced by 2.68-, 2.07-, 2.8-, and 4.5-fold and the expression levels of anti-apoptotic proteins Bcl-2 and Bcl-XL were reduced by 3.5- and 5.2-fold in PC-3 cells. Proteomic (antibody microarray) analysis suggests that the mechanism of action of trabectedin may be exerted via the induction of both intrinsic and extrinsic apoptotic pathways. The antibody microarray platform can be utilised to explore the molecular mechanism of action of novel anticancer agents.

Keywords : trabectedin, prostate cancer, omic protein expression profile, apoptosis
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