PYGO in Cancer Pathway

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Abstract

Several molecules are involved in cancer molecular network. Pygopus family plant homeodomain (PHD) finger (Pygo) is a component of Wnt/β-catenin transcription complex. Pygo has two homologs, Pygo1 and Pygo2, in mammalian cells. Pygo2 has an important role as a component of β-catenin-B-cell CLL/lymphoma 9 (Bcl9)-TCF/LEF complex. In this Editorial, a role of Pygo in Wnt/β-catenin signaling related to cancer pathway is summarized.
Introduction

What is PYGO?
Pygopus family plant homology domain (PHD) finger (Pygo) is a dedicated component of the Wnt/β-catenin transcription complex [1]. Pygo is required for MYC, a basic helix-loop-helix leucine zipper protein, -dependent activation of mitosis-related genes and an essential component of MYC oncogenic activity [1]. Pygo has two homologs in mammalian cells, which are Pygo1, dispensable for normal murine development, and Pygo2, related to malignant growth in different cancers [1]. Pygo2 binds specific histone marks of activation such as H3K4me3, which promotes an open euchromatic structure as transcribing genes [1]. Pygo2 participates in the expression of highly transcribed RNAs essential for DNA replication and cell-cycle progression [1].

PYGO in Wnt/β–catenin signaling
Pygo is necessary for virtually all canonical Wnt signaling-dependent responses [2]. It has been demonstrated that mutations in B-cell CLL/lymphoma 9 (Bcl9) and Pygo genes result in congenital heart defects by tissue-specific perturbation of Wnt/β-catenin signaling in zebrafish [2]. The interaction between Pygo2 and di- and trimethylated lysine 4 of histone H3 (H3K4me2/3) is essential for mouse development and Wnt signaling-dependent transcription [3]. Pygo2 is more popular than Pygo1 in development, while Pygo1 and Pygo2 are considered to be tissue-specific Wnt pathway components [4]. Pygo2 is recruited by Bcl9 and Bcl9-like (Bcl9l) (Bcl9/9l) and sustains Pax6 expression to ensure a correct lens development in mice, independent of β-catenin [4].

PYGO in therapeutic-resistant cancer
It has been reported that the interactions of Bcl9/Bcl9L with β-catenin and Pygo promote breast cancer growth, invasion, and metastasis [5]. Bcl9/Bcl9L bind to Pygo and to the N-terminal domain of b-catenin via the homology domain 1 (HD1) and HD2 domains [5,6]. PYGO2 gene expression was down-regulated in diffuse-type gastric cancer compared to intestinal-type gastric cancer [7]. Diffuse-type gastric cancer demonstrates epithelial-mesenchymal transition-like phenotype which is related to therapeutic resistance in cancer [8]. Some correlations between PYGO2 expression and therapeutic-resistant cancer have been reported. Pygo promotes transcriptional activation of Wnt-target genes via β-catenin [6]. It may be possible that PYGO2 in Bcl9-TCF complex contributes to cancer progression in terms of Wnt/β-catenin pathway.

Conclusion
Pygo2 play a role in cancer pathway especially in correlation of Wnt/β-catenin pathway. PYGO2 expression seems to be associated with cancer phenotypes, whereas precise mechanism of the Pygo2-promoted therapeutic resistance in cancer is a way of the future.
References


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