Erratum

Erratum to “Ethanol Extracts of Fruiting Bodies of *Antrodia cinnamomea* Suppress CL1-5 Human Lung Adenocarcinoma Cells Migration by Inhibiting Matrix Metalloproteinase-2/9 through ERK, JNK, p38, and PI3K/Akt Signaling Pathways”

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(1) Would you please change the Abstract section with this following?

Metastatic cancer attributes to a major cause of cancer death. In this pioneer study, we aimed to investigate how *Antrodia cinnamomea* (*A. cinnamomea*), indigenous to Taiwan, affects migration ability of highly metastatic human adenocarcinoma lung cancer cells CL1-5. Our result demonstrated that noncytotoxic ethanol extract of fruiting bodies of *A. cinnamomea* (EEAC) exhibited a dose-dependent inhibitory effect on motility and migration of the highly metastatic CL1-5 cells. Results of a gelatin zymography assay illustrated that *A. cinnamomea* repressed the activities of matrix metalloproteinase- (MMP-) 2 and 9 in a dose-dependent manner. *A. cinnamomea* administration decreased MMP-9 and MMP-2 protein expressions from Western blotting assay, whereas the expression of the tissue inhibitors of MMP (TIMP-1 and TIMP-2) increased. Additional study disclosed that *A. cinnamomea* suppressed FAK, ERK1/2, p38, AKT, and JNK1/2 phosphorylation, and also PI3K and Rac-1 were found decreased. Further, treatment of CL1-5 cells with inhibitors specific for PI3K (LY294002), ERK1/2 (PD98059), JNK (SP600125), and p38 MAPK (SB203580) decreased the expression of MMP-2

and MMP-9. Taken together, EEAC induced FAK phosphorylation and exhibited its antimigration activities via the PI3K/AKT and MAPK signalings in CL1-5 cells. This is the pioneer study verifying the antimigration activity of *A. cinnamomea* against human lung adenocarcinoma CL1-5 cancer cells.

(2) Would you please change the Introduction section with this following?

Lung cancer develops as the number one cancer cause of death in several countries, and it accounts for more fatalities than total of prostate cancer, breast cancer, and colorectal cancer [1]. Human lung adenocarcinoma cell lines CL1-0, L1-1, CL1-5, and CL1-5-F4 are a series of sublines with progressively invasive ability established by in vitro invasion screening. CL1-5 cells are a human lung adenocarcinoma cell line derived from the parental CL1 cells by five successive matrigel selections. CL1-5 cells showed a 4- to 6-fold higher invasive ability than the parental cells, and their production of 92-kDa MMP-9 also exhibited a drastic increase over that of their parental cells [2].

Overgrowth and metastasis are the two major characteristics of malignancy with poor clinical outcome. Malignant tumor progression depends upon the capacity to invade,

FIGURE 2

metastasize, and promote the angiogenic host response. The dynamics of extracellular matrix (ECM) remodeling has been the focus of intense investigation for many years. The degradative process is mainly mediated by matrix metalloproteinases (MMPs), which are a family of at least 20 zinc-dependent endopeptidases best known for their ability to hydrolyze ECM components [3]. MMP-9 is in large quantities expressed in human lung cancer cells A549 and might play an important role in tumor invasion [4]. Therefore, the inhibition of MMP-9 activity is critical for the prevention of lung cancer cell migration and metastasis. CL1-5 cells expressed an abundant quantity of MMP-2 and MMP-9 and showed a highly metastatic capability [2, 5]. MMP-2 and MMP-9 are activated by plasmin, which is generated from specifically cleaved zymogen plasminogen through the enzyme urokinase-type plasminogen activator (uPA) on associating with its receptor (uPAR). Moreover, the balance between MMPs and the natural tissue inhibitors of MMPs, TIMPs, including TIMP-1, -2, -3, and -4, attributes to homology and structural identity [6]. Also, in the present study, we investigate if ethanol extract of fruiting bodies of *Antrodia cinnamomea* (EEAC) affects the mitogen-activated protein kinase (MAPK) signaling pathways, which is involved in cell growth, differentiation, apoptosis, and metastasis [7]. Besides, EEAC was conducted to investigate its effects on phosphatidylinositol-3-kinase/serine/threonine protein kinase (or protein kinase B) (PI3K/Akt) signal transduction pathway, which is strongly correlated with the development, progression, and metastasis of various tumors [8–10].

Antrodia cinnamomea (*A. cinnamomea*) has been traditionally consumed among Asian countries to prevent inflammation and liver cancer [11]. Much evidence suggests that *A. cinnamomea* protects ethanol-, CCl_4 -, and cytokine-induced liver injury [12], anti-inflammation [13], and antioxidation [14]. Some reports have suggested that extracts of mycelia and fruiting bodies of *A. cinnamomea* could be a potential chemotherapeutic agent against hepatoma, as well as prostate, breast, bladder, and lung cancer cells [15–20]; however, the antimigration effect of *A. cinnamomea* in lung adenocarcinoma CL1-5 cancer cells remains unclear. In this study, we investigated the antimigration effects of *A. cinnamomea* on highly metastatic CL1-5 cell lines and also explored its molecular mechanisms.

(3) In the Results section, we did wrong calculation; however, we correct it (in *italic font*) in a new one as follows.

3.2. EEAC Inhibited Cell Mobility with Wound Healing Assay. Wound healing assay was conducted to study the effect of EEAC on the mobility/migration of CL1-5 cells. Under wound healing assay, the confluent monolayer was scraped with a sterile micropipet tip to create a scratch wound. Our result demonstrated that EEAC inhibited the migration of CL1-5 cells in a dose-dependent manner, with *21.85% and 32.03%* inhibition at 0.5 and 1.0 µg/mL after incubation for 36 h, respectively (Figures 2(a) and 2(b)).

(4) I would like to replace Figure 2(a) with the new one shown earlier.