BAP1 Gene

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BRCA1 associated protein 1

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1. Normal Function

The *BAP1* gene provides instructions for making a protein called ubiquitin carboxyl-terminal hydrolase BAP1 (shortened to BAP1). This protein functions as a deubiquitinase, which means it removes a molecule called ubiquitin from certain proteins. The presence of ubiquitin molecules on a protein can affect the activity of the protein and its interactions with other proteins. The ubiquitin "tag" also promotes breakdown (degradation) of a protein. By removing ubiquitin, BAP1 helps regulate the function of many proteins involved in diverse cellular processes. The BAP1 protein is thought to help control cell growth and division (proliferation) and cell death. Studies suggest that it is involved in the progression of cells through the step-by-step process they take to replicate themselves (called the cell cycle) and that it plays roles in repairing damaged DNA and controlling the activity of genes.

Although the exact mechanism is unclear, the BAP1 protein acts as a tumor suppressor. Tumor suppressor proteins help prevent cells from growing and dividing too rapidly or in an uncontrolled way.

2. Health Conditions Related to Genetic Changes

2.1. BAP1 tumor predisposition syndrome

Mutations in the *BAP1* gene cause *BAP1* tumor predisposition syndrome. People with this condition have an increased risk of developing many types of noncancerous (benign) and cancerous (malignant) tumors, particularly certain tumors of the skin (atypical Spitz tumors, cutaneous melanoma, and basal cell carcinoma); eyes (uveal melanoma); kidneys (clear cell renal cell carcinoma); and a tissue called the mesothelium that lines the chest, abdomen, and internal organs (malignant mesothelioma). Researchers are still determining whether other forms of cancer are linked to *BAP1* tumor predisposition syndrome.

Affected individuals inherit a mutation in one copy of the *BAP1* gene. These mutations, which are present in essentially every cell of the body, are classified as germline mutations. Most germline *BAP1* gene mutations lead to an abnormally short BAP1 protein that is likely broken down prematurely. Other germline mutations change single protein building blocks (amino acids) in the BAP1 protein and likely impair its function. In most cases, a second, non-inherited (somatic) mutation occurs in the normal copy of the gene in cells that give rise to tumors. Together, the germline and somatic mutations lead to a loss of BAP1 protein function in tumor cells.

Reduction or loss of this protein's function likely prevents the removal of ubiquitin molecules from certain proteins. Although it is unclear exactly how changes in BAP1 function lead to *BAP1* tumor predisposition syndrome, researchers speculate that altered activity of proteins normally regulated by BAP1 deubiquitination may promote cell proliferation or survival, resulting in tumor formation.

2.2. Cholangiocarcinoma

Cholangiocarcinoma

2.3. Melanoma

Melanoma

2.4. Other cancers

Somatic *BAP1* gene mutations have been found in uveal melanoma, malignant mesothelioma, and clear cell renal cell carcinoma tumors in the absence of a germline *BAP1* gene mutation. In these cases, the cancers occur in people with no family history of the cancer and are considered sporadic. Affected individuals do not develop additional tumor types associated with *BAP1* tumor predisposition syndrome (described above).

3. Other Names for This Gene

- BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase)
- cerebral protein 6
- cerebral protein-13
- HUCEP-13
- hucep-6
- KIAA0272
- ubiquitin carboxyl-terminal hydrolase BAP1
- UCHL2

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