Resveratrol significantly inhibits the occurrence and development of cervical cancer by regulating *PLSCR1*.

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Abstract

Cervical cancer is currently the most common female malignancies, and resveratrol is a polyphenol isolated from the skins of grapes that has been reported to significantly alter the cellular physiology of tumor cells, as well as block the process of initiation and progression. Little is known about the role of *PLSCR1* in the occurrence and development of cervical cancer. Here, we demonstrated that resveratrol significantly inhibited both the growth of HeLa cells and expression of *PLSCR1*, which can be recovered by gain of function of *PLSCR1*. These results suggest that resveratrol mediated cell growth inhibition can be regulated by *PLSCR1*.

Keywords: Resveratrol, Cervical cancer, *PLSCR1*.

Introduction

Cervical Cancer (CC) is currently the most common female tumors worldwide with an extremely poor prognosis, accounting for more than 60% of the gynecological cancer burden in developing countries. Every year, more than 500,000 women are diagnosed with CC, and CC accounts for more than 275,000 deaths globally [1,2].

The antioxidant 3, 4', 5 tri-hydroxystilbene (resveratrol) is a polyphenol compound found in various nutrients that was found in various nutrients such as peanuts, mulberries, and red wine. It had been shown to have immunomodulatory, anti-cancerogenic, and cardioprotective effects [3]. It has been increasingly recognized that resveratrol possesses cancer-preventive and -suppressive activities. More importantly, resveratrol has little cytotoxic effect on normal tissues in vitro and in vivo at effective anticancer doses, reflecting its potential value in cancer treatments when administered appropriately [4-8].

Phospholipid scramblase 1 is a calcium-dependent endofacial plasma membrane protein. The first function ascribed to *PLSCR1* was to catalyse rapid, bidirectional and non-specific distribution of phospholipids (lipid scrambling) between the inner and outer leaflet of the plasma membrane resulting in collapse of the phospholipid asymmetry [9-18]. However, little is known about the role of *PLSCR1* in the occurrence and development of cervical cancer. In this study, we evaluated effects of resveratrol as individual agents on the occurrence and development of cervical cancer and explore the *PLSCR1*-related mechanism behind the observed efficacy.

Materials and Methods

Cell lines and cell culture

We specifically used cervical cancer cell lines Hela. All the cell lines used in this study were purchased from the Shanghai Cell Bank, Shanghai Institute for Biological Sciences, China Academy of Sciences. All cell lines were maintained in RPMI-1640 medium supplemented with 10% Fetal Bovine Serum (FBS) at a 37°C humidified atmosphere containing 5% CO₂.

Cell proliferation assay

Cells were plated in 96-well plates and examined at 24, 48, 72, 96 h after plating (n=8). Cells were incubated with CellTiter 96 AQueous (MTS) solution for 3 h. The absorbance at 490 nm was then measured on the microplate reader (BioTek).

Cell viability assay

Cell Counting Kit-8 (CCK-8) assay was used to detect the cell growth status according to manufacturer’s instruction. Cells were cultured at a density of 5 × 10⁴ cells per well in flat bottomed 96-well plates with various concentrations of resveratrol. After 72 h, 10 μl of CCK-8 Solution Reagent was added to each well according to the manufacturer’s instructions. After 4 h in culture, cell viability was measured via reading the absorbance at 450 nm using a Spectramax 190 microplate reader (Molecular Devices, Sunnyvale, CA, USA), and the relative cell viability of surviving cells from each group relative to controls, defined as relative cell viability 1.0, was determined by reduction of WST-8.