3. Results (continued)

Figure 3. DLL3 is expressed in a large subset of in vivo samples. (A) Cell-surface DLL3 expression using a flow cytometry assay revealed that DLL3 expression using a flow cytometry assay revealed that DLL3 expression in PDXs was strongly regulated, with >90% of tumor cells expressing DLL3. (B) Representative images of DLL3 expression using a flow cytometry assay revealed that DLL3 expression in PDXs was strongly regulated, with >90% of tumor cells expressing DLL3. (C) Representative images of DLL3-expressing cells within tumors. (D) Representative images of DLL3-expressing cells within tumors.

Figure 4. Anti-DLL3 antibody is effectively internalized. (A) Immunofluorescence studies revealed that DLL3 is internalized by these cells, and (B) that DLL3 internalization is efficiently blocked by an antibody against DLL3. (C) Representative images of DLL3 expression using a flow cytometry assay revealed that DLL3 expression in PDXs was strongly regulated, with >90% of tumor cells expressing DLL3.

Figure 5. Cancellation Analysis. (A) Representative images of DLL3 expression using a flow cytometry assay revealed that DLL3 expression in PDXs was strongly regulated, with >90% of tumor cells expressing DLL3. (B) Representative images of DLL3 expression using a flow cytometry assay revealed that DLL3 expression in PDXs was strongly regulated, with >90% of tumor cells expressing DLL3.

Table 3. Statistical aspects of in vivo studies.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fold change</td>
<td>2.49</td>
<td>0.0257</td>
</tr>
<tr>
<td>Internalization of anti-DLL3 antibody</td>
<td>0.370</td>
<td>0.1795</td>
</tr>
<tr>
<td>Statistical significance</td>
<td>0.001</td>
<td>0.05</td>
</tr>
</tbody>
</table>

4. Conclusions

DLL3 is expressed in the plasma membrane in the majority of neuroblastoma PDXs. DLL3 expression is effectively internalized by these cells, and antibody against DLL3 efficiently blocks DLL3 internalization. DLL3 expression above background levels is not the only biomarker of response. These studies describe a paradigm that targeting DLL3 using an ABC approach in neuroblastoma should be effective therapeutic strategy.

New information: [www.bcpp.org]

Acknowledgements: [N. M. McCormick, J. M. Maris, and Y. P. Mossé]

Support: [NIH grant CA115293 and R01 CA199299]

References: [N. M. McCormick, J. M. Maris, and Y. P. Mossé]

Figure 1. The efficacy of the anti-DLL3 antibody in vivo.

Figure 2. The efficacy of the anti-DLL3 antibody in vivo.

Figure 3. The efficacy of the anti-DLL3 antibody in vivo.

Figure 4. The efficacy of the anti-DLL3 antibody in vivo.

Figure 5. The efficacy of the anti-DLL3 antibody in vivo.

Figure 6. The efficacy of the anti-DLL3 antibody in vivo.

Figure 7. The efficacy of the anti-DLL3 antibody in vivo.

Figure 8. The efficacy of the anti-DLL3 antibody in vivo.