Effect of CDDP on A549 cells. To elucidate the inhibitory effect of CDDP on A549 cells, the cells were treated with different concentrations of CDDP for 48 h, and then dose-response evaluation was performed. The CCK-8 assay revealed that the cell survival rate decreased with increasing CDDP concentrations (Fig. S1). The inhibitory concentration of CDDP achieving 50% cell death (IC_{50}) was 2.04±0.39 μg/ml.

miR-1273a in exosomes enhances the sensitivity of A549 cells to CDDP. To further confirm the role of exosomal miR-1273a in sensitivity of NSCLC cells to CDDP, A549 cells were treated with CDDP, or transfected with miR-1273 mimic or inhibitor. As shown in Fig. S2A, miR-1273a mimic transfection increased the miR-1273a expression levels in cells, whereas CDDP treatment and miR-1273a inhibitor transfection significantly reduced the miR-1273a expression levels. Next, exosomes were isolated from the above mentioned cells and labeled as $EXOC^{DDP}$, EXO^{mimic} and $EXO^{inhibitor}$, respectively. The level of exosomal miR-1273a was determined by RT-qPCR analysis and exhibited the same trend as that in the cells (Fig. S2B). These results indicated that miR-1273a may be encapsulated into exosomes and the expression level of exosomal miR-1273a is likely affected by the miR-1273a expression level of the parent cells.

We next examined the effect of exosomal miR-1273a on the sensitivity of A549 cells to CDDP. After inhibiting miR-1273a expression in A549 cells, the cells were incubated with EXO^{mimic} and exosomes from miR-1273a mimic negative control (NC)-infected cells. After an additional 48 h of culture, the expression level of miR-1273a was determined by RT-qPCR analysis, and the results demonstrated that the expression of miR-1273a was increased in EXO^{mimic}-treated A549 cells (Fig. S2C). In addition, cell survival was assessed by the CCK-8 assay and it was observed that EXO^{mimic} treatment significantly enhanced CDDP-mediated cytotoxicity (Fig. S2D). Flow cytometry further confirmed that EXO^{mimic} incubation significantly increased the number of apoptotic cells under CDDP treatment (Fig. S2E). Taken together, these results indicated that the delivery of exosomal miR-1273a may affect the sensitivity of receptor cells to CDDP.

Figure S1. Dose response relationship between viability of A549 cells (%) and concentration of CDDP for 48 h. CDDP, cisplatin.

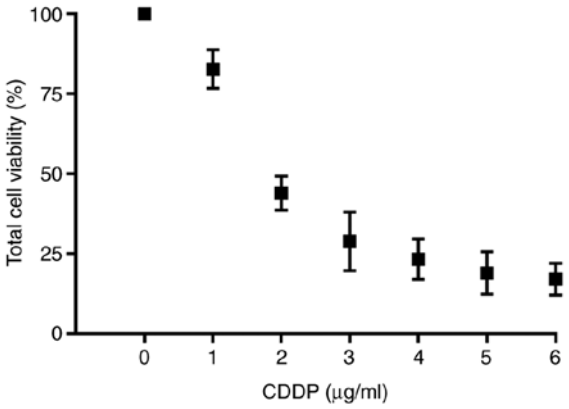

Figure S2. Delivery of exosomal miR-1273a enhances the sensitivity of A549 cells to CDDP. (A) Relative expression level of miR-1273a in A549 cells following treatment with CDDP, miR-1273a mimic or miR-1273a inhibitor (*P<0.05, **P<0.01). (B) Relative expression level of miR-1273a in exosomes secreted from A549 cells following treatment with CDDP, miR-1273a mimic, or miR-1273a inhibitor (**P<0.01, ***P<0.001). (C) After 48 h of treatment of A549 cells with EXO^{mimic} or negative control (NC), the relative expression level of miR-1273a was determined by reverse transcription-quantitative PCR analysis (**P<0.01). (D) After incubating A549 cells with EXO^{mimic} or NC for 48 h, these cells were further incubated with the indicated concentrations of CDDP for additional 48 h, and cell viability was detected by the Cell Counting Kit-8 assay (*P<0.05, **P<0.01). (E) Apoptosis rates in cells incubated with EXO^{mimic} and negative control were analyzed by flow cytometry. The number of apoptotic cells was significantly increased in cells treated with EXO^{mimic} (*P<0.05). EXO^{mimic}, exosomes from miR-1273a mimic-transfected cells; CDDP, cisplatin.

