

The Relevance of Women's Diseases, Jun Activation-domain Binding Protein 1 (JAB1) and p27^{kip1}

Mijin Kim¹, Tae-Hee Kim², Hae-Hyeog Lee²

¹Department of Interdisciplinary Program in Biomedical Science, Soonchunhyang University, Asan, ²Department of Obstetrics and Gynecology, Soonchunhyang University College of Medicine, Bucheon, Korea

The Jun activation-domain binding protein 1 (Jab1) recognize a potential coactivator of activator protein 1 (AP-1) such as c-fos, c-jun transcription factor and the fifth subunit of the COP9 signalosome complex. Also, Jab1 activate the c-jun gene resulted cell proliferation. Not only a powerful tumor suppressor but also regulator of apoptosis negative cdk inhibitor p27^{kip1} are involved in the cell cycle. This is Jab1 and p27^{kip1} interact with each other, Jab1 accelerate p27^{kip1} from nuclear to cytoplasm through ubiquitin/proteasome pathway. However, information about the relationship between Jab1 and p27^{kip1} is not known much. Taken together, the results of this study identify function and structure of Jab1 and p27^{kip1} were described in a recent article on the basis of relevant. Besides Jab1 and p27^{kip1} will organize the relationship between the disease and women. (**J Menopausal Med 2016;22:6-8**)

Key Words: Breast neoplasms · Cyclin-dependent kinase inhibitor p27 · Endometriosis · Ovarian neoplasms

Introduction

The Jun activation-domain binding protein 1 (Jab1) is initially identified as a coactivator of activator protein (AP-1) transcription factor and found a component of the COP9 signalosome (CSN) complex, contained modulating signal transduction, gene transcription, and protein stability.^{1,2} Jab1 interacted with p27^{kip1} and translocate it's from nuclear to cytoplasm which resulted in acceleration of p27^{kip1} degradation through the ubiquitin-dependent/proteasome pathway and promotes cell-cycle progression.³ p27^{kip1} is an inhibitor of cyclin-dependent kinases (CDKs), performing potential tumor suppressor gene in diversity of human's cancer. CDK is a family of protein kinases, the activity of the serine/threonine kinases known as cdk that are under the strict control of positive and negative regulators. Until now studies

have found that p27^{kip1} promotes apoptosis, growth inhibition and cell cycle arrest.^{4,5} Reduction of p27^{kip1} protein means high resistance and poor prognosis to anticancer drug. Down regulation of p27^{kip1} protein is often discovered by human cancers including breast and ovarian cancer and is normally correlated with poor clinical outcome. As a result, the concentration of the p27^{kip1} protein can be expressed as an important marker in the development of human cancer. Accordingly, this study examines a correlation of p27^{kip1} and Jab1, will reveal the relevant disease in women.

Jab1, p27^{kip1} Structure and Function

Jab1 has been involved to the tumorigenic process, therefore, jab1 have the potential to be an effective beneficial

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Address for Correspondence: Tae-Hee Kim, Department of Obstetrics and Gynecology, Soonchunhyang University Bucheon Hospital, 170 Jomaru-ro, Bucheon 14584, Korea

Tel: +82-32-621-5380, Fax: +82-2-6008-6874, E-mail: heeobgy@schmc.ac.kr

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target that affect the interaction of many tumor stage. Size of Jab1 is an ~40 kDa soluble protein, also Jab1 is located on chromosome 8, Jab1 interacted with p27^{kip1} and improved its cytoplasmic translocation which resulted in acceleration of p27^{kip1} degradation through the ubiquitin and proteasome pathway. It is well known that p27^{kip1} protein levels are mainly regulated through degradation by ubiquitin-dependent proteolysis. Control of p27^{kip1} and Jab1 is important process in cancer progression, which is controlled by both the positive and negative regulators. p27^{kip1} is a kind of cdk inhibitors, suppresses the G1-to-S cell cycle progression, functions as a main negative regulator of apoptosis and is, thus, considered a tumor suppressor.⁶ The main function of this p27^{kip1} is to inhibit the CDK2-cyclin E complex by controlling at the G1 to S transition in normal cells,

