Gene Section
Mini Review

MYC (v-myc myelocytomatosis viral oncogene homolog (avian))

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Identity

Other names: C-MYC. Identified as the oncogene of the MC29 avian myelocytomatosis virus
HGNC (Hugo): MYC
Location: 8q24

![c-MYC (8q24) in normal cells: PAC 944B18 (top) and PAC 968N11 (below)](image)
- Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Transcription
Alternative splicing; coding sequences: 1318 and 1362 bp for proteins p64 and p67 respectively.

Protein

Description
439 amino acids and 48 kDa in the p64; 454 amino acids in the p67 (15 additional amino acids in N-term; contains from N-term to C-term: a transactivation domain, an acidic domain, a nuclear localization signal, a basic domain, an helix-loop-helix motif, and a leucin zipper; DNA binding protein.

Expression
Expressed in almost all proliferating cells in embryonic and adult tissues; in adult tissues, expression correlates with cell proliferation; abnormally high expression is found in a wide variety of human and rodent tumours.

Localisation
Located predominantly in the nucleus.

Function
The encoded myc oncoproteins are apparently transcription factors known as basic region-helix-loop-helix-leucine zipper (b-HLH-Zip) proteins; like other b-HLH-Zip proteins, they modulate the expression of target genes by binding to specific DNA sequences. In this case, however, the binding requires dimerization to another b-HLH-Zip protein, namely Max (the latter can also form heterodimers with Mad as well as homodimers with itself). Myc/Max complexes activate transcription and promote cell proliferation and transformation. Mad/Max complexes, however, repress transcription and block myc-mediated cell transformation. All three complexes bind to the same DNA sequence and are competitors.
Expression of c-myc is required for proliferation; it can over-ride p53-induced GI-arrest by inducing an inhibitor of the cyclin kinase inhibitor WAFI(p21). The latter (located at 6p21) normally coordinates S and M phases of the cell cycle. If absent, cells with damaged DNA arrest not in GI but in a G2-like state from which they can pass through additional S phases without intervening normal mitoses (the deformed polyploid cells that result may then die by apoptosis). The uncoupling of S and M may contribute to the acquisition of the chromosomal abnormalities manifested by most tumour cells when apoptotic pathways have been circumvented.

Homology
The human myc family also includes N-myc and L-myc, rather specifically implicated in neuroblastoma and small-cell lung carcinoma, respectively, in which amplified copy numbers have been found.

Implicated in
Burkitt's lymphoma

The gene is activated by translocation next to an immunoglobulin constant gene. Most frequently, it is positioned near the immunoglobulin heavy-chain (IgH) constant region on chromosome 14 but, in some tumours, near the light-chain region chromosome 2 (IgK) or 22 (IgL). It is now known that immunoglobulin joining enzymes may be involved in recombinations associated with a variety of chromosomal translocations in B and T cells.

Amplification has been described in many types of tumour, including breast, cervical and colon cancers, as well as in squamous cell carcinomas of the head and neck, myeloma, non-Hodgkin's lymphoma, gastric adenocarcinomas and ovarian cancer

Prognosis
C-myc involvement is by no means universally found in these cancers; there may be a correlation with the more advanced stages, suggesting a value as a prognostic indicator (although this has not been demonstrated in some studies for breast, ovarian and cervical cancers).

Oncogenesis
C-myc gene activation (enhanced expression and/or amplification) may result from chromosomal duplication as well as translocation, and from retroviral as well as point mutation. Multiple copies of the gene may be evidenced in homogeneously staining chromosomal regions and in double minutes.

Role of c-myc in other conditions

Disease

In adult respiratory distress syndrome the degree of diffuse alveolar damage and consequently the prognosis may be related to the intensity of expression of c-myc in the alveolar cells which, if severe, may contribute to deregulation of cellular proliferation and apoptosis. In endometriosis, c-myc expression is a possibly important regulator of cellular proliferation.

To be noted

Note
Although c-myc appears to be active in variety of tumours, it is important to realise that in common with other mechanistic pathways to cancer induction and progression no single genetic event (including c-myc deregulation) will prove to be necessary in the light of the inherent complexity and diversity of cellular pathways leading to neoplasia.

References

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