

# MYCN (N-MYC) Gene Amplification by FISH

## DETECTION OF MYCN AMPLIFICATION AS A PROGNOSTIC INDICATOR IN PATIENTS WITH NEUROBLASTOMA

### Test Highlights

- Fluorescent in situ hybridization (FISH) analysis provides sensitive detection of *MYCN* amplification. *MYCN* amplification status supplies significant prognostic information for the workup of neuroblastoma and medulloblastoma.

### Disease Overview

- Neuroblastoma is one of the more common solid tumors occurring in children. Neuroblastomas arise in derivatives of the primitive neural crest, including adrenal medulla, paravertebral sympathetic ganglia, and sympathetic paraganglia. Several prognostic factors have been identified, including patient age and stage of disease.
- MYCN* oncogene amplification status is one of the most important prognostic markers currently available and is amplified in approximately 25 percent of neuroblastomas.
- MYCN* amplification is associated with progression and poor prognosis in neuroblastomas. Rates of survival at 18 months depend on the level of *MYCN* amplification. Five-year survival rates for patients whose tumors have one, three to ten, and greater than ten *MYCN* copies are 70,30, and 5 percent, respectively. Thus, detection of *MYCN* amplification is of significant utility in identifying high-risk cases of neuroblastoma independent of clinical and histomorphologic findings.
- Medulloblastoma is also known to be associated with *MYCN* and *MYCC* amplification. Amplification of *MYCC* occurs in a minority of medulloblastomas but is associated with clinically aggressive neoplasms. *MYCN* amplification occurs in approximately five percent of medulloblastomas and, as with *MYCC*, may be associated with a poor prognosis.
- MYCN* amplifications also occur in a variety of other neoplasms, including those of the hematopoietic system and lung, where their influence on prognosis is less clear.

### Epidemiology

Neuroblastomas are the fourth most frequent malignant tumor in children under 15 years of age.

### Genetics

- MYCN* is a proto-oncogene found on the short arm of chromosome 2 (2p23-24). Overexpression of this proto-oncogene appears to block differentiation and increase cell proliferation.
- MYCN* amplicons can be detected in two forms in metaphase chromosomes: homogeneously staining regions (HSRs) or centromere-free extrachromosomal double-minutes (DMs).

### Indication for Ordering

Patients diagnosed with neuroblastoma or medulloblastoma as determined by morphology or immunophenotypic studies.

### Additional Ordering Notes

- The biopsy site and fixative used should be provided.
- The submitted sample should contain sufficient viable tumor.

### Interpretation

Presence of *MYCN* amplification is strongly predictive of a poor prognosis.

### Limitations

Tissues fixed in alcohol-based or non-formalin fixatives have not been tested using this method.

### Methodology

This test uses a commercially available DNA FISH probe.

### References

- Vysis<sup>®</sup> LSI *MYCN* (2p24)/CEP2 Probe (package insert). Des Plaines, IL: Abbott Molecular; 2009.
- Aldosari N, et al. *MYCC* and *MYCN* oncogene amplification in medulloblastoma. A fluorescence in situ hybridization study on paraffin sections from The Children's Oncology Group. *Arch Pathol Lab Med* 2002; 126:540-4.
- Deyell RJ and Attiyeh EF. Advances in the understanding of constitutional and somatic genomic alterations in neuroblastoma. *Cancer Genetics* 2011;204:113-21.

## Test Information

**0049235**

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For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).

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