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ORIGINAL ARTICLE

hsa_circ_0003218 Mitigates Trophoblast Dysfunction in Gestational Diabetes by Regulating TLR4/MyD88/NF-κB and NLRP3 Inflammasome

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SUMMARY

Background: **This investigation sought to determine hsa_circ_0003218's role and mechanism in trophoblast dysfunction during gestational diabetes mellitus (GDM).**
Methods: **The study involved forty pregnant women, comprising twenty with GDM and twenty with normal pregnancies. hsa_circ_0003218 expression levels in serum and placental tissues were detected by RT-qPCR. hTR8/SVneo cells were exposed to high glucose (HG) *in vitro* and assayed for proliferation, apoptosis, migration, and invasion by CCK-8, flow cytometry, and Transwell tests, respectively. Inflammatory factors were detected by ELISA. TLR4/MyD88/NF-κB cascade and NLRP3 inflammasomes-associated proteins were detected by Western blot.**
Results: **hsa_circ_0003218 was lowly expressed in placental tissues from GDM patients and HG-treated trophoblasts. hsa_circ_0003218 overexpression lessened HG-induced inhibition of trophoblast proliferation, migration, and invasion, and stimulation of apoptosis and inflammatory factor production. Furthermore, hsa_circ_0003218 prevented the activation of both the TLR4/MyD88/NF-κB cascade and the NLRP3 inflammasome.**
Conclusions: **hsa_circ_0003218 improves trophoblast function in GDM by blocking the TLR4/MyD88/NF-κB cascade and preventing NLRP3 inflammasome activation.**
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Supplementary Data

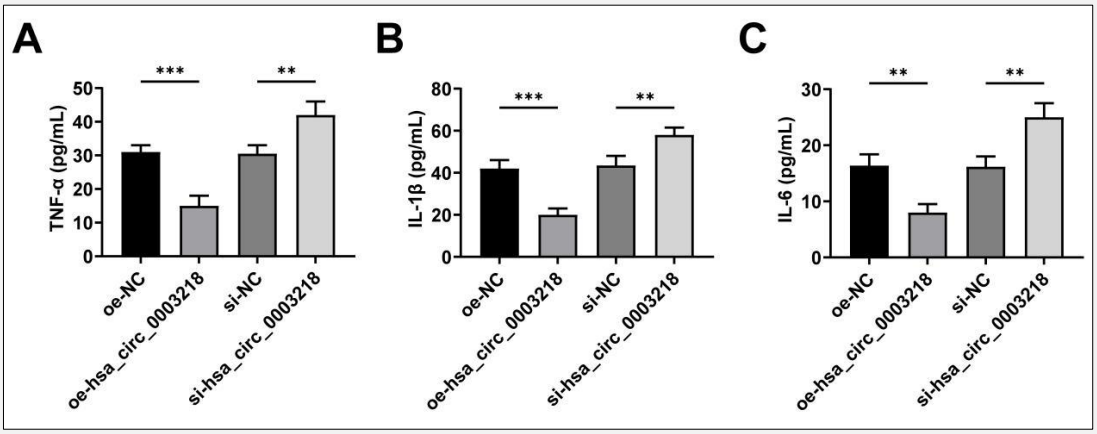

Figure S1. Upregulation of hsa_circ_0003218 ameliorates HG-induced trophoblast dysfunction.

A - C) ELISA to detect inflammatory factors (TNF-α, IL-1β, and IL-6).
*** indicates p < 0.05, ** indicates p < 0.01, *** indicates p < 0.001, **** indicates p < 0.0001.**

