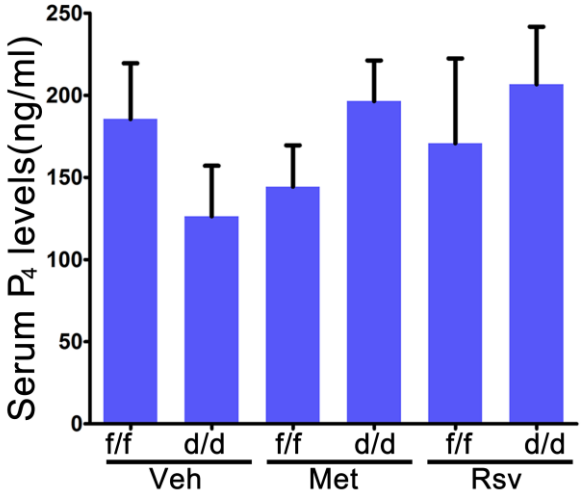
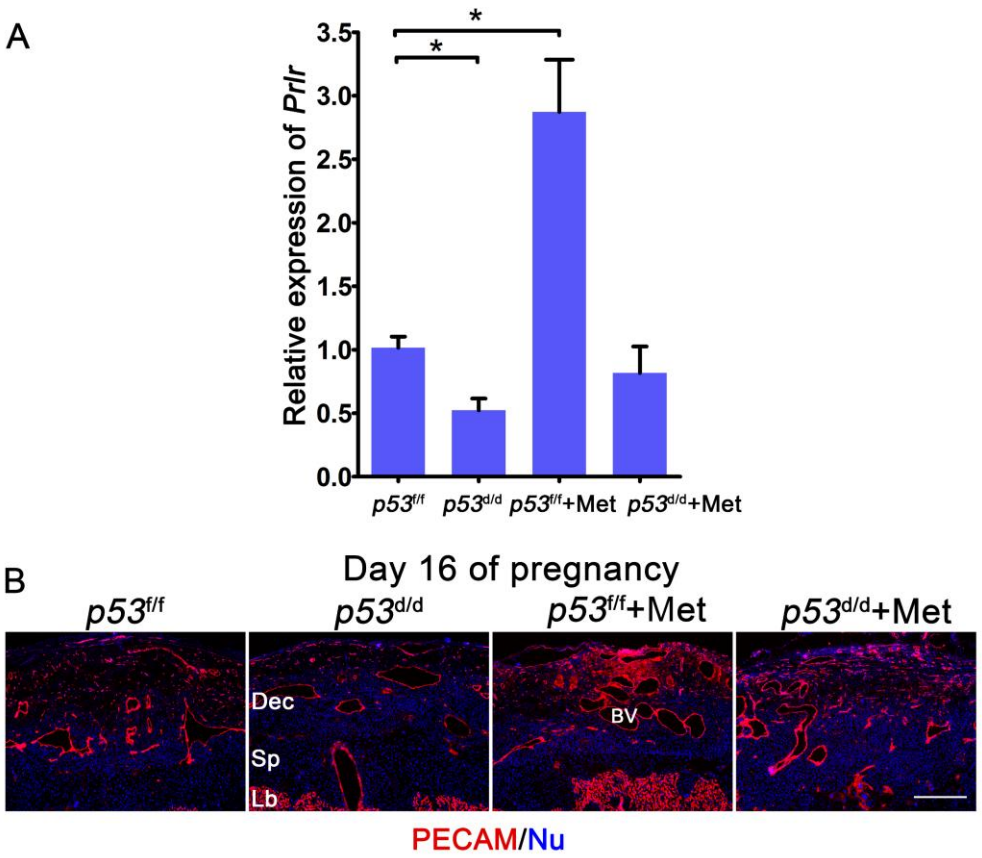
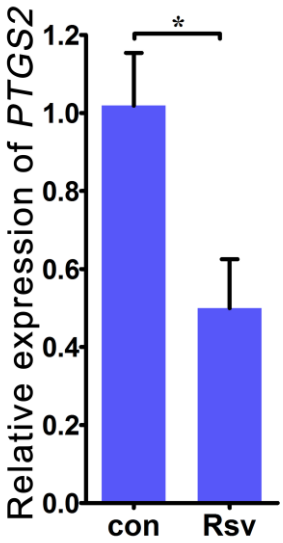
Supplementary Figures



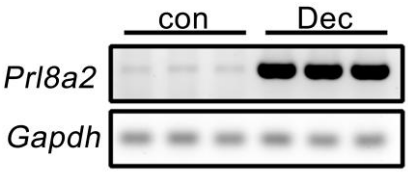
Supplementary Figure 1. Serum progesterone (P_4) levels in Met or Rsv pretreated *p53*$^{f/f}$ and *p53*$^{d/d}$ females on day 16 (n=4). No significant changes in P_4 levels were noted between the two groups.



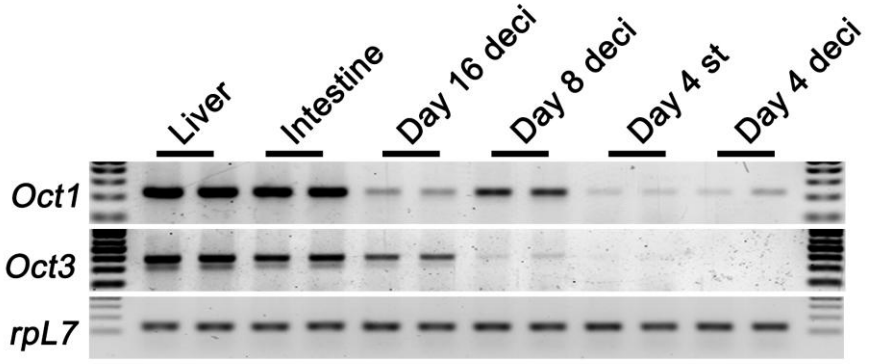
Supplementary Figure 2. Met increases *Prlr* mRNA expression and blood vessel density in *p53*$^{d/d}$ mice. (A) Expression of *Prlr* mRNA was decreased in day 16 *p53*$^{d/d}$ deciduae while Met significantly increased *Prlr* mRNA in *p53*$^{f/f}$ deciduae with more than 50% increasing but not reach into significant in *p53*$^{d/d}$ deciduae. (N=4, *p<0.05, mean ± SEM, ANOVA). (B) Density of PECAM-positive blood vessels was lower in *p53*$^{d/d}$ deciduae, but was upregulated in Met pretreated *p53*$^{d/d}$ deciduae. Dec: Decidua; Sp: spongiotrophoblast; Lb: labyrinth; BV: blood vessel (Bar, 500 μm).



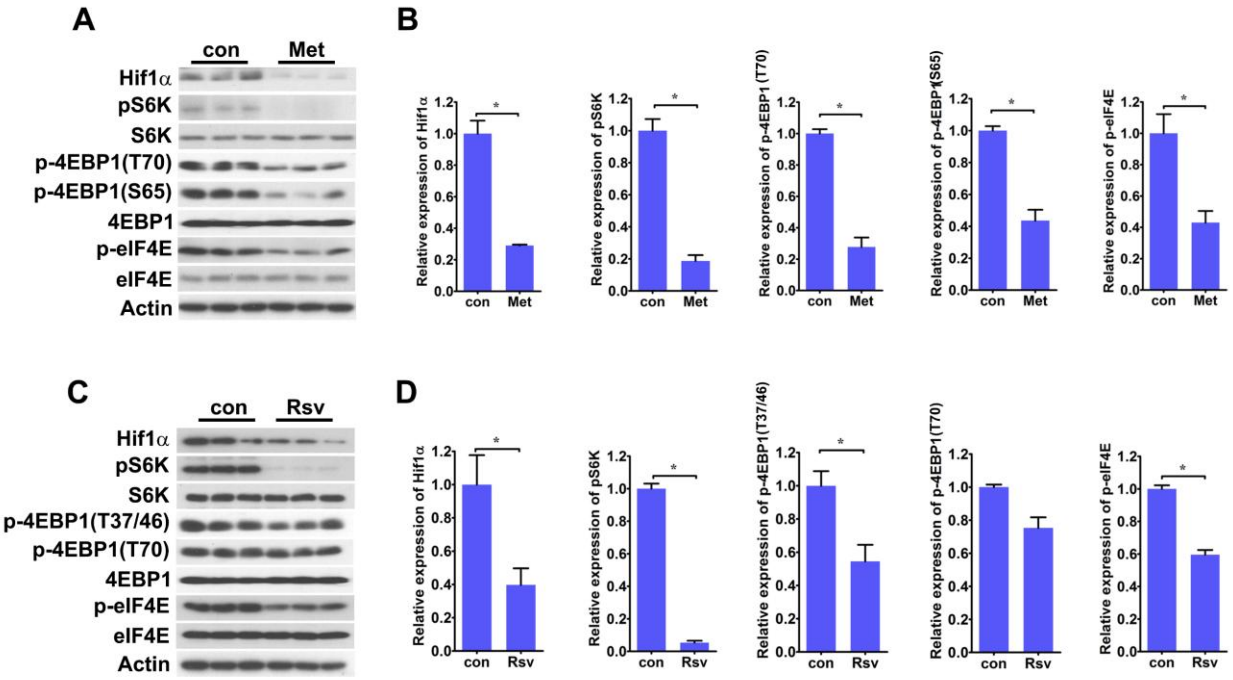
Supplementary Figure 3. Rsv inhibited *PTGS2* expression in human decidualized cells differentiated in vitro from human uterine fibroblast cells (HuF) (N=3, *p< 0.05, mean ± SEM, Student's *t* test).



