DYNAMICS OF SIGNALING PROCESSES IN GLIOBLASTOMA D54MG CELLS INDUCED BY SUB-LETHAL PHOTODYNAMIC TREATMENT WITH 5-AMINOLEVULINIC ACID

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Photodynamic therapy (PDT) that induces oxidative stress is a promising mode for treatment of brain tumors, specifically gliomas. The proteomic study using Panorama Ab Cell Signaling Microarray (Sigma-Aldrich), which assays 224 cellular proteins, demonstrated that sublethal PDT mediated by 5-aminolevulinic acid induced diverse biochemical changes in glioblastoma D54Mg cells. Phosphorylation of Raf, the central enzyme of Ras/Raf/MEK/ERK pathway, and expression of protein kinase C occurred at earlier response stages. Phosphorylation of adhesion-related proteins FAK, Pyk2, microtubule-associated protein tau, increase of microtubule protein MAP-1beta along with simultaneous decease of proteins dystrophin, vinculin, MAP2 and various cytokeratins reflect cytoskeleton reorganization associated with changes in cell adhesion. The expression of proteins regulating cell cycle was also changed. At 30 min after PDT, levels of cyclin D1, c-Myc, checkpoint proteins chk1 and chk2 that arrest G0/G1, G1/S and G2/M transitions were reduced. At 1 hour, levels of cyclins A and D3, protein kinases cdk6 and cdc27 were decreased that also delayed transitions G0/G1, G1/S and G2/M. However, simultaneous increase in cyclin D1, transcription factors E2F1 and Smad4 could facilitate transitions Go/G1 and G1/S. The anti-apoptotic protein Bcl-xL was elevated and caspase 9 was reduced demonstrating protective cell response. Decrease of neuro-specific proteins S100-beta, CNPase and increase of beta-synuclein and proapoptotic NGF receptor p75 were also observed. Thus, the complex response of glioblastoma cells to sub-lethal PDT treatment included dynamic changes of signaling proteins associated with cell adhesion, cytoskeleton reorganization, cell cycle control and apoptosis.