OMP-59R5 (Anti-Notch2/3) inhibits tumor growth and reduces cancer stem cell frequency in patient derived Small Cell Lung Cancer xenografts

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ABSTRACT

OMP-59R5 (Anti-Notch2/3) inhibits tumor growth and reduces cancer stem cell frequency in patient-derived Small Cell Lung Cancer xenografts. OMP-59R5 modulates the proportion of cells expressing neuroendocrine and epithelial lung markers as well as genes implicated with cancer stem cells. Furthermore, we observed an increase in expression in neuroendocrine differentiation and tumorigenicity studies with the Notch2/3 antibody alone or in combination with chemotherapeutic agents. The Notch pathway is active in Small Cell Lung Cancer and investigated combinatorial treatment with chemotherapeutics.

RESULTS

OMP-59R5 reduces the cancer stem cell frequency, reversing the enrichment of cancer stem cells by chemotherapy in a Small Cell Lung Cancer PDX

OMP-59R5 modulates the expression of Notch pathway, neuroendocrine, tumor regrowth and tumorigenicity genes

SUMMARY

1. The Notch pathway is activated in Small Cell Lung Cancer
2. Cells which express Notch2 and/or Notch3 are highly tumorigenic
3. OMP-59R5 antagonizes the Notch pathway and reduces tumor growth
4. OMP-59R5 modulates genes associated with Notch signaling both in the tumor cells and the tumor microenvironment.
5. OMP-59R5 reduces the cancer stem cell frequency, reversing the enrichment of cancer stem cells in chemotherapeutic agents.