

Proteomic analysis of ovarian cancer cells reveals dynamic processes of protein secretion and shedding of extra-cellular domains

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Elucidation of the repertoire of secreted and cell surface proteins of tumor cells is relevant to molecular diagnostics, tumor imaging and targeted therapies. We have characterized the cell surface proteome and the proteins released into the extra-cellular milieu of three ovarian cancer cell lines, CaOV3, OVCAR3 and ES2 and of ovarian tumor cells enriched from ascites fluid. To differentiate proteins released into the media from protein constituents of media utilized for culture, cells were grown in the presence of [(13)C]-labeled lysine. A biotinylation-based approach was used to capture cell surface associated proteins. Our general experimental strategy consisted of fractionation of proteins from individual compartments followed by proteolytic digestion and LC-MS/MS analysis. In total, some 6,400 proteins were identified with high confidence across all specimens and fractions. Protein profiles of the cell lines had substantial similarity to the profiles of human ovarian cancer cells from ascites fluid and included protein markers known to be associated with ovarian cancer. Proteomic analysis indicated extensive shedding from extra-cellular domains of proteins expressed on the cell surface, and remarkably high secretion rates for some proteins (nanograms per million cells per hour). Cell surface and secreted proteins identified by in-depth proteomic profiling of ovarian cancer cells may provide new targets for diagnosis and therapy.