

Fig. S1. Fetal and placental growth from E12.5 to E18.5 among the different IVF procedure groups.
Each data point represents an individual conceptus from a minimum of three litters ($n=13-22$ per group for ART groups, $n=39-45$ per group for natural control groups). These are the same individuals shown in Figure 1.

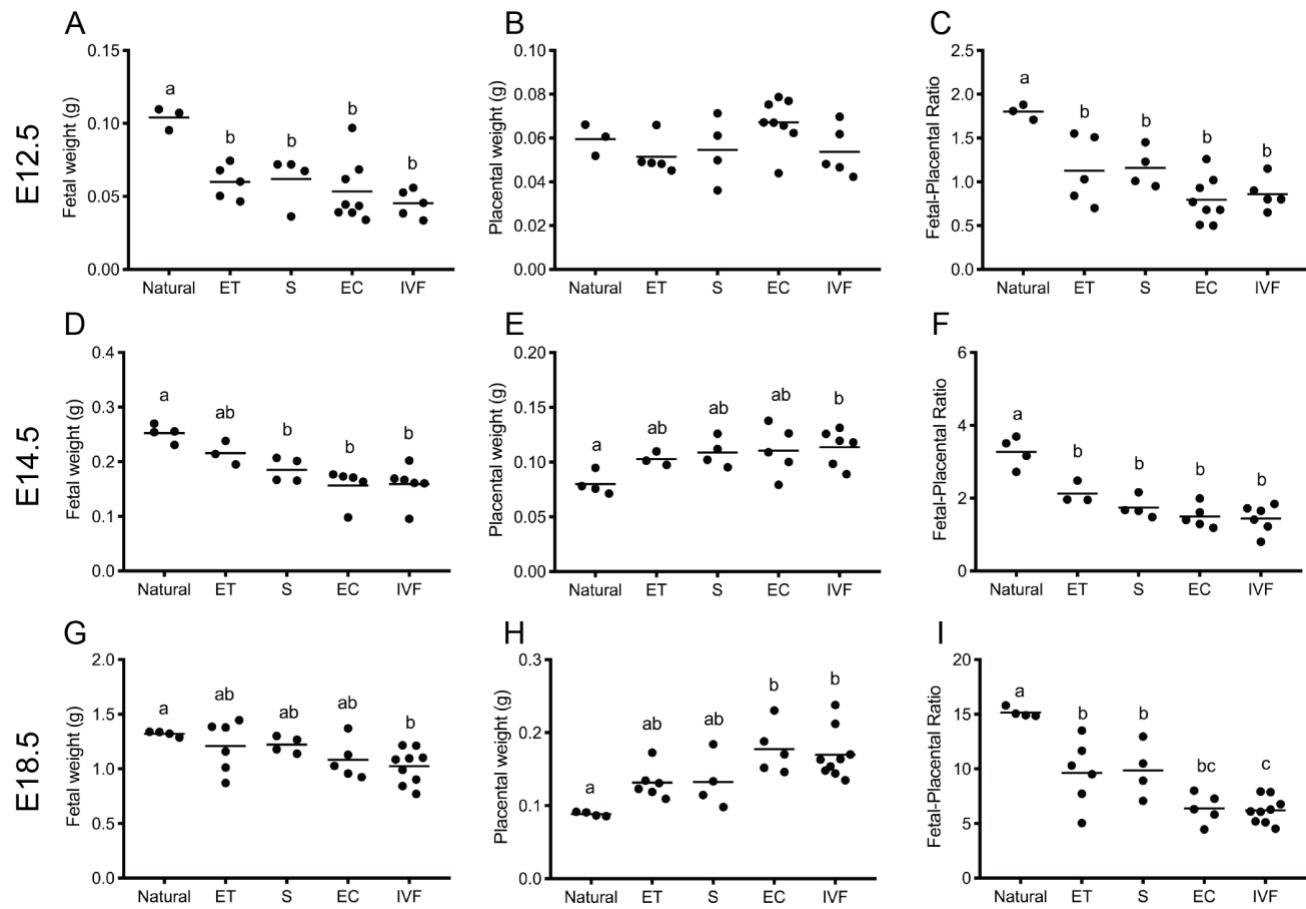


Fig.S2. Fetal and placental weight after IVF procedures at E12.5, E14.5, and E18.5 averaged by litter. Each data point represents the mean for all conceptus from a single litter ($n=3-9$ per group). Statistical significance was determined for each end point by one-way ANOVA ($p<0.05$) with Tukey's multiple comparisons test. Groups with different letters denote significant differences between groups ($p<0.05$); similar letters indicate no difference.

