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CHRD
CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

Submitter Name
Andrew (Wai Hei) Tse

Email
atse@chrim.ca

Title
Transplacental transfer of IgG-modified nanoparticles by the maternal-fetal transfer of passive immunity for prenatal therapies

Background
Surgical intervention and drug therapies for congenital diseases are limited in their ability to rescue underlying pathomorphological changes and possess pharmacokinetic challenges, respectively. Nanoparticles (NPs) surface-modified with IgG isoform antibodies can safely deliver encapsulated life-changing medication to the fetus via the maternal circulation. We hypothesize the maternal-fetal transfer of passive immunity can be harnessed to safely transport IgG-modified NPs across the placenta.

Objective
The neonatal Fc receptor (FcRn) responsible for the maternal-fetal transfer of passive immunity, will be studied as a mechanism to induce the transplacental transport of IgG-modified NPs for prenatal therapy.

Methods
Human BeWo placental epithelial cells (1X106 cells/cm2) were grown on 3 μm polyester transwell membranes. Transfer was assessed after 18 hours of exposure to chitosan NPs synthesized by ionic gelation, covalently modified with human IgG antibodies, and FITC-tagged. Barrier function was assessed with transepithelial electrical resistance (TEER) and immunofluorescence for E-cadherin and Zonula Occludens-1.

Results
Transport of IgG-modified NPs across the placental epithelial barrier established in an in vitro transwell model is possible (Figure 1). A 2.8 times increase ($p = 0.0264$) of IgG-modified NPs was transported across barrier compared to similarly sized bare NPs. Transfer of IgG-modified NPs was reduced in a dose-dependent manner when co-administered with free IgG; which was not observed for bare NPs. Colocalization of FcRn and FITC-tagged IgG-modified NPs