

ERK-phosphorylation, a valuable Biomarker to invest the effectiveness of MEK-inhibitors as Antivirals against Influenza

Inhalt

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The interest is increasing rapidly in the use of biomarkers and surrogate markers as primary measures of the effectiveness of investigational drugs in definitive drug trials. We develop MEK-inhibitors as antivirals against influenza. Here, the status of ERK-phosphorylation represents a perfect surrogate marker of the drug effectiveness.

There are various tools available to detect ERK-phosphorylation. The most sensitive one is the analysis of the phosphorylation sites of ERK using mass spectrometry. This method is very time and cost intensive. Another approach is to analyze the phosphorylation either with Western Blot Analysis (WBA) or with ELISA. The latter is a quantitative method but not very sensitive. WBA is more sensitive but only a qualitative method. WES (Simple Western™), a relatively new analysis approach uses capillary electrophoresis to identify and quantitate a protein of interest and in addition also the phosphorylation status of a protein. We have used this method to characterize, the phosphorylation status of ERK.

We present a method, where lymphocytes can be collected from a blood sample that will be used for pharmacokinetic (PK) analysis. Simply after centrifugation of the blood sample, the cell free plasma will be collected for PK analysis and normally cells would be thrown away. From these cells we collect the lymphocytes that will be analyzed for ERK phosphorylation. This allows the direct correlation of drug plasma concentration with the status of ERK-phosphorylation and consequently MEK activity.

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