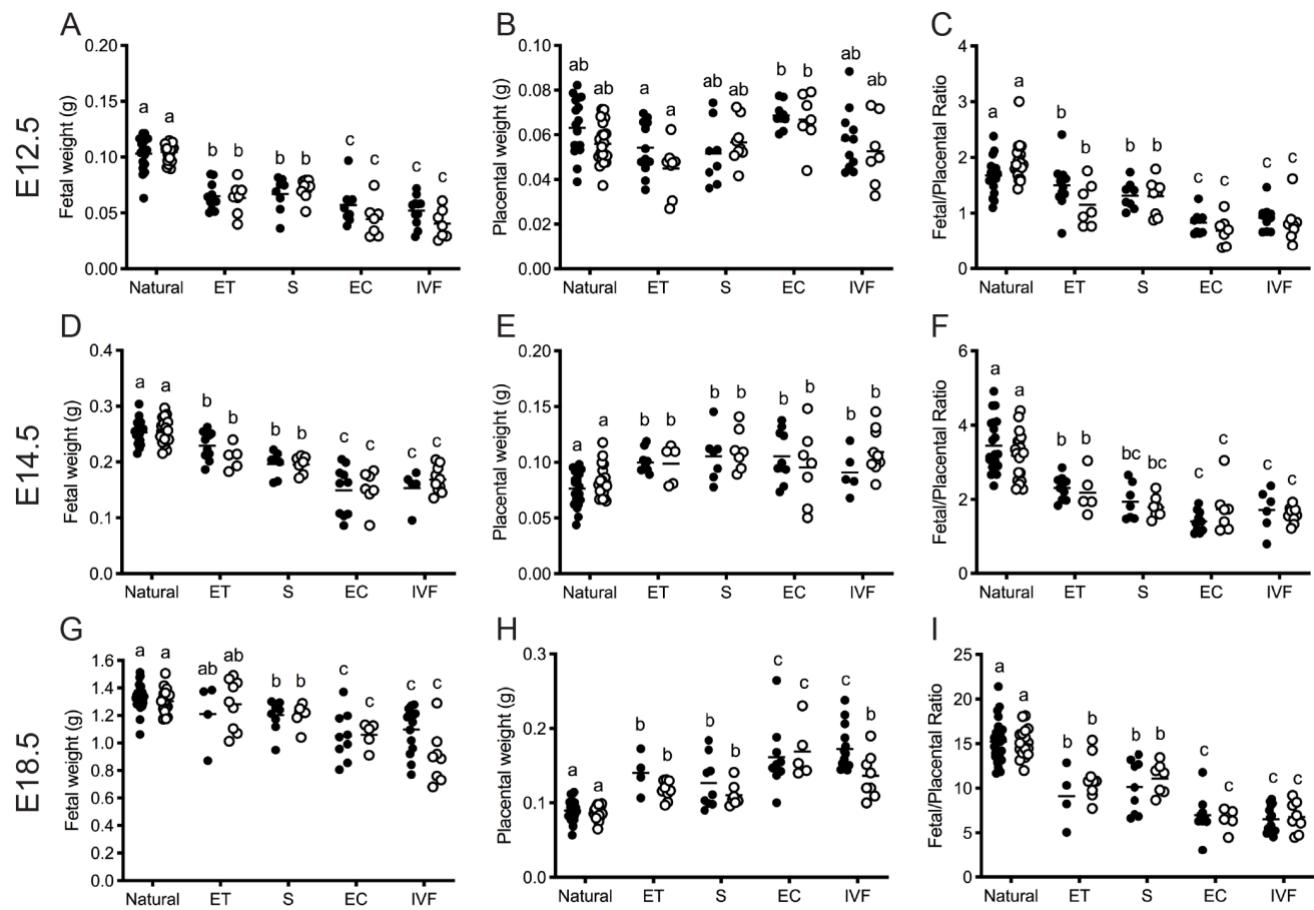


Fig. S3. Fetal and placental weight in male and female ART concepti at E12.5, E14.5, and E18.5.
 Each data point represents an individual conceptus from a minimum of three different litters ($n=13$ - 45 /group), then separated based on sex. Black circles=male concepti, white circles=female concepti.