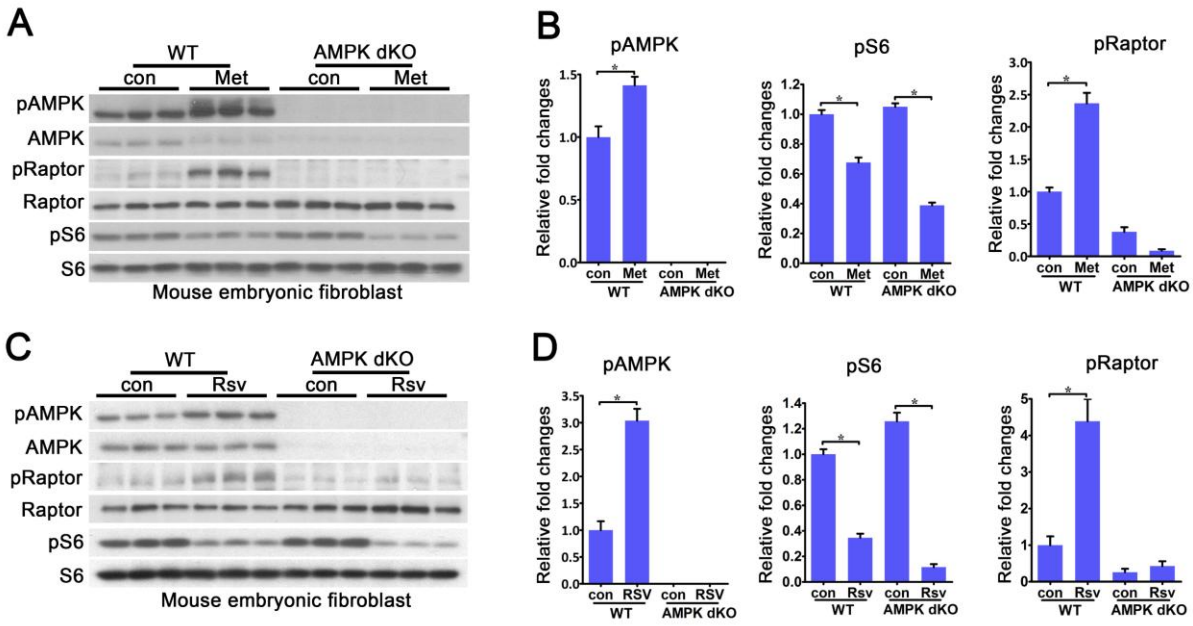
Supplementary Figure 4. Expression of *Prl8a2 (*decidual marker gene) in stromal cells decidualized in vitro. *Prl8a2* was highly expressed in decidual cells *in vitro* exposed to 10 nM estradiol-17β and 1 μM P_4. *Gapdh* was used as an internal control, con: Non-decidualized, Dec: Decidualized.



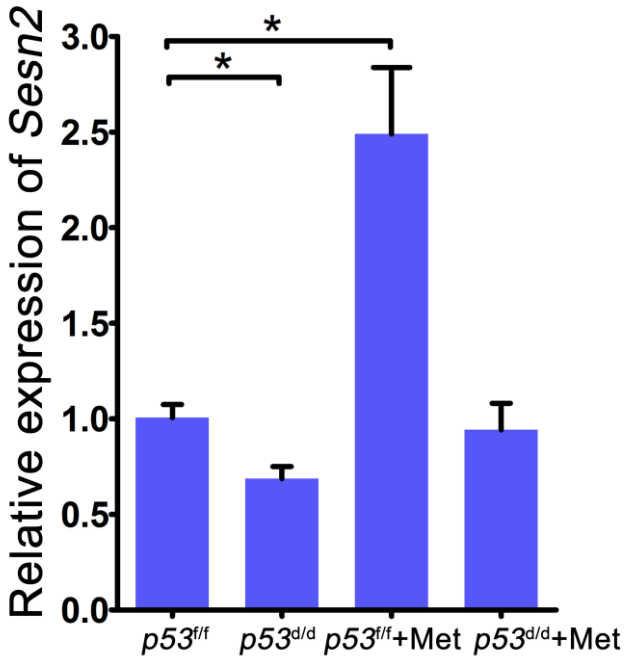
Supplementary Figure 5. *Oct1* and *Oct3* expression in different tissues and comparison of AMPK-mTORC1 signaling in floxed versus WT decidual cells. Levels of *Oct1* and *Oct3* transcripts, as determined by RT-PCR, in liver, intestine, day 16 deciduae, day 8 deciduae, as well as day 4 isolated stromal cells and decidualized stromal cells in vitro. Deci, decidua; Day 4 st, stromal cells isolated on day 4; Day 4 deci, day 4 stromal cells decidualized in vitro.



