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Epithelial-mesenchymal transition (EMT) linked with stem-cell properties

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Abstract

Glioblastoma (GB) is the most devastating type of human cancer, whereas a subset of the patients responds well to the current treatment modalities including temozolomide. Recent genetic profiling has revealed a mesenchymal subtype possesses the most aggressive characteristics among four genetic subtypes. To establish a more detailed sub-classification based on the protein level, we applied an antibody microarray targeting 165 signal transduction proteins to the human GB clinical materials, and found that the pluripotent stem-cell marker, alkaline phosphatase, and the epithelial- mesenchymal transition (EMT) marker, Arf6, were most significantly up-regulated in the treatment-refractory GBs. These two factors highly correlated to each other, and also with expression of the putative gliomastem-like cell marker, CD133. We used two-dimensional gel electrophoresis (2DE) combined with matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) to identifythe proteins closely-related to tumor aggressiveness such as invasion and angiogenesis. Among the candidate proteins, the small GTP-binding proteins, Rac1 and RhoA which play a key role in cell motility and migration, were identified as a highly expressed protein in the patients with shorter survival, and significantly correlated with Arf6 expression. Plasminogen-activator inhibitor-1 (PAI-1), a protease contributing to modification of the extracellular matrix, has also found in the proteomic study, and its serum level can be used as a biomarker for tissue production. Since the expressions of PAI-1 and Arf6 were significantly correlated, EMT occurred in gliomatissues could be predicted pre-operatively. These multidisciplinary proteomic data obtained from the patients' tumor tissues and sera collectively offer certain evidence that EMT linked with the stem-cell properties actually contribute to the aggressivenessof the human GB.

Biography

Dr. Iwadate received his M.D. and Ph.D. from Chiba University in Japan. He acquired the board certified qualification of the Japan neurosurgical Society and is engaged in the clinical diagnosis and treatment of the gliomapatients.Utilizing more than 500 fresh frozen glioma samples, he is now collaborating with the Department of Genetics and Biochemistry in Chiba University to search for novel biomarkers and molecular targets in gliomas.His recent basic research has focused on immunological environment of gliomasto establish an oncolytic viral therapy combined with cytokine gene therapy.