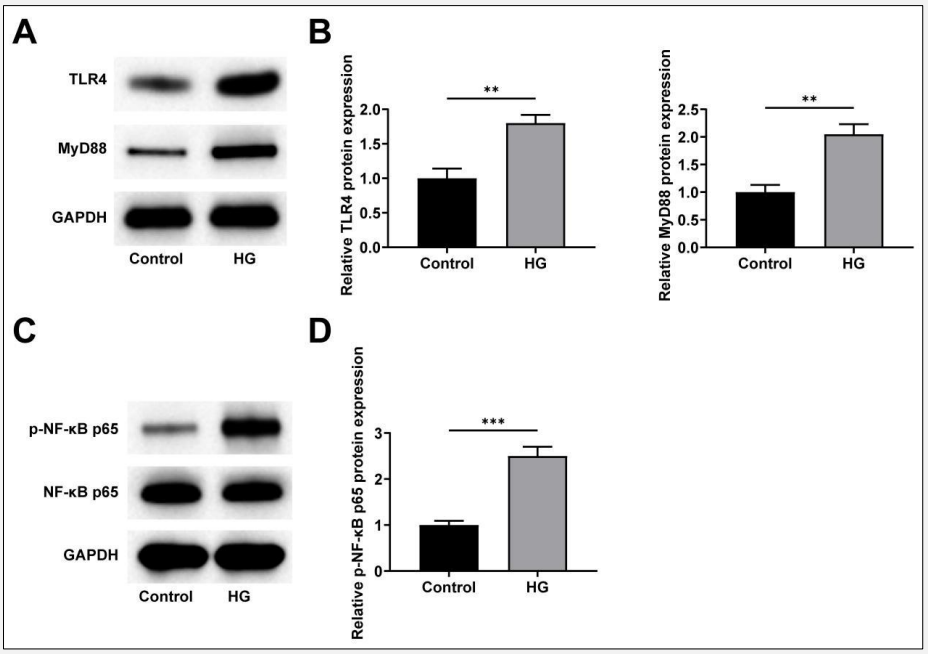

Figure S2. Upregulation of hsa_circ_0003218 inhibits HG-induced TLR4/MyD88/NF-κB signaling pathway activation in trophoblasts.

A - D) Western blot detection of TLR4/MyD88/NF-κB signaling cascade-related protein expression after HG treatment.
*** indicates p < 0.05, ** indicates p < 0.01, *** indicates p < 0.001, **** indicates p < 0.0001.**

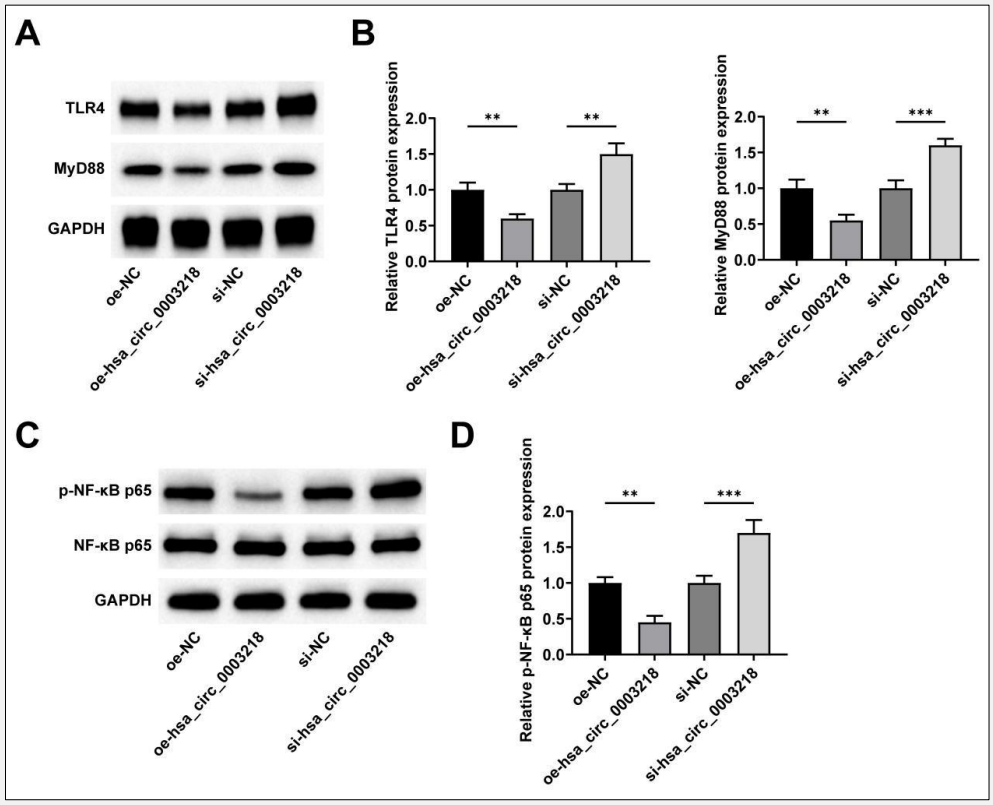

Figure S3. Upregulation of hsa_circ_0003218 inhibits HG-induced TLR4/MyD88/NF-κB signaling pathway activation in trophoblasts.

A - D) Western blot detection of TLR4/MyD88/NF-κB signaling cascade-related protein expression after regulating hsa_circ_0003218 expression.
*** indicates p < 0.05, ** indicates p < 0.01, *** indicates p < 0.001, **** indicates p < 0.0001.**

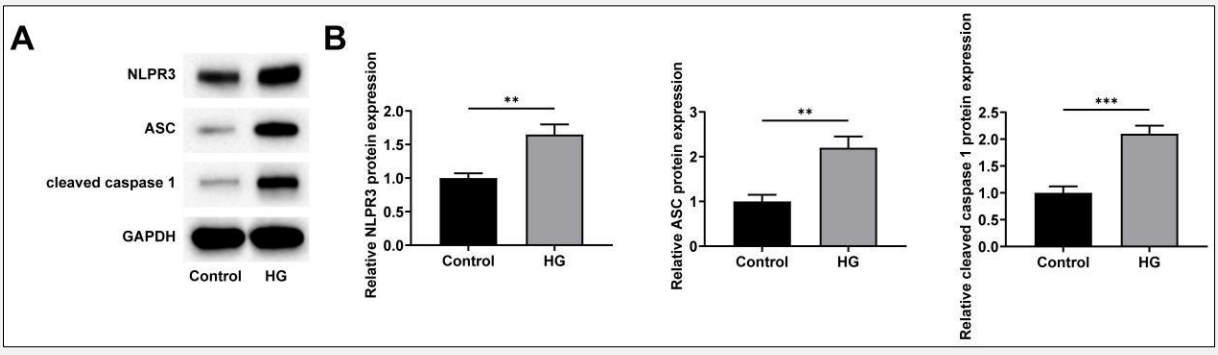

Figure S4. Upregulation of hsa_circ_0003218 inhibits HG-induced NLRP3 inflammasome activation in trophoblast cells.

A/B) Western blot detection of NLRP3 inflammasomes-associated protein expression after HG treatment.
*** indicates p < 0.05, ** indicates p < 0.01, *** indicates p < 0.001, **** indicates p < 0.0001.**

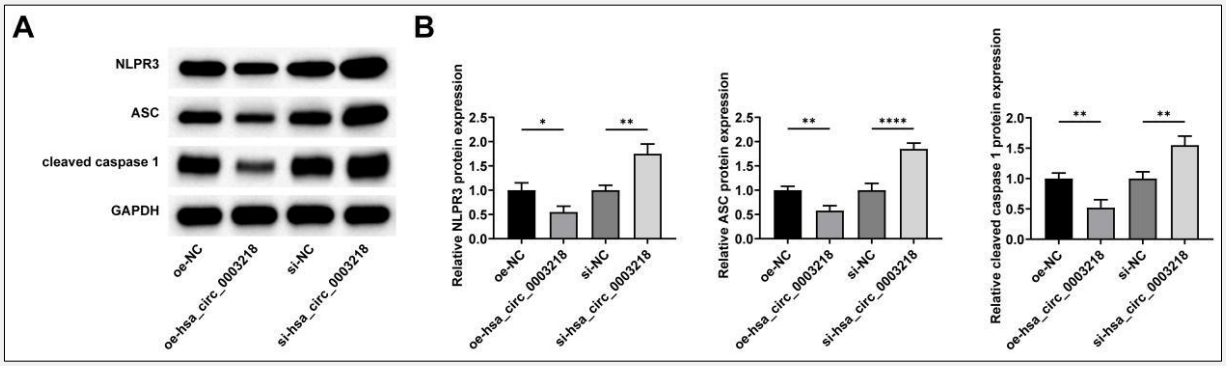

Figure S5. Upregulation of hsa_circ_0003218 inhibits HG-induced NLRP3 inflammasome activation in trophoblast cells.

A/B) Western blot detection of NLRP3 inflammasomes-associated protein expression after regulating hsa_circ_0003218 expression.
*** indicates p < 0.05, ** indicates p < 0.01, *** indicates p < 0.001, **** indicates p < 0.0001.**