Id proteins involved in all processes associated with development of neural tumors.

- VEGF Signaling
- Integrins, MMP2
- Angiogenesis
- Anaplasia
- Proliferation
- Tissue Invasion
- Id
- Metalloproteinases
- Lineage Specific bHLH
- Rb, bHLH, Ets, Pax
THE FUTURE : Anti Id2 therapeutics

- Growth arrest
- Differentiation
- Increased cell death
- Inhibition of angiogenesis
Underlying challenge: how to control stem cells
Control brain tumor/neural stem cell behavior

N-Myc

Stem cell

Huwe1

Glia

Neuron

N-Myc

X

X

X
Loss of Huwe1 expands the neural stem cell population.
Loss of Huwe1 impairs neural stem cell differentiation
Focal deletions and decreased expression of *Huwel* in GBM

TCGA

Oncomine

<table>
<thead>
<tr>
<th>Normal brain</th>
<th>GBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=23</td>
<td>n=77</td>
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</tbody>
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P-value: 9.3E-10
Expression of Huwe1 is lost in primary neuroblastomas displaying accumulation of N-Myc protein
Lineage commitment
Differentiation
Cell cycle arrest

Neural stem cell

Growth factors → N-Myc → Tumor stem cell

N-Myc → Huwe1

Growth arrest
Maturation

N-Myc

Growth factors

Tumor growth
Malignant gliomas invade the normal brain.