

Supplemental Materials

Title: High Maternal Serum Estradiol Levels Induce Dyslipidemia in Human Newborns via a Hepatic HMGCR Estrogen Response Element

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Table S1 Nucleotide sequences of primers used for quantitative Real-time PCR and PCR

Gene Name	Accession Number	Sequences (5'->3')		Length
Human HMGCR	NM_000859.2	Forward	TGAGGGCTCCTTCCGCTCCG	78bp
		Reverse	ACTAGAGGCCACCGAACCCCG	
Human CYP7A1	NM_000780.3	Forward	TCTTACAAGGCGGGACACAC	166bp
		Reverse	GTTCTCGTGCCTCAAGCTCT	
Human LCAT	NM_000229.1	Forward	CCCATGGCAGTGGGTGACG	148bp
		Reverse	CAGCCGGGCACGAGGATGAC	
Human LPL	NM_000237.2	Forward	GTGGACTGGCTGTCACGGGC	168bp
		Reverse	GCCAGCAGCATGGGCTCCAA	
Human GAPDH	NM_002046.5	Forward	CAGGGCTGCTTTTAACTCTGG	102bp
		Reverse	TGGGTGGAATCATATTGGAACA	
Mouse Hmgcr	NM_008255.2	Forward	CCACGCAGCAAACATTGTCA	199bp
		Reverse	GCAGGCTTGCTGAGGTAGAA	
Mouse Gapdh	NM_001289726.1	Forward	TGACGTGCCGCCTGGAGAAA	98bp
		Reverse	AGTGTAGCCCAAGATGCCCTTCAG	
Human HMGCR (ChIP)	NC_000005.10	Forward	ACGGAGCCTTAGCTGCCTTC	174bp
		Reverse	GCTCACACTCCTCAGCCCTT	

Abbreviations: HMGCR: 3-hydroxy-3-methylglutaryl-CoA reductase; CYP7A1: cholesterol 7 α -hydroxylase; LCAT: lecithin-cholesterol acyltransferase; LPL: lipoprotein lipase, GAPDH: glyceraldehyde-3-phosphate dehydrogenase.

Figure S1

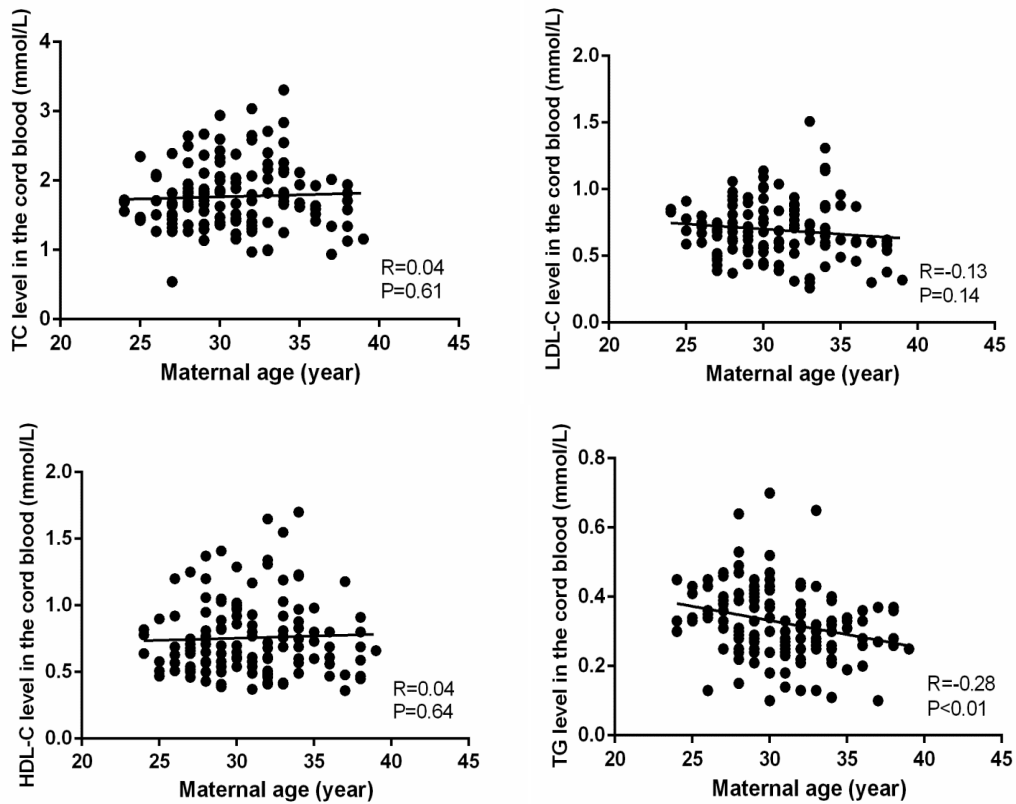


Figure S1. The correlation between lipid levels and the maternal age in the umbilical cord blood of newborns.

The amounts of TC, LDL-C, HDL-C and TG had no correlation with the maternal age in the 44 newborns ($R = 0.04$, $P = 0.61$; $R = -0.13$, $P = 0.14$; $R = 0.04$, $P = 0.64$; $R = -0.28$, $P < 0.01$; respectively). TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride.

Figure S2

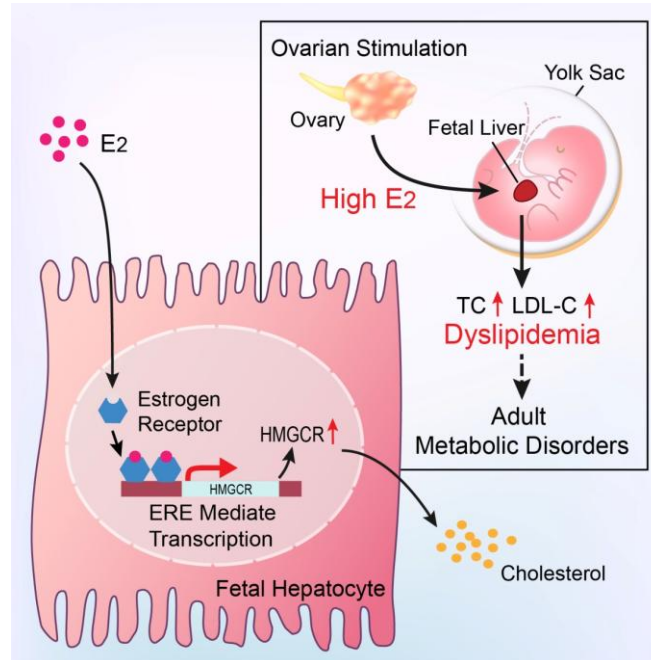


Figure S2. Hypothetical schematic representation of dyslipidemia induced by high E₂ in human newborns.

OS at IVF-ET procedure can induce maternal high E₂ throughout pregnancy. Intrauterine high E₂ can up-regulate the cholesterol synthesis rate-limiting enzyme HMGCR expression in fetal hepatocytes via an ERE in the promoter and induces elevated levels of TC and LDL-C levels in offspring that may be related to increased risk of metabolic diseases in adulthood. OS: ovarian stimulation; E₂: estradiol; IVF-ET: *in vitro* fertilization and embryo transfer; HMGCR: 3-hydroxy-3-methylglutaryl-CoA reductase; ERE: estrogen response element; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol.