C7. **Signaling pathways in cancer cells**

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Background: Signaling pathways from growth factor receptors and integrins are cross-talking at a non-receptor tyrosin kinase, focal adhesion kinase (FAK) and overexpression of integrins was associated with increased phosphorylation of protein kinase B (PKB or Akt) and extracellular-signal-regulated kinases (ERK) in cancer cells. The aim of this study was to provide new insides the signaling pathways in seven cancer cell lines.

Methods: Three suspension cell lines: NB-4 (human acute promyelocitic leukemia), SEM (human B cell precursor leukemia), K-562 (human chronic myeloid leukemia in blast crisis) and four adherent cell lines: HT-29 (human colon adenocarcinoma), NTERA-2 (human embryonal carcinoma/teratocarcinoma), A-594 (human lung carcinoma) and A-431 (human epidermoid adenocarcinoma) were cultured according to their specifications. The samples, 10^6 cells/ sample, were stained for surface- and intracellular markers followed by measurements using Becton-Dickinson FACS Canto II and Beckman Coulter Gallios flow cytometers. The data were analyzed using DIVA and respectively, Gallios software. A-431 cells were treated for 30 minutes and 48 h with epigallocathechin 3-*O* gallate (EGCG) and the effect of the flavonoid was evaluated on the signaling proteins. An Akt-inhibitor (Calbiochem) was applied for 48 h to the leukemic cell lines and its effects were investigated on the signaling proteins and by clonogenic assay.

Results: The following signaling proteins were evaluated by flow cytometry: FAK/pFAK, Akt/pAkt, ERK/pERK, pSTAT3, pSTAT5 and in the leukemic cell lines additionally the surface markers: CD13, CD15, CD33. In the investigated cancer cell lines: pFAK and pAkt displayed an increased expression level. The Akt inhibitor applied in different concentrations 5, 10 and 20 μM modulated the expression level of pAkt and the number of colonies evaluated by clonogenic assay. EGCG administrated to A-431 cell line induced a reduction in pFAK expression level at 30 minutes and 48 h of incubation.

Conclusions: Our results recommend pFAK and pAkt as new biological markers for clinical investigations and support the anti-cancer activity of the natural compounds, like EGCG.

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