TNKS (tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase)

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### Identity

**Other names:** PARP-5a; PARP5A; PARPL; TIN1; TINF1; TNKS1; pART5

**HGNC (Hugo):** TNKS

**Location:** 8p23.1

### DNA/RNA

**Description**

Spans 226410 bp, 27 exons.

**Transcription**

9599 bp long mRNA, containing 3984 bp long ORF.

### Protein

**Description**

Isoform 1 (1327 amino acids) contains region with homopolymeric runs of His, Pro, and Ser (HPS domain, aa 1-181), 15 ankyrin repeats (ANK 1 to 15, aa 215-934), multimerization domain homologous to the sterile alpha motif (SAM domain, aa 1112-1317). Isoform 2 (643 amino acids) contains only HPS domain and 9 ANK repeats.

**Expression**

Ubiquitous, high expression in brain and ganglions, skin and cardiac tissue.

**Localisation**

Nuclear and cytoplasmic.

### Function

Poly(ADP-ribosylation) (PARsylation) of target proteins: TNKS itself, TNKS2/TNKL, TRF1, IRAP, TAB182/TNKS1BP1, EBNA-1, Mcl-1L, Mcl-1S, NuMA, AXIN1, AXIN2.

TNKS PARsylates TRF1 (telomeric repeat-binding factor 1), a negative regulator of telomere length maintenance. PARsylated TRF1 dissociates from telomeres, enhancing telomerase-mediated telomere elongation (Smith and de Lange, 2000; Cook et al., 2002).

PARsylation of NuMA (nuclear mitotic apparatus protein) by TNKS contributes to mitotic spindle pole assembly (Sbodio and Chi, 2002).

TNKS can PARsylate Mcl-1L and Mcl-1S and inhibit their anti- and pro-apoptotic function correspondingly (Bae et al., 2003).

TNKS inhibits Epstein-Barr virus OriP function by binding and modifying Epstein-Barr nuclear antigen 1 (EBNA1) (Deng et al., 2002; Deng et al., 2005).

PARsylation activity of TNKS increases after phosphorylation by mitogen-activated protein kinase (MAPK) upon insulin stimulation (Chi and Lodish, 2000).

TNKS together with its partner IRAP enhances insulin-stimulated exocytosis of GLUT4 (Yeh et al., 2007).

TNKS PARsylates AXIN1 and AXIN2 components of beta-catennin (the Wnt pathway transcription factor) destruction complex (Huang et al., 2009).

TNKS is a target of the FANCD2, the key protein involved in development of Fanconi anemia. FANCD binds tankyrase-1 and inhibits its PARsylation at telomeres (Lyakhovich et al., 2011).
**TNKS protein.** HPS: region containing homopolymeric runs of His, Pro, and Ser; ANK: ankyrin domain; SAM: multimerization domain homologous to the sterile alpha motif; PARP: PARP catalytic domain.

**Homology**
With TNKS2/TNKL.

**Mutations**
**Somatic**
Frameshift mutations are found in exons 9 and 10 in gastric and colorectal malignant tumors (Kim et al., 2011).

**Implicated in Cancer**
**Note**
TNKS is considered as a potential target for anticancer treatment.

Inhibition of PARP activities of TNKS blocks Wnt/beta-catenin pathway and increases efficiency of telomerase inhibitors (Seimiya et al., 2005; Huang et al., 2009; Zhang et al., 2010).

**Disease**
TNKS expression increased in some tumors (compared to adjacent normal tissues), including breast, bladder and gastric cancer (Gelmini et al., 2004; Gelmini et al., 2007; Poonepalli et al., 2008; Gao et al., 2011), but in other tumors, e.g. malignant glioma and colorectal cancer TNKS expression might be downregulated (Shervington et al., 2007; Shebzukhov et al., 2008), Fanconi anemia (Lyakhovich et al., 2011).

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