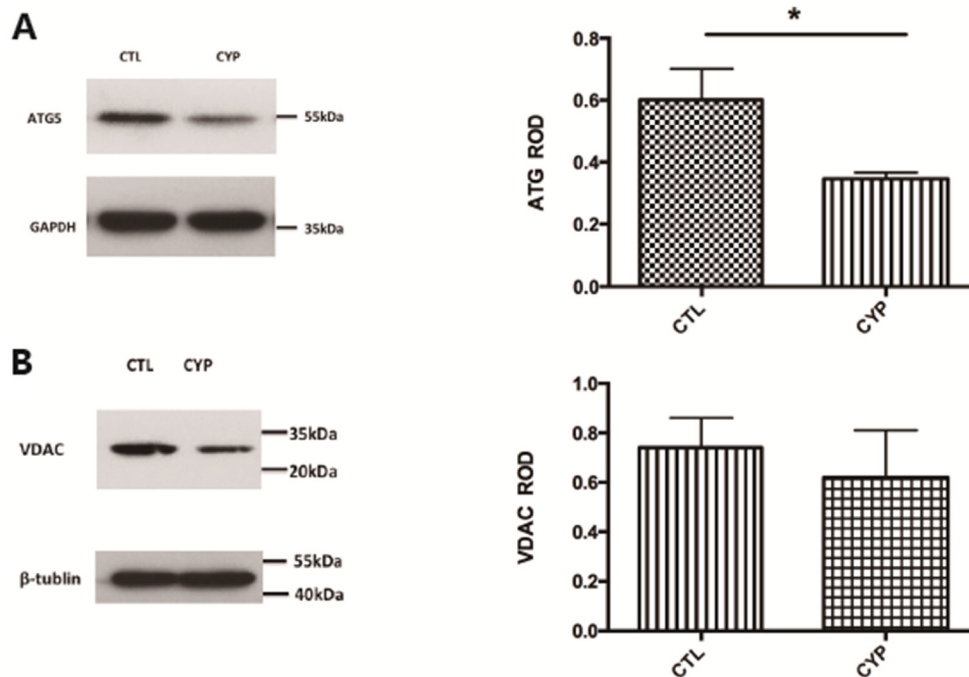
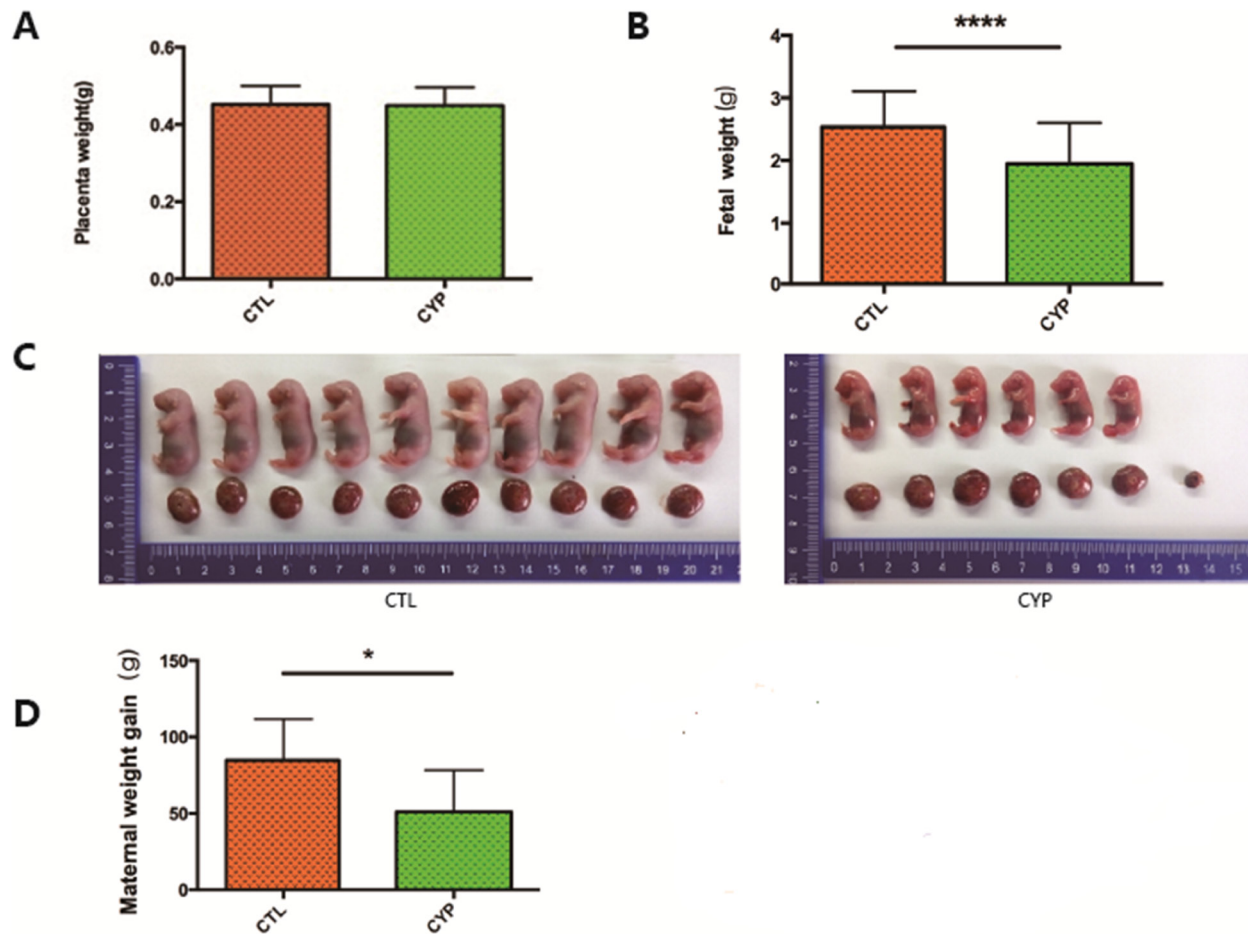


