WNT1 (wingless-type MMTV integration site family, member 1)

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Abstract
Review on WNT1, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity
**Other names:** BMND16, INT1, OI15
HGNC (Hugo): WNT1
**Location:** 12q13.12

DNA/RNA
**Description**
The WNT1 gene spans a genomic region of 4161 bases on plus strand.
The DNA of WNT1 consists of 4 exons and the coding sequence starts in the first exon.

**Transcription**
The WNT1 gene has one protein coding transcript which consists of 370 amino acids.

Protein
**Description**
Ligand for members of the frizzled family of seven transmembrane receptors.
In some developmental processes, is also a ligand for the coreceptor RYK, thus triggering Wnt signaling.

**Localisation**
Secreted, extracellular space, extracellular matrix.

Function
Probable developmental protein.
May be a signaling molecule important in CNS (central nervous system) development.
Is likely to signal over only few cell diameters.
Has a role in osteoblast function and bone development.

Mutations
**Somatic**
There are several WNT1 mutations identified related with osteogenesis imperfecta.
Several confirmed somatic mutations of the WNT1 gene have also been reported, according to COSMIC, which are associated with carcinomas of the endometrium, lung, large intestine, prostate and kidney.
Implicated in

**Esophageal cancer**

**Note**
It has been shown, in cell cultures of esophageal cancer, that WNT1 results in cytoplasmic accumulation of beta-catenin and activates TCF-dependent transcription (Mizushima et al., 2002). Overexpression of mRNA and protein levels of WNT1 have been positively associated with lymph node metastasis, advanced pathological stage and prognosis of patients with esophageal squamous cell carcinoma (Lv et al., 2012).

**Breast cancer**

**Note**
WNT1 has been shown to be markedly elevated in grade I tumors, but declined as tumor grade declined (Wong et al., 2002). Ectopic expression of WNT1, triggers the DNA damage response (DDR) and an ensuing cascade of events resulting in tumorigenic conversion of primary human mammary epithelial cells. WNT1-transformed cells have high telomerase activity and compromised p53 and Rb function, grow as spheres in suspension, and in mice form tumors that closely resemble medullary carcinomas of the breast (Ayyanan et al., 2006). siRNA anti-WNT1 has been shown to induce apoptosis in human breast cancer cell lines (Wieczorek et al., 2008). WNT1 immunoreactivity has been found to be inversely related to histological grade, Ki-67 and p53, positively to , HER-2 and caspase-3 and has been correlated with favorable prognosis of patients with stage II breast cancer (Mylona et al., 2013).

**Basal cell carcinoma of head and neck**

**Note**
Overexpression of WNT1 has been positively associated with cytoplasmic beta-catenin (Lo Muzio et al., 2002).

**Sarcoma**

**Note**
WNT1 blockade by either monoclonal antibody or siRNA induces cell death in sarcoma cells (Mikami et al., 2005).

**Non-small cell lung cancer (NSCLC)**

**Note**
The expression of WNT1 has been positively correlated with c-Myc, cyclin D1, VEGF-A, MMP-7, Ki-67 and intratumoral microvesSEL density and has been found to negatively influence patients' survival (Huang et al., 2008). WNT1 overexpression has been positively associated with the Ki-67 proliferation index and c-Myc and has been found to exert an unfavorable impact on patients' survival (Nakashima et al., 2008). WNT1 expression has been found to be an independent prognostic factor of poor survival (Xu et al., 2011).

**Gastric cancer**

**Note**
The expression levels of WNT1 are positively correlated with tumor size, tumor invasive depth,
lymph node metastasis, pTNM stage and negatively influences patients’ 5-year survival rate (Zhang and Xue, 2008).

**Neuroblastoma**

**Note**

Knockdown of endogenous WNT1 expression results in cell death and inhibits cell growth (Zhang et al., 2009).

**Osteogenesis imperfecta (OI)**

**Note**

This disease is a heritable bone fragility disorder that is usually due to dominant mutations in COL1A1 or COL1A2 and is characterized by reduced bone mass and recurrent fractures. Genetic variations in WNT1 define the bone mineral density quantitative trait locus 16 (BMND16) [MIM:615221]. Variance in bone mineral density influences bone mass, contributes to size determination in the general population, and is a susceptibility factor for osteoporotic fractures. The disease is caused by mutations affecting the gene of susceptibility factor for osteoporotic fractures. The WNT1 gene is associated with variations affecting the gene of osteoporotic fractures. The disease is caused by mutations affecting the gene of osteoporotic fractures. The disease susceptibility factor for osteoporotic fractures. The disease is caused by mutations affecting the gene of osteoporotic fractures. The disease susceptibility factor for osteoporotic fractures.

**Osteoporosis (OSTEOP)**

**Note**

A systemic skeletal disorder characterized by decreased bone mass and deterioration of bone microarchitecture without alteration in the composition of bone. The result is fragile bones and an increased risk of fractures, even after minimal trauma. Osteoporosis is a chronic condition of multifactorial etiology and is usually clinically silent until a fracture occurs. Disease susceptibility is associated with variations affecting the gene of osteoporotic fractures. WNT1 (Fahiminiya et al., 2013; Faeqeh et al., 2013; Laine et al., 2013; Pyott et al., 2013).

**References**


This article should be referenced as such: