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Metabonomics of deadherent cancer cells

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Abstract

Anchorage independence is an essential characteristic of metastasizing cells. While normal cells undergo apoptosis consecutive to loosing contact with their substratum, cancer cells can survive in the circulation for extended periods of time. In fact, the major limiting factor in the process of metastasis formation is the death of the tumor cells before their implantation in the target organs. The metastasis gene osteopontin is expressed at high levels by various cancers and contributes importantly to their invasive potential. A splice variant, osteopontin-c, is selectively produced by cancer cells and supports anchorage-independent expansion. Osteopontin-c induces the expression of oxidoreductases, many of which belong to the mitochondrial respiratory chain or to the hexose monophosphate shunt or regulate the hexose monophosphate shunt. Therefore, biochemical pathways that affect the energy metabolism are likely to be important mediators of the osteopontin-c effects on breast tumor cells. We confirmed in functional assays that anchorage independence is supported by peroxide signaling and that the induction of oxidoreductases by osteopontin-c generates the required peroxides. The osteopontin-c induced metabolite profile in deadherent breast cancer cells, derived from NMR analysis, identified creatine, glycine, glutamine, glutamate, glutathione, O-phosphocholine, and O-phosphoethanolamine to be upregulated. These results indicate that biochemical processes associated with the energy metabolism are important contributors to anchorage-independence, and consecutively to metastasis formation, by breast tumor cells.

Biography

Georg F. Weber attended medical school in Wuerzburg, Germany. He worked at the Dana-Farber Cancer Institute, Harvard Medical School from 1990 through 1999 and is currently on the faculty at the University of Cincinnati. Georg F. Weber has published over 70 scientific reports, including many in the most respected professional journals, and various monographs, most recently a textbook on molecular oncology. He holds several patents. As a component of his mission to research cancer dissemination, Georg F. Weber is the founder and chief executive officer of MetaMol Theranostics, a company specialized in diagnosis and treatment of cancer metastasis.