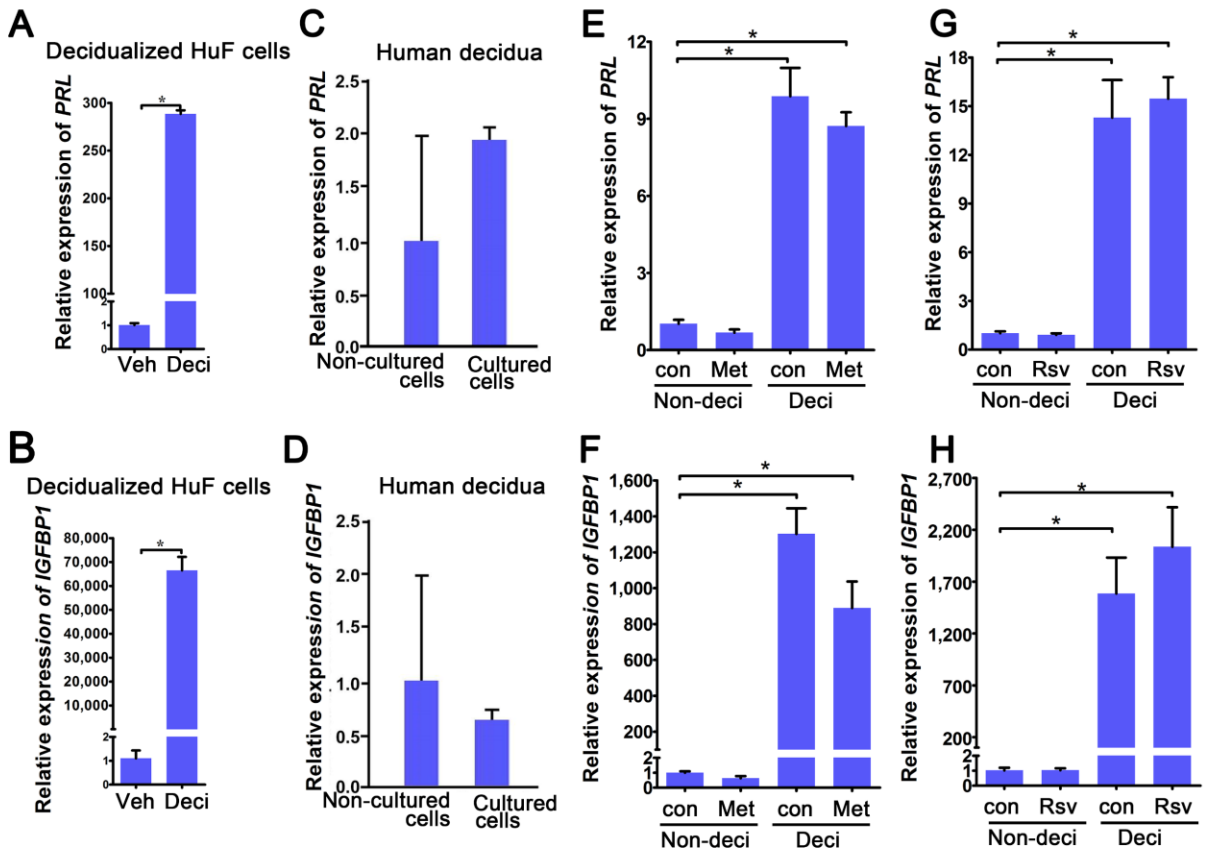
Supplementary Figure 6. Met and Rsv attenuate several other mTORC1 targets in stromal cells decidualized in vitro. (A-D) levels of Hif1α, pS6K (Thr389), p-4EBP1 (Thr37/46), p-4EBP1 (Thr70), p-4EBP1 (Ser65) and p-eIF4E (Ser209) are downregulated by Met and Rsv, respectively (N=3, *p<0.05, mean ± SEM, Student's *t* test).