## Abnormal CYP11A1 gene expression induces excessive autophagy, contributing to the pathogenesis of preeclampsia

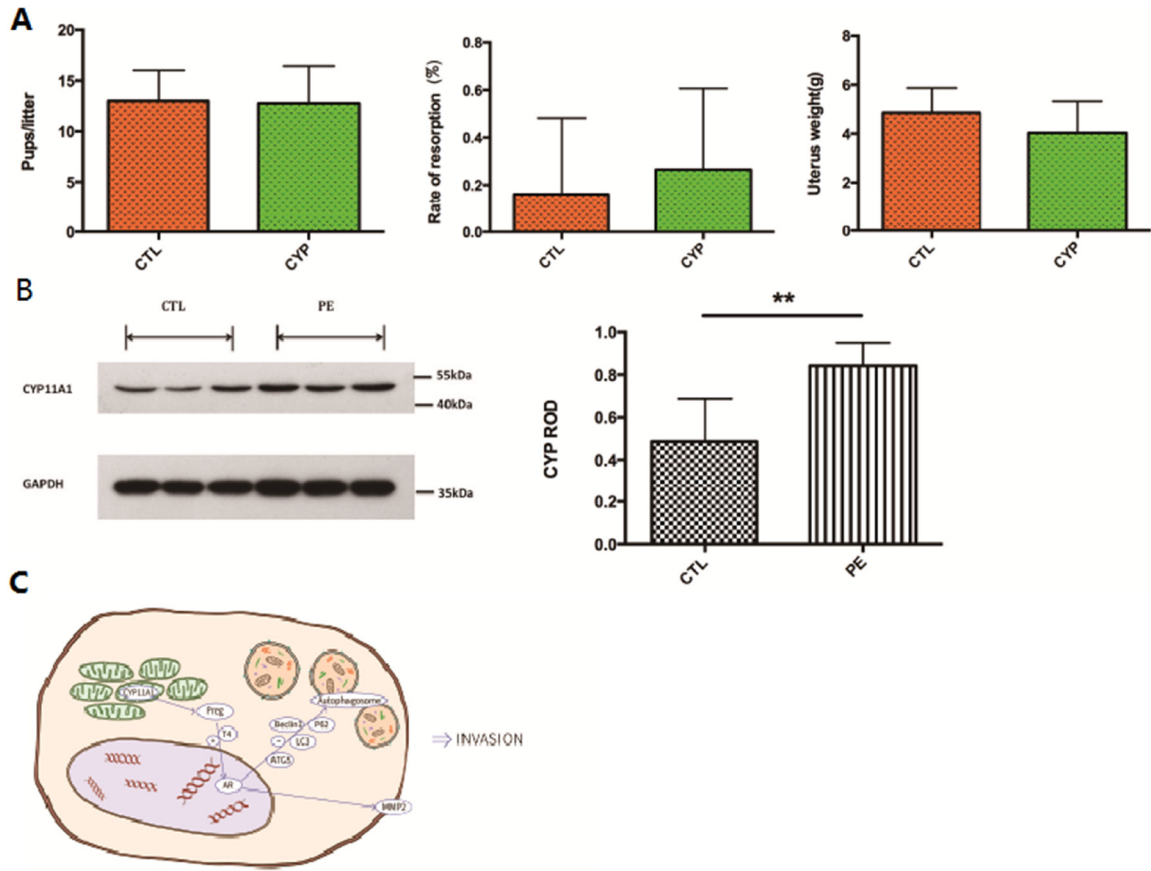
### SUPPLEMENTARY MATERIALS



**Supplementary Figure 1:** (A, B) Western blot shows that ATG5 and VDAC1 expression are suppressed in CYP11A1 overexpression BeWo cells. \* means  $P < 0.05$ .



**Supplementary Figure 2: *In vivo* overexpression of CYP11A1 leads to decreased placenta, fetal weight and reduced maternal weight gain in rats.** (A) Placenta weight shows significant decrease after overexpression of CYP11A1. (B, C) Offspring weights shows significant decrease after overexpression of CYP11A1. (D) Overexpression of CYP11A1 Rats' maternal weight gain from GD 0.5 to GD 19.5 is significant lower than the control group. \* means  $P < 0.05$ , \*\* means  $P < 0.01$ , \*\*\* means  $P < 0.001$ , \*\*\*\* means  $P < 0.0001$ .



**Supplementary Figure 3:** (A) Pregnancy loss and fetal number shows modest decrease after overexpression of CYP11A. (B) Western blot result shows that the expression of CYP11A1 is significantly increased in placenta of preeclampsia patients ( $N = 24$  for control group;  $N = 24$  for PE group); (C) The diagram shows the proposed mechanism of how overexpressed CYP11A1 leading to compromised