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Multiplexing Analysis of Signaling Pathways in Glioblastoma †

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Abstract: Glioblastoma is the most common high-grade adult brain tumor, with a poor prognosis exhibited by most patients, with a median survival time of fewer than 2 years. The progression of brain tumors has been associated with multiple signaling deregulations. By monitoring an array of phosphorylation-dependent signaling molecules, we aim to better understand the events in glioblastoma progression. Data were obtained using two cutting-edge proteomic profiling technologies - xMAP array Luminex200 and Proteome Profiler Dot-Blot Array, on U87 cell cultures with/without stimulation with epidermal growth factor (hrEGF). Using phosphokinases array, out of 43 analyzed molecules, 10 proteins, such as mTOR(S2448), p38a(T180/Y182), Lyn(Y397), STAT3(Y705), p53(S46), PLCγ1(Y783) recorded an increased level of activation, ranging from 50% to 300% (treated vs. non-treated cells). For other 15 molecules, such as EGFR(Y1086), ERK1/2(T202/Y204, T185/Y187), AKT1/2/3(S473), p70S6 kinase(T421/S424), a moderate level of activation was observed, from 10% to 50%. A subsequent 11-plex xMAP analysis revealed that the phosphorylated levels of several proteins: IRS1(Ser636), Akt(Ser473), mTOR(Ser2448), PTEN(Ser380), and TSC2(Ser 939), were considerably stimulated -stimulation index between 60-90%, while GSK3a(Ser21) was inhibited by more than 50%. Analysis of modulation by phosphorylation of signal transduction proteins, induced by hrEGF, using the two assays (Dot-blot and xMAP), revealed several intracellular targets significantly modified, which could serve further as molecular targets for glioblastoma treatment. These results are consistent with other studies, mainly based on genomic and/or transcriptomic approaches, pointing out similar molecular targets.

Keywords: glioblastoma; signaling pathways; multiplex analysis.

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Conflicts of Interest

The authors declare no conflict of interest.