YAP1 expression in Merkel Cell Carcinoma

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Yes-associated protein 1 (YAP1) is a transcriptional regulator of Hippo signaling pathway that controls cell proliferation, tissue growth and organ development.

YAP1 also regulates the biological effects of the Wnt signaling pathway


Upregulation of YAP1 expression in human tumors

YAP1 expression is upregulated in skin Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC).

YAP-1 expression is abolished in high-grade neuroendocrine tumors

-Loss of YAP1 correlates with expression of neuroendocrine markers.

-Loss of YAP1 expression in 98% of small cell lung carcinoma (SCLC)

What about Merkel Cell Carcinoma (MCC)?

- MCC is a high-grade primary neuroendocrine carcinoma of the skin

- It has been suggested that the ST oncoprotein of Merkel Cell Polyoma Virus (MCPyV) activates nuclear translocation of YAP


Aims

- Investigate YAP1 expression pattern in primary and metastatic nodal Merkel Cell Carcinoma

- Correlate YAP1 expression with the presence of Merkel Cell Polyoma Virus (MCPyV)
Cohort characteristics

20 patients, 10 males-10 females, age 49-90

22 tissue samples
-12 cutaneous (two from one patient- recurrent lesions)
-9 nodal (without known primary) + 1 nodal (with known primary)

Immunohistochemical profile of MCC cases
- CK20 expression 22/22 (3 focal expression) 100%
- Synaptophysin 21/21 100%
- Chromogranin 19/21 (5 focal expression) 90%
- Neurofilament 14/14 (3 focal expression) 100%
- CD56 19/19 100%
- MCPyV 17/22 78%
- TTF1 0/22 0%

Immunohistochemical analysis of YAP expression using FFPE sections
Clone: Ab52771 (Abcam)
Dilution: 1/200
## YAP1 expression is abolished in MCC

**Immunohistochemical characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>CK20 expression</td>
<td>22/22</td>
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<td>78%</td>
</tr>
<tr>
<td>TTF1</td>
<td>0/22</td>
<td>0%</td>
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<tr>
<td>YAP1</td>
<td>0/22</td>
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</tbody>
</table>

Cut-off for (+) expression of YAP1: Cytoplasmic and nuclear staining in >10% of neoplastic cells

## YAP1 expression patterns

<table>
<thead>
<tr>
<th>Samples</th>
<th>No YAP1 (+) cells</th>
<th>Few scattered YAP1 (+ nuclear) cells</th>
<th>Clusters of YAP1 (+ cytoplasmic) cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Cutaneous</td>
<td>3</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>10 Nodal</td>
<td>5</td>
<td>5</td>
<td>0</td>
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</tbody>
</table>
Loss of YAP1 in cutaneous MCC (1)
Loss of YAP1 in cutaneous MCC (2)
Loss of YAP1 in both MCPyV+ and MCPyV- MCC
Loss of YAP1 in nodal MCC
YAP1 expression in scattered cells
Cytoplasmic YAP1 staining in clusters of MCC cells
Conclusion

• YAP1 expression is lost in primary and metastatic MCC, regardless of MCPyV positivity.

• YAP1 loss is a robust marker of neuroendocrine differentiation in MCC

Open questions

• Mechanism? Involvement of miR-375?

• Implications in MCC histogenesis- How early is the neuroendocrine differentiation event in the course of MCC development?
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