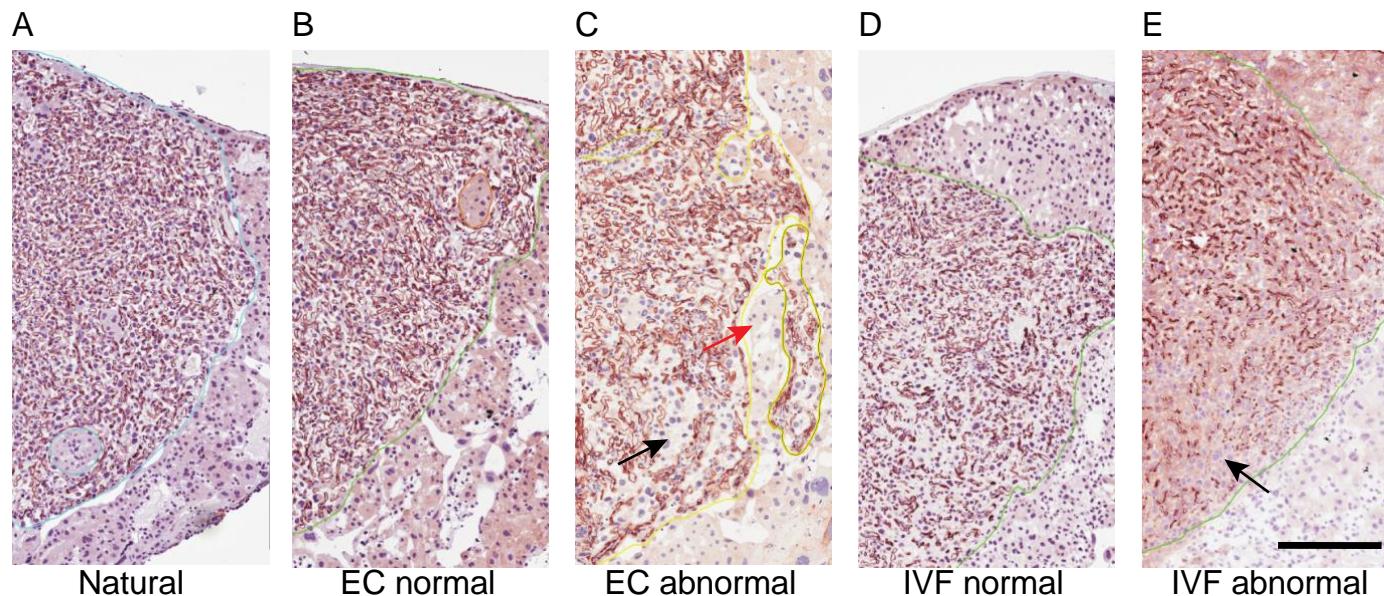


Fig. S4. Representative E18.5 placentas from EC and IVF groups. CD34 immunostaining counterstained with hematoxylin was used to visualize fetal endothelial cells. Examples of the range of labyrinth fetal endothelial cell morphology. 20x magnification. Scale bar=300 um. Black arrows indicate areas of uneven distribution of CD34-positive fetal endothelial cells within CD34-negative labyrinth trophoblast cells. Red arrow points to area of junctional zone/labyrinth border, where border is less distinct.

