Aggressive mucosa associated lymphoid tissue lymphomas are associated with mutations in Bcl10

Structurally, wild type Bcl10 protein consists of a caspase recruitment domain (CARD), which has significant homology with other known CARDs, and a novel N-terminal caspase recruitment domain (CARD) homologous to that found in several apoptotic molecules. Bcl10 and E10 activated NF-κB but caused apoptosis of 293 cells. Bcl10 expressed in a MALT lymphoma exhibited a frameshift mutation resulting in truncation distal to the CARD. Truncated Bcl10 activated NF-κB but did not induce apoptosis. Wild-type Bcl10 suppressed transformation, whereas mutant forms had lost this activity and displayed gain-of-function transforming activity. Similar mutations were detected in other tumor types, indicating that Bcl10 may be commonly involved in the pathogenesis of human malignancy.

Comment

Low grade B cell lymphomas of mucosa associated lymphoid tissue (MALT) are tumours with characteristically indolent behaviour. They have relatively low proliferation index, benign cellular morphology and histology, and the tumour cells are often interspersed among chronic inflammatory cells. Some cases of low grade gastric MALT lymphoma are dependent on local infection with Helicobacter pylori, compounding their image as very low grade malignancies. The advent of sensitive polymerase chain reaction methods however showed that these are indeed tumours which can advance, both in stage, and from low to high grade. Within this group of relatively non-threatening tumours, there are some clinically aggressive ones. Cells from some of these tumours proliferate spontaneously in tissue culture and have a chromosomal translocation between chromosomes 1 and the immunoglobulin heavy chain locus on chromosome 14 (t(1;14);p12;q32)). Tumours without the translocation die in culture. Willis et al have identified and described the properties of a novel gene, Bcl10, which is located at the chromosomal breakpoint. They characterised both wild type Bcl10 which maps to chromosome 1p22, and the mutated Bcl10 which was used by an aggressive MALT lymphoma variant. Mutation resulted in the production of a truncated protein with different functional properties.
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