Introduction:

- Liver kinase B1 (LKB1/ STK11) is a protein kinase
- Tumor suppressor and a check point for metabolic stress
- Activates AMPK related down-stream kinases

![LKB1-AMPK pathway](adapted from reference 1)

- Loss of LKB1 has seen in 30-40% of lung non-small cell lung cancer (NSCLC) tumors
- However, underlying pathway remains unclear

Goals

- To use phosphoproteomics to identify the role of phosphorylation in LKB1-dependent NSCLC
- To compare and contrast differentially regulated proteins in LKB1-deficient (vector) and add-back (Wild-type and Kinase-dead) cell lines
- To identify changes in phosphoproteins that lead to pathway specific differential down-stream protein expressions

Methods

<table>
<thead>
<tr>
<th>A</th>
<th>HCC15</th>
<th>A549</th>
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<tbody>
<tr>
<td>Vector</td>
<td>KD</td>
<td>W</td>
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Phosphoproteome Proteome

- Analyzed by 2D LC-mass spectrometry (15-fractions)

Fold change p-value

PATHWAY ANALYSIS

2D LC (high pH fractionation followed by low pH separation)

Figure 1: LKB1-AMPK pathway (adapted from reference 1)

Results: Pathway map

- Morphological changes observed in HCC15 cell line

![Wild-type shows slow growing much larger, irregular shaped cells](adapted from reference 1)

- To determine the effect of MEK inhibitors on discovered pathway proteins

Future directions

- To validate differentially regulated phospho and non-phospho peptides by targeted mass spectrometry and western blots
- To determine the effect of MEK inhibitors on discovered pathway proteins

References


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