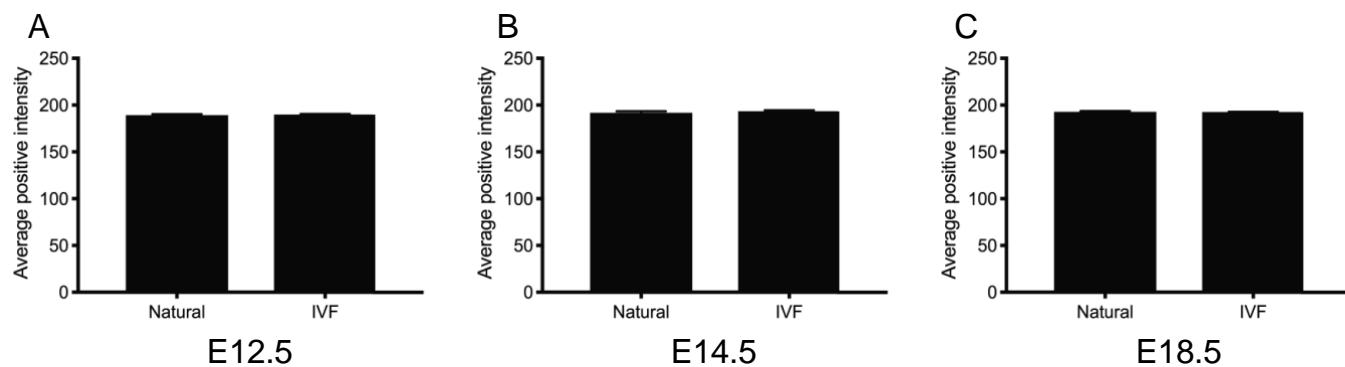


Fig. S5. Placental glycogen content in Natural and IVF placentas. Placental glycogen content was measured in a subset of Natural and IVF placental sections stained with Periodic Acid-Schiff reagents ($n=6$) from a minimum of three different litters. Statistical significance was determined for each time point by Student's t-test ($p>0.05$). Bars represent SEM.

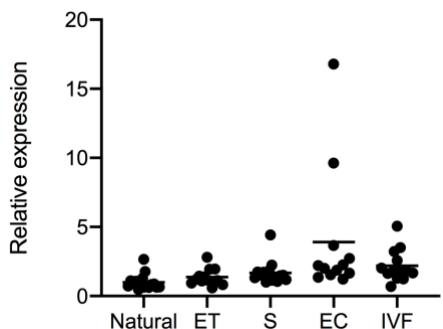


Fig. S6. E18.5 placental s Flt1 expression including outliers. Each data point represents the sFlt1 expression normalized to housekeeping gene, *B2m*. Statistical significance was determined for each end point by one-way ANOVA ($p<0.05$) with Tukey's multiple comparisons test. Groups with different letters denote significant differences between groups ($p<0.05$); similar letters indicate no difference.

Table S1. Control and ART Procedure groups

	Procedure					
	Hormone stimulation	Fertilization		Development		Embryo transfer
		In Vitro	In Vivo	In Vitro	In Vivo	
Natural			+		+	
ET			+		+	+
S	+		+		+	+
EC	+		+	+		+
IVF	+	+		+		+

ET= embryo transfer; S=Hormone stimulation; EC=embryo culture; IVF= in vitro fertilization.

Table S2. Litter characteristics

	Group	Individuals (litters)	Mean litter size ¹	Litter size range	Live pups (%) ²	Number of resorptions ³
E12.5	Natural	54 (4)	12.75 ± 0.48	12-14	--	1
	ET	21(5)	4.20 ± 1.07	2-8	42.00%	12
	S	17 (4)	4.25 ± 2.02	1-10	42.50%	0
	EC	17 (8)	2.13 ± 0.58	1-6	21.25%	29
	IVF	18 (5)	3.60 ± 0.75	1-5	36.00%	21
E14.5	Natural	54 (4)	13.50 ± 1.32	10-16	--	6
	ET	15 (3)	5.00 ± 2.31	1-9	50.00%	1
	S	14 (4)	3.50 ± 1.19	1-6	35.00%	2
	EC	17 (5)	3.40 ± 1.17	1-7	34.00%	16
	IVF	15 (6)	2.50 ± 1.12	1-8	25.00%	10
E18.5	Natural	46 (4)	11.50 ± 1.19	8-13	--	3
	ET	13 (6)	2.16 ± 0.54	1-4	21.67%	1
	S	16 (4)	4.00 ± 1.00	1-5	40.00%	3
	EC	14 (5)	2.80 ± 1.11	1-6	28.00%	19
	IVF	16 (7)	2.44 ± 0.44	1-4	22.86%	20

