MAPK/ERK Pathway

Technical Bulletin

A Pro-Cell Survival Pathway Implicated in Cancer

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The MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase) pathway is responsible for regulating cellular proliferation, migration and differentiation in response to extracellular stimuli. Therefore, malfunctions or dysregulation of this pathway lead to abnormal cell growth and often the development of cancer.

MAPK/ERK signaling can be activated by several membrane receptors; one of these is the receptor tyrosine kinase (RTK), epidermal growth factor receptor (EGFR). Not surprisingly, mutations that activate EGFR are directly linked to cancer (1). The small GTPase Ras binds and activates MAP3Ks; thus connecting EGFR to downstream MAPK/ERK signaling. Because of its key role in several intracellular pathways including MAPK/ERK, Ras is the focus of many cancer drug development programs. However, Ras remains an elusive target despite over thirty years of research and numerous attempts to attenuate the function of this small GTPase (2).

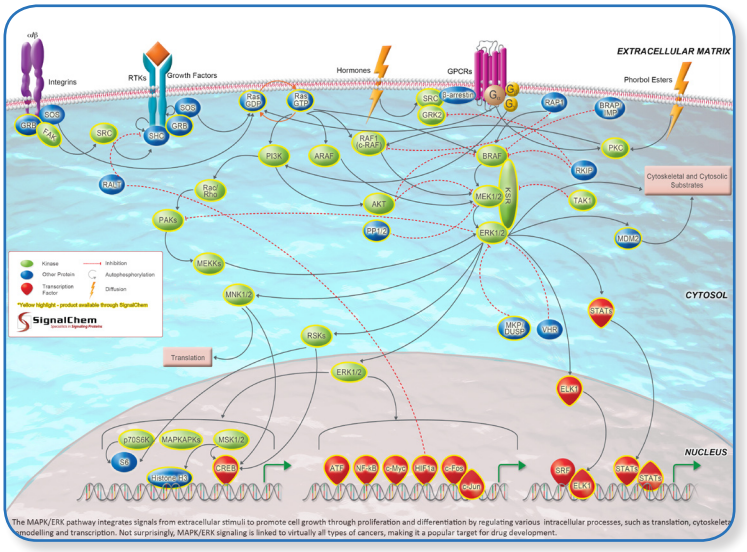

Figure: MAPK/ERK Pathway

Mutations that activate Ras mutations are found in almost a third of all cancers. Like Ras, BRAF has many disease-relevant mutations. While there are more than 40 known mutations that affect BRAF, BRAF (V600E) is found in 90% of all BRAF-related cancers, making it the most clinically relevant variant (3). Moreover, crosstalk between the MAPK/ERK signaling and the PI3K/AKT pathway has significant implications towards cancer (4).

The MAPK/ERK pathway is an important target for pharmaceutical studies and drug development. Currently, several drugs that target MAPK/ERK related proteins are available on the market. The BRAF inhibitors Tafinlar® and Zelboraf® and the MEK inhibitor Mekinist® are used to treat melanoma. Zelboraf® is also effective for treating certain colorectal cancers. Many other MAPK/ERK pathway inhibitors are still undergoing clinical trials for treating a wide range of cancers (5).

SignalChem manufactures products to support studies on the MAPK/ERK pathway. These products include wild type and mutant active kinases, as well as many recombinant signaling proteins. We also provide various inhibitory compounds, siRNAs, antibodies, growth factors and active enzymes to facilitate comprehensive studies and drug-development efforts that target this cancer-relevant pathway.

References:

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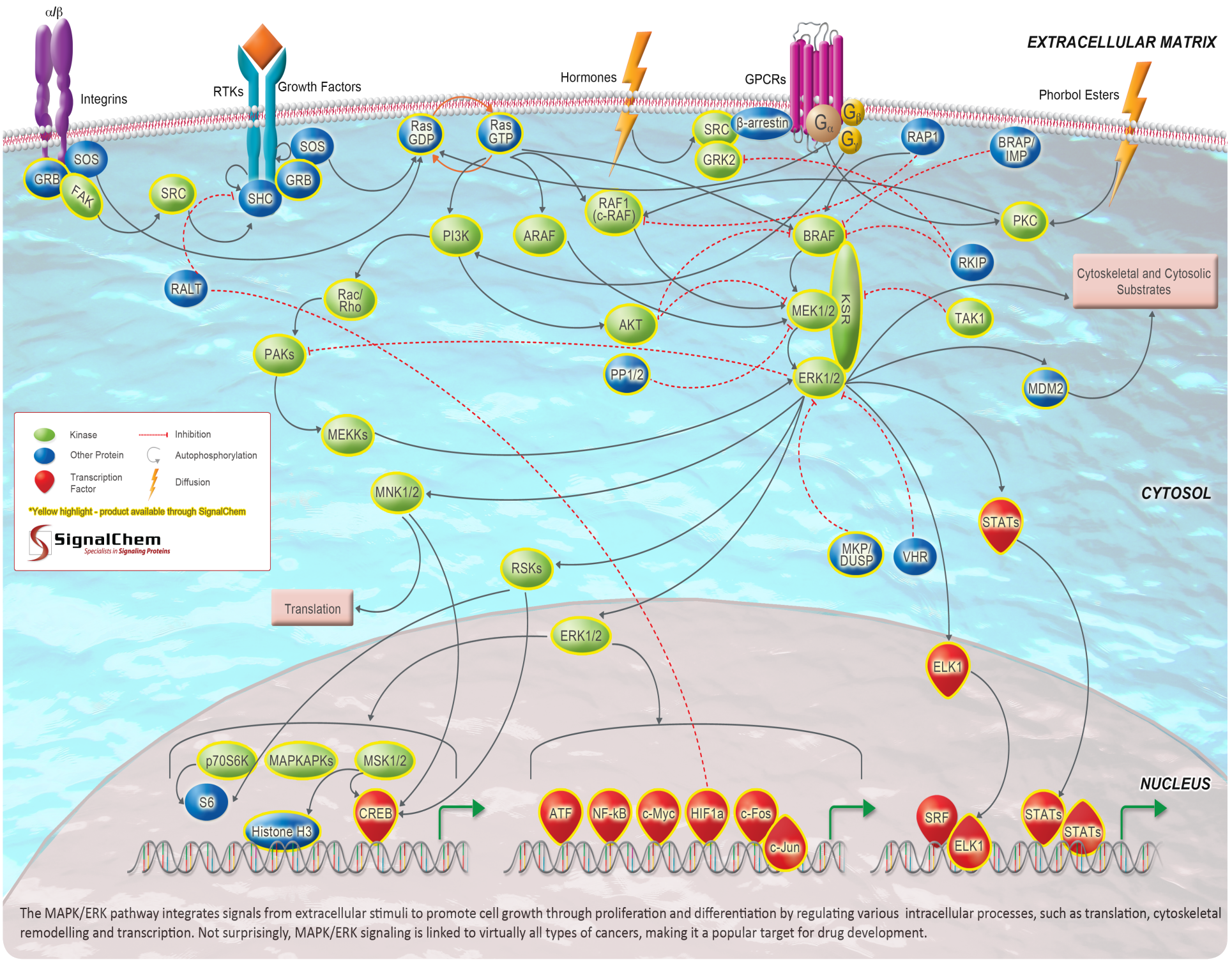

The MAPK/ERK pathway integrates signals from extracellular stimuli to promote cell growth through proliferation and differentiation by regulating various intracellular processes, such as translation, cytoskeletal remodelling and transcription. Not surprisingly, MAPK/ERK signaling is linked to virtually all types of cancers, making it a popular target for drug development.