Mapping the hypoxic regulation of IFNγ and TNFα-mediated kinase pathways in melanoma

#4128

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Introduction

Background:

Activation of hypoxia signaling pathways has been linked to cancer cell-intrinsic immune evasion and resistance. IFNγ and TNFα are immune cell-derived effector cytokines critical for tumor immunity. However, the effect of these cytokines in the hypoxic tumor microenvironment is less well studied.

Aim of the study:

To investigate how hypoxia modulates the kinase signaling pathways activated by the cytokines IFNγ and TNFα in melanoma cells, and to identify potential mechanisms underlying immune evasion in the tumor microenvironment.

Method:

Murine B16F10 melanoma cells were treated with 40 ng/ml of IFN-gamma and TNF-alpha under Normoxia (21 % oxygen) and hypoxia (1% oxygen) conditions for 6 or 24 hours. Tyrosine and Serine/threonine kinase activity profiles were generated using PamGene's KinomePro technology.

PamGene's KinomePro technology

With the advanced PamChip® technology, we can simultaneously measure the activity of over 380 kinases, providing a comprehensive view of kinase signalling pathways in a wide range of cell types and tissues.

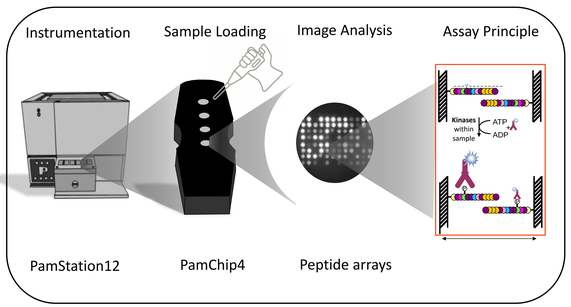

Fig.1. Kinase activity profiling on PamChip® microarrays

KinomePro Coverage

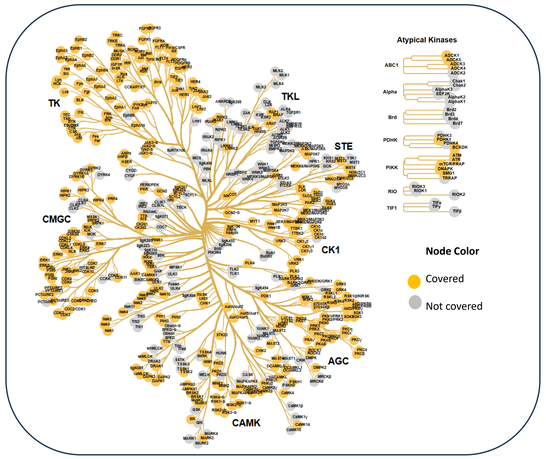

Fig.2. Kinases covered by PamChip® microarrays

Kinases affected upon Hypoxia

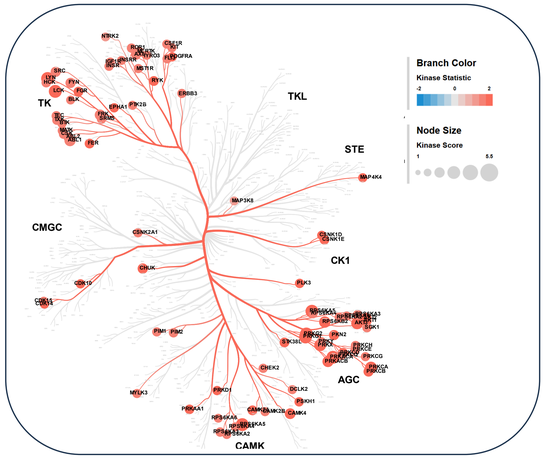

Fig.3. Kinases activated by hypoxia treatment of B16F10 cells

Tyrosine and Serine/Threonine kinases affected upon IFN-γ and TNF-α treatment

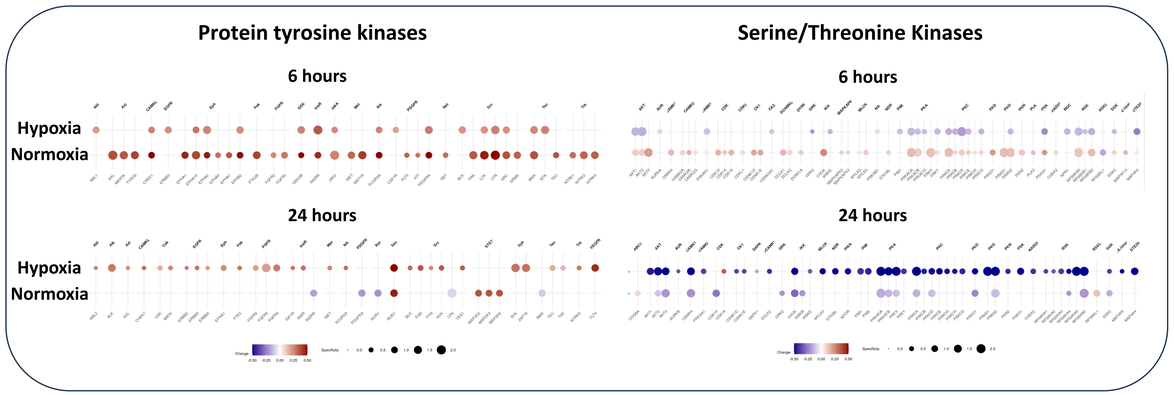

Fig.4. Protein tyrosine kinases (*left*) and serine/threonine kinases (*right*) differentially up-(*red*) or down-(*blue*) regulated upon IFNγ and TNF-α treatment for 6 hours (*top*) or 24 hours (*bottom*) in Normoxia or Hypoxia treated cells. Size of circle depicts specificity of kinase change.

Pathways enriched by IFN-γ & TNF-α treatment

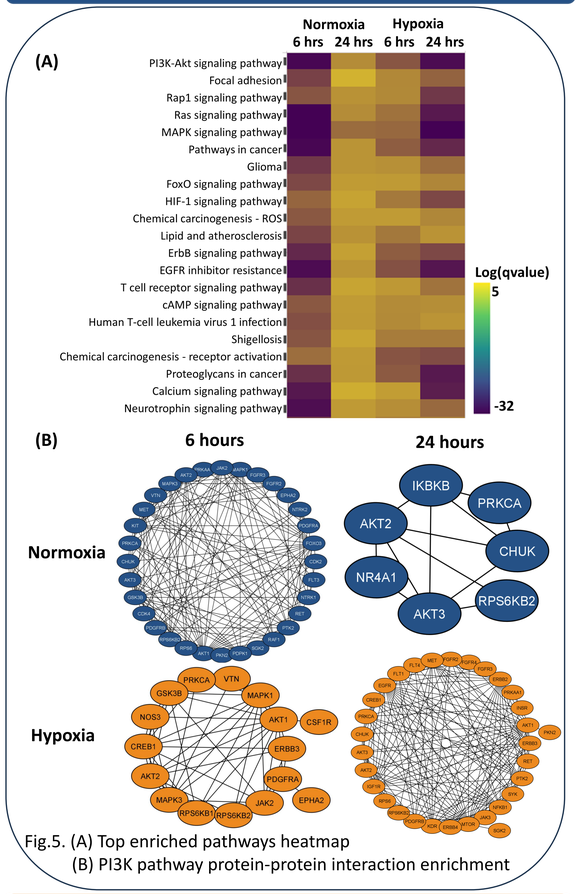

Fig.5. (A) Top enriched pathways heatmap
(B) PI3K pathway protein-protein interaction enrichment

Kinome profiling enables deeper insights into complex hypoxia biology and opens new avenues for drug target discovery

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