**Decreased DHRS2 expression is associated with HDACi resistance and poor prognosis in ovarian cancer**

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**Supplementary Figure 1**

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**Supplementary Figure 1 DHRS2 expression was upregulated by HDAC inhibitors in SK-OV-3 cells. A-C.** qRT-PCR and western blot showing DHRS2 expression in SK-OV-3 cells after treatment with SAHA (A), apicidin (B) and TSA (C) for 48 h.

**Supplementary Table 1: Correlation analysis between HDAC inhibitors sensitivity and DHRS2 expression in cells from any primary site/subtype, adherent.**

|  |  |  |
| --- | --- | --- |
| Compound | Correlation\* | Target |
| Apicidin | -0.0722 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |
| SAHA | -0.0847 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |
| Belinostat | -0.111 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |
| Panobinostat | -0.096 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |
| ISOX | -0.0536 | HDAC6 |
| Tacedinaline | -0.0.785 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |
| Entinostat | -0.0788 | HDAC1, HDAC2, HDAC3, HDAC6, HDAC8 |

\* Pearson correlation coefficients between HDAC inhibitors sensitivity data, expressed as areas under concentration-response curves (AUCs), with DHRS2-expression measurements, expressed as log2 robust-multi-array-average values.

**Supplementary Figure 2**

**Supplementary Figure 2 Suppression Suppression of DHRS2 caused resistance to HDAC inhibitors in ES2 cells. A.** ES2 cells transfected with DHRS2 siRNAs were treated with TSA and Apicidin for 48 hours, and cell apoptosis was detected by flow cytometry.

**Supplementary Figure 3**



**Supplementary Figure 3 Suppression of DHRS2 caused resistance to HDAC inhibitors in ES2 cells. A.** ES2 cells transfected with DHRS2 siRNAs were treated with TSA and Apicidin for 48 hours, and cell cycle was detected by flow cytometry.

**Supplementary Figure 4**

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**Supplementary Figure 4 Suppression of DHRS2 caused resistance to HDAC inhibitors in A2780 cells. A.** A2780 cells was transfected with the indicated siRNAs for 48 h and the mRNA level of DHRS2 was measured using qRT-PCR. **B.** After A2780 cells were transfected with NC siRNA or DHRS2 siRNA-2 for 48 h, 1 μM TSA, 2 μM SAHA and 3 μM apicidin was added to each group. 48 h later, crystal violet dye was used to stain the adherent cells and take photographs. **C.** Cells transfected with NC siRNA or DHRS2 siRNA-2 were treated with SAHA, TSA,and Apicidin for 48 hours and the apoptotic cells were detected using flow cytometry. **D.** The cells transfected with NC siRNA or DHRS2 siRNA-2 were treated with SAHA, TSA,and Apicidin for 48 hours and the cell cycle was measured using flow cytometry.

**Supplementary Table 2**

|  |  |  |
| --- | --- | --- |
|  | **Patient characteristics** |  |
| **Normal (n=4)** | **Range of age (years)** | 21-50 |
|  |  | Number |
| **Malignant (n=80)** | **Range of age (years)** |  |
|  | 0~40 | 20 |
|  | 41~70 | 60 |
|  | **cTNM stage** |  |
|  | cT1 | 42 |
|  | cT2 | 15 |
|  | cT3 | 11 |
|  | **Histological grade** |  |
|  | 1 | 13 |
|  | 2 | 14 |
|  | 3 | 24 |
|  | **Tumor stage** |  |
|  | I | 32 |
|  | II | 13 |
|  | III | 11 |
|  | IV | 2 |
|  | **Histological type** |  |
|  | Adenocarcinoma | 42 |
|  | Clear cell carcinoma | 4 |
|  | Dysgerminoma | 3 |
|  | Endodermal sinus carcinoma | 5 |
|  | Granular cell tumor | 4 |
|  | Squamous cell carcinoma | 1 |
|  | Theca cell tumor | 1 |
|  | Undifferentiated carcinoma | 1 |

**Supplementary Table 2 The clinicopathological parameters of cases used in IHC.**