Papillary renal cell carcinoma (RCC) is the second most common type of kidney cancer (1 in 10 renal cell carcinomas).

**MET:**
MET, a membrane receptor protein, is found to be over-expressed in these particular types of tumors.

The Big Question:
After inhibiting the function of MET in two different ways (RNA interference vs. pharmacologic inhibition), it was found that only knockdown actually slowed cell proliferation. This is surprising because both methods should inhibit MET function to a similar degree.

shRNA Chronic MET Expression Knockdown:
- inhibited cellular proliferation

INCB028060 Acute MET Activity Inhibition:
- did not inhibit cellular proliferation

Methods

**Types of Cells Used:**
- HK2: Normal human kidney cell line
- SKRC39: Malignant Papillary RCC line
- Caki2: Malignant Papillary RCC line

Western Blotting:

**Results**

Validation of MET shRNA Chronic Knockdown:

Validation of INCB MET Acute Inhibition:

**Table 1:** Various conditions examining the effect of INCB on cell proliferation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Testing</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varying Doses of Drug</td>
<td>Impact of drug concentration on growth</td>
<td>Effective knockdown of MET and no affect on proliferation</td>
</tr>
<tr>
<td>Immediately after Plating Cells</td>
<td>Impact on initiating cell cycle</td>
<td>Effective knockdown of MET and no affect on proliferation</td>
</tr>
<tr>
<td>Soft Agar Assay</td>
<td>Impact on 3D growth</td>
<td>Preliminary results show reduced growth in INCB condition compared to control</td>
</tr>
</tbody>
</table>

**Conclusions**

- **Chronic knockdown** of MET expression (shRNA) is effective in limiting proliferation in two dimensions
- **Acute inhibition** of MET activity (INCB028060) is not effective in limiting proliferation in two dimensions
- **Acute inhibition** of MET activity (INCB028060) may be effective in limiting proliferation in 3D

**Future Directions**

- Replicate results obtained from the soft agar assay
- Find additional methods for testing INCB effectiveness in 3D growth
- Test the effectiveness of INCB in low nutrient media conditions

**References**

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