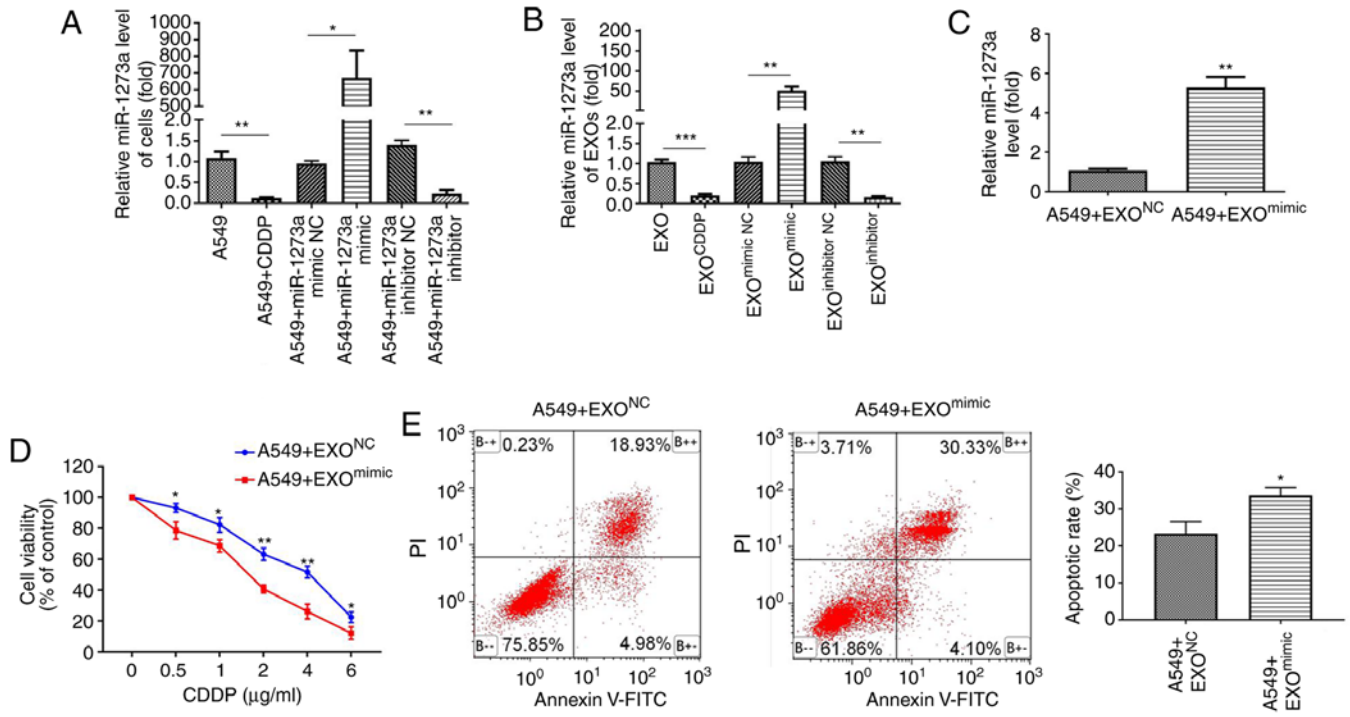

Table SI. Characteristics of the NSCLC patients.

Characteristics	Data values
Age, years（means ± SD）	57.0±9.8
Sex, n (%)	
Male	32 (65.3)
Female	17 (34.7)
Tumor stage, n (%)	
IIIA	4 (8.2)
IIIB	2 (4.1)
IV	43 (87.7)
Chemotherapy regimens, n (%)	
Platinum-pemetrexed	43 (87.8)
Platinum-paclitaxel	6 (12.2)
Chemotherapy outcome, n (%)	
CR+PR	19 (38.8)
SD+PD	30 (61.2)

NSCLC, non-small cell lung cancer; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.