Jab1, p27^{kip1} and Breast Cancer

Jab1 is an important protein in breast cancer progression comes from the recent study that it is a downstream target for HER2-2/neu.⁷ Amplification and overexpression of HER-2/neu was established in many cancers and upregulating of this oncogene was associated with increased metastasis and prognosis. Especially, HER-2/neu oncogene (known for erbB2) is a critical biomarker, target of therapy for roughly 30% of breast cancer patients and expression of HER-2/neu is upregulated in the existence of tamoxifen, leading to tamoxifen resistance in breast cancer. The role of Jab1 interacts with c-myc gene in breast cancer cells.⁸ C-myc is regulator gene, including apoptosis, transformation, metabolism and cell cycle progression. On the other hand, the lower level of p27 in breast tumors was high grade. Estrogen receptor-negative and progesterone receptor-positive p27 showed a positive correlation between low levels in breast cancer.

P27^{kip1} and Endometriosis

Endometriosis is the endometrial tissue in the uterus that should be present in the abdominal cavity outside the uterus,⁹ a common disease that occurs in approximately 10 to

15% woman of childbearing age. The cause of endometriosis, though not known as yet, regurgitation of menstrual blood, immunological factors, genetic factors and family history factors have been established occurrence of endometriosis. According to previous research compared to the healthy women were reported for endometriosis and endometriosis in infertile women, following studies have been reported to demonstrate the changes in the endometrium of women with disease.^{10,11} Moreover the before-mentioned transformation demanded the establishment of the endometrium in the peritoneal, recent evidence indicated that uterine mucosal cells of patients with endometriosis do not follow the normal growth pattern and apoptosis.¹²⁻¹⁴ In the midst of CDK inhibitors, we should be focused on p27^{kip1}. The critical function of p27^{kip1} is to inhibit CDK-cyclin E complex by controlling a checkpoint in the G1 in normal cells. When p27^{kip1} is not present in the cells, cells are not follow a cell cycle control signal and proliferation.¹⁵ Because endometrial cell cycle changes may be involved in cell cycle regulation of endometriosis in women with diseases significance of p27^{kip1} protein level it can be seen that a change in the lining of a particular cell cycle is important.

Jab1, p27 and Ovarian Cancer

Ovarian cancer is malignant tumor, the most widely occurring between 50 to 70 years old woman.^{16,17} The second most common cause of gynecologic cancer in succession cervical cancer has been identified as a family history, a lot of ovulation number. No proven method for ovarian cancer is often rapidly progressive and fatal disease early symptoms rarely.⁵ As a negative regulator of the cell cycle, p27^{kip1} is tumor suppressor,⁶ which inhibits cyclin-CDK in a dosage dependent manner to control cell cycle progression.^{7,8} Recently, decreased expression of p27^{kip1} has been frequently detected in human cancers,^{5,10-15} including ovarian carcinoma. Recently, the expression of Jab1 and p27^{kip1} in a malignant epithelial ovarian cancer, was found to be correlated with the reverse p27^{kip1} expression levels as a result Jab1 negative regulator.¹⁸ That is a negative regulator of p27^{kip1} Jab1 has been associated with the development of the ovarian tumor, progression and prognosis.

Summary

Jab1 is a protein that enhances the activity of the c-jun gene and induce cell proliferation, p27^{kip1} is a strong reduction in the tumor suppressor gene p27^{kip1} has a high resistance and poor prognosis in cancer. Also p27^{kip1} has an important role cell cycle regulatory factors. Recently, Jab1 and p27^{kip1} has been reported that many women involved in diseases such as breast cancer, endometriosis and ovarian cancer. As well as Jab1 and p27^{kip1} started to reveal that the association became known widely in hepatocellular carcinoma, laryngeal carcinoma and nerves. In conclusion, a wide range of research on Jab1 and p27^{kip1} is expected to play a major role in reproductive system, kidney, blood vessel tissues and nerves system further physiological pathophysiological.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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