trophoblast invasion, therefore contributing preeclampsia pathogenesis. Over-activated CYP11A1 increases androgen production, which stimulate androgen receptor (AR) transcriptional activity. Androgen receptor (AR) could then activate the expression of mitophagy related proteins, including LC-3, Beclin 1, P62, et. al. The excessive mitophagy inhibits the trophoblast invasion through regulating MMP2 expression.

**Supplementary Table 1: Clinical characteristics of patients in the current study**

	<b>Healthy pregnant (n = 24)</b>	<b>Preeclampsia (n = 24)</b>	<b>P value</b>	<b>P significant</b>
Age (years old)	30.02 ± 0.6790	32.34 ± 1.209	0.1021	ns
gestational age (weeks) at end of pregnant	39.79 ± 0.1836	34.98 ± 0.9715	< 0.0001	****
number of parity	1.417 ± 0.1797	2.792 ± 0.2885	0.0002	***
number of gestation	1.083 ± 0.05763	1.292 ± 0.1123	0.0723	ns
fetal weight (g)	3358 ± 61.45	2264 ± 263.5	0.0005	***
fetal length (cm)	49.79 ± 0.2169	43.45 ± 1.724	0.0016	**
placenta weight (g)	601.2 ± 21.77	431.3 ± 34.57	0.0001	***
BMI at beginning of pregnant (kg/m <sup>2</sup> )	20.25 ± 0.4121	22.49 ± 0.8989	0.0403	*
BMI at deliver (kg/m <sup>2</sup> )	25.44 ± 0.3993	28.08 ± 0.8163	0.0071	**
SPB (mm/Hg)	110.4 ± 1.340	149.2 ± 3.468	< 0.0001	****
DPB (mm/Hg)	67.59 ± 2.460	95.45 ± 2.230	< 0.0001	****