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TRANSPLACENTAL DELIVERY OF NANOPARTICLES FOR PRENATAL THERAPY

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Background:
Current prenatal interventions - surgery and drug therapy - do not address the underlying pathomorphological changes in congenital diaphragmatic hernia and its underlying abnormal lung development. Our proposed nanoparticle model can safely encapsulate and deliver medication introduced from the maternal circulation to the fetus. Nanoparticles surface-modified with IgG antibodies provide the necessary tissue specificity to mitigate unintentional drug exposure.

Objective:
We aim to study the maternal transfer of passive immunity as a mechanism to induce the transplacental transport of IgG-modified nanoparticles for prenatal therapy.

Methods:
Human BeWo placental epithelial cells ($1X10^6$ cells/cm^2) were grown on 3 μm polyester transwell membranes. Barrier function was monitored with transepithelial electrical resistance (TEER) and immunostaining for E-cadherin and zonula occludens-1. Placental integrity was assessed after 24 hours of exposure to chitosan nanoparticles synthesized by ionic gelation, covalently modified with human IgG antibodies, and fluorescently-tagged with FITC.

Results:
We successfully established an *in vitro* transwell model of the placenta epithelial layer. TEER measurements indicated no significant change in barrier function ($p > 0.05$) after 24 hours of nanoparticle exposure. This is verified by the intact E-cadherin and zonula occludens-1 junction proteins observed with immunostaining. Transplacental transport of nanoparticles was determined fluorometrically to be a function of size and presence of IgG functionalization. A 2.7 fold increase of IgG-modified nanoparticles (414 nm) was transported across the placental barrier compared to bare nanoparticles (376 nm).

Conclusion:
The transplacental delivery of IgG-modified nanoparticles is a novel solution to the limited prenatal therapies for CDH. TEER measurements indicated the placental integrity was maintained after exposure to nanoparticles. Together with immunostaining, the results suggest that nanoparticles pose no adverse effect to the placental barrier. The increased transport of IgG-modified nanoparticles suggests an active transport mechanism - the maternal transfer of passive immunity - is involved. We intend to explore the transplacental efficiency *in vivo*.