Supplementary Figure 7. Met or Rsv downregulated mTORC1 signaling in AMPK dKO MEFs. (**A** to **D**) levels of pS6 were downregulated in WT and AMPK dKO (AMPKα1 and AMPKα2) MEFs by Met and Rsv with increased levels of pAMPK and its target pRaptor in WT MEFs (N=3, *p<0.05, mean ± SEM, Student's *t* test).



Supplementary Figure 8. Expression of *Sesn2* mRNA decreased in D16 $p53^{d/d}$ deciduae. Met significantly increased *Sesn2* mRNA in $p53^{f/f}$ deciduae and more than 37% in $p53^{d/d}$ deciduae which did not reach statistical significance (N=4, *p<0.05, mean ± SEM, ANOVA).



Supplementary Figure 9. Expression of human decidual cell makers in HuF cells and non-cultured and cultured decidual cells, as determined by real-time PCR. (**A and B**) Markers of human decidual cells *IGFBP1* and *PRL*, were strongly induced in human uterine fibroblasts (HuF) cells after decidualization with E_2 (10 nM), MPA (1 μM) and PGE_2 (10 nM) (N=3, *p<0.05, mean ± SEM, Student's *t* test). **(C and D)** *PRL* and *IGFBP1* transcript levels were comparable between non-cultured and cultured decidual cells (N=3, *p<0.05, mean ± SEM, Student's *t* test). **(E to H)** Decidual markers were highly expressed in HuF cells decidualized in vitro compared with much lower levels in non-decidualized cultured cells. Met or Rsv treatment maintained the expression of decidual cell markers in vitro (N=3, *p<0.05, mean ± SEM, ANOVA).

Use	Antibody	Source	Catalog No.	Dilution	Type	Fixative
IHC	γH2AX	Millipore	05-636	1:500	Paraffin	NBF
IHC	Sesn2	proteintech	10795-1-AP	1:200	Paraffin	NBF
IF	pAMPK(Thr172)	Cell Signaling	2535s	1:100	Frozen	PFA
IF	PECAM	BD	553370	1:300	Frozen	PFA
IF	Hoechst 33342	Life technology	H3570	1:500	Frozen	PFA
WB	pAMPK(Thr172)	Cell Signaling	2535s	1:1000	N.A.	N.A.
WB	AMPK	Cell Signaling	5831s	1:1000	N.A.	N.A.
WB	pRaptor (Ser792)	Cell Signaling	2083s	1:1000	N.A.	N.A.
WB	Raptor	Cell Signaling	2280s	1:1000	N.A.	N.A.
WB	pS6 (Ser235/236)	Cell Signaling	2211s	1:2000	N.A.	N.A.
WB	S6	Cell Signaling	2217s	1:2000	N.A.	N.A.
WB	Sesn2	Proteintech	10795-1-AP	1:2000	N.A.	N.A.
WB	p53	Santa Cruz	sc-6243	1:1000	N.A.	N.A.
WB	Actin	Santa Cruz	sc-1615	1:1000	N.A.	N.A.
WB	pS6K (Thr389)	Cell Signaling	9234	1:1000	N.A.	N.A.
WB	S6K	Cell Signaling	2708	1:1000	N.A.	N.A.
WB	Hif1α	Cell Signaling	14179S	1:1000	N.A.	N.A.
WB	p-4EBP1(Thr37/46)	Cell Signaling	2855	1:2000	N.A.	N.A.
WB	p-4EBP1(Ser65)	Cell Signaling	9451	1:2000	N.A.	N.A.
WB	p-4EBP1(Thr70)	Cell Signaling	9455	1:2000	N.A.	N.A.
WB	p-eIF4E (Ser209)	Cell Signaling	9741	1:2000	N.A.	N.A.
WB	eIF4E	Cell Signaling	2067	1:2000	N.A.	N.A.
WB	PDCD4	Cell Signaling	9535	1:1000	N.A.	N.A.
WB	α-Tubulin	Cell Signaling	2144	1:2000	N.A.	N.A.
WB	Anti-Flag	Sigma	F-3165	1:1000	N.A.	N.A.

Supplementary Table 1. Antibodies and applications. Specific antibodies are listed along with dilutions used for immunohistochemistry (IHC), immunofluorescence (IF), or Western blotting (WB). Fixatives used for optimal immunostaining is also shown, when applicable. NBF, Neutral buffered formalin; PFA, Paraformaldehyde.