¹ Mean litter size ± SEM

² Number of live pups/number of blastocysts transferred × 100

³ Number of visible implantations that were not viable concepti

Table S3. Individual outcomes at E12.5, E14.5, and E18.5 for EC and IVF concepti

	Group	Pup ID	F:P ratio	CD34	Labyrinth trophoblast marker expression			JZ	pTGC count	s <i>FLT1</i> expression	ICR DNA methylation				LUMA
					S-TGCs	SynT I	SynT II				H19	Kcnq1ot1	Peg3	Snrpn	
					--	--	--				--	--	--	--	
E12.5	EC	A-1	↓	↓	↓	↓	↓	--	--	--	↓	↓	--	--	--
	EC	A-2	↓	↓	↓	↑	--				↓	↓	↓	↓	↓
	EC	B-1	↓	--	↓	↓	↓				↓	--	↓	--	↓
	EC	B-2	↓	↓	↓	--	↓				↓	--	↓	--	↓
	EC	C-1	↓	↓	↓	--	--				↓	↓	↓	↓	↓
	EC	C-2	--	↓	↓	↓	↓				↓	↓	--	↓	↓
	EC	D-1	↓	↓	↓	--	--				↓	↓	--	--	↓
	EC	D-2	↓	--	↓	--	↓				↓	↓	--	--	↓
	EC	E-1	--	--	--	--	--				--	--	↓	--	↓
	EC	F-1	--	↓	↓	--	--				--	↓	↓	↓	--
	EC	F-2	↓	↓	↓	↑	--				↓	↓	↓	--	--
	IVF	A-1	↓	↓	↓	--	↓	--	--	--	↓	↓	↓	↓	--
	IVF	B-1	↓	--	↓	↓	↓				↓	↓	↓	↓	--
	IVF	B-2	↓	--	↓	--	↑				↓	↓	↓	↓	--
	IVF	B-3	↓	↓	↓	--	--				↑	↓	--	--	--
	IVF	C-1	↓	↓	↓	--	↓				--	↓	↓	↓	--
	IVF	C-2	↓	↓	↓	--	--				--	↓	↓	↓	--
	IVF	D-1	↓	--	↓	--	--				--	↓	--	↓	--
	IVF	D-2	↓	↓	↓	↓	--				--	↓	--	↓	--
	IVF	E-1	↓	--	↓	↓	↓				--	↓	--	↓	--
	IVF	E-2	↓	--	↓	↓	↓				--	--	--	↓	--
	IVF	E-3	↓	↓	↓	--	--				--	↓	--	--	↓

	Group	Pup ID	F:P ratio	CD34	Labyrinth trophoblast marker expression			JZ	pTGC count	s <i>FLT1</i> expression	ICR DNA methylation				LUMA
					S-TGCs	SynT I	SynT II				H19	Kcnq1ot1	Peg3	Snrpn	
					--	--	--				--	--	--	--	
E14.5	EC	A-1	↓	--	--	--	--	--	--	--	--	--	--	--	↓
	EC	B-1	↓	--	↓	--	--				↑	--	↓	--	--
	EC	B-2	↓	--	--	--	↓				↑	↑	--	↓	--
	EC	B-3	↓	--	--	↑	--				↑	↑	--	--	--
	EC	B-4	↓	--	↓	--	↓				--	--	↓	--	--
	EC	C-1	↓	--	↓	↑	--				--	↑	--	--	↓
	EC	C-2	↓	--	↓	--	↓				--	--	↓	↓	--
	EC	C-3	↓	--	↓	--	--				--	↑	--	--	--
	EC	D-1	↓	--	↓	↓	--				↑	↑	--	--	--
	EC	D-2	↓	↓	--	--	--				--	--	↓	↓	--
	EC	D-3	--	--	--	--	--				↑	--	--	↓	--
	IVF	A-1	↓	--	--	↑	--	--	--	--	↑	--	--	↓	--
	IVF	A-2	↓	--	--	--	--				↑	↑	--	↓	--
	IVF	A-3	↓	--	--	--	--				↑	↑	↑	↓	--
	IVF	A-4	--	--	↓	--	--				↑	↑	--	↓	--
	IVF	B-1	↓	--	↓	--	--				--	↑	--	↓	--
	IVF	C-1	↓	--	↓	--	--				↑	--	--	↓	--
	IVF	C-2	↓	--	--	--	--				--	--	--	↓	--
	IVF	D-1	↓	--	--	--	--				--	--	--	--	--
	IVF	E-1	↓	--	↓	--	--				--	--	↓	--	--
	IVF	F-1	↓	--	--	--	--				--	↑	--	--	--
	IVF	F-2	↓	--	--	--	--				↑	↑	--	↓	--

	Group	Pup ID	F:P ratio	CD34	Labyrinth trophoblast marker expression			JZ	pTGC count	<i>sFLT1</i> expression	ICR DNA methylation				LUMA
					S-TGCs	SynT I	SynT II				<i>H19</i>	<i>Kcnq1ot1</i>	<i>Peg3</i>	<i>Snrpn</i>	
					--	--	--				--	--	--	--	
E18.5	EC	A-1	↓	--	--	--	--	↑	--	--	--	--	↓	--	--
	EC	B-1	--	↑	--	--	--	↑	↑	↑	--	--	↓	--	↓
	EC	B-2	↓	↑	↓	--	--	↑	↑	--	--	--	↓	--	--
	EC	B-3	↓	--	--	--	--	↑	↑	--	--	--	↓	--	--
	EC	B-4	↓	↑	--	--	--	↑	--	--	--	--	--	--	↓
	EC	C-1	↓	--	--	--	--	↑	--	--	--	--	↓	--	--
	EC	D-1	↓	--	--	--	--	↑	↑	--	↓	↓	↓	↓	
	EC	E-1	↓	--	--	--	--	↑	↑	--	↓	--	--	--	--
	EC	E-2	↓	--	--	--	--	↑	↑	↑	--	--	↓	↓	--
	EC	E-3	↓	--	--	--	--	↑	↑	↑	--	↓	↓	↓	↓
	EC	E-4	↓	--	↓	↑	--	↑	--	--	↓	↓	↓	↓	--
	IVF	A-1	↓	--	--	↓	↑	--	--	--	↓	--	↓	--	--
	IVF	A-2	↓	--	--	↓	--	↑	--	--	--	--	↓	--	--
	IVF	B-1	↓	--	--	--	--	↑	↑	↑	↑	↓	--	↓	↓
	IVF	C-1	↓	--	--	--	↑	↑	--	--	--	--	--	--	--
	IVF	D-1	↓	--	↓	--	--	--	--	--	--	--	↓	--	↓
	IVF	E-1	↓	↓	↓	--	--	↑	--	↑	--	--	↓	--	↓
	IVF	E-2	↓	--	↓	--	↑	↑	--	--	--	--	↓	--	--
	IVF	F-1	↓	--	↓	--	↑	↑	↑	--	--	↓	↓	↓	--
	IVF	F-2	↓	--	--	↓	--	↑	↑	↑	--	↓	↓	↓	↓
	IVF	G-1	↓	--	↓	--	--	--	↑	--	--	--	↓	--	--
	IVF	G-2	↓	--	↓	↓	↑	--	↑	--	--	--	↓	--	--

Arrow direction determined using range of Natural individuals: Down arrow (↓) and up arrow (↑) denote individual had a value lower than lowest Natural value and higher than highest Natural value, respectively. Dashes (--) denote individual was within Natural range. Gray boxes denote experimental group was not statistically different from Naturals for that specific phenotype/timepoint. Black boxes denote that the analysis was not performed for that phenotype/timepoint.

Table S4. In situ hybridization primers

Gene	Primer	Sequence	Reference
<i>Prl8a8</i>	Forward	TCCTGCTGCTACTGTTGTCAAAC	This study
	Reverse	ATCCACCTAACGGTCACGCAGA	
<i>Tpbpa</i>	Forward	TGAAGAGCTGAACCAGTGGA	This study
	Reverse	CAATTGCCTCACAAAACCTGA	

Table S5. Real-time PCR primers

Gene	Primer	Sequence	Reference
<i>B2m</i>	Forward	CTCGGTGACCCTGGTCTTC	(1)
	Reverse	GGATTCAATGTGAGGCCGG	
<i>Ctsq</i>	Forward	GTGATCTGAGGCAGTAGTGGT	This study
	Reverse	TGACAGGATTCCAAGCACA	
<i>Slc16a1</i>	Forward	TCCTAGGGCCACCACTTTAG	This study
	Reverse	TGATGAGGATCACGCCACAA	
<i>Slc16a3</i>	Forward	AGCACACCATTGTGGAGAGA	This study
	Reverse	GGCTGCTTCACCAAGAACT	
<i>sFlt1</i>	Forward	AGGTGAGCACTGCGGCA	(2)
	Reverse	ATGAGTCCTTAATGTTGAC	

References

1. Avgustinova A, et al. (2018) Loss of G9a preserves mutation patterns but increases chromatin accessibility, genomic instability and aggressiveness in skin tumours. *Nat Cell Biol* 20(12):1400–1409.
2. Muthig V, et al. (2007) Upregulation of Soluble Vascular Endothelial Growth Factor Receptor 1 Contributes to Angiogenesis Defects in the Placenta of α_{2B} -Adrenoceptor-Deficient Mice. *Circ Res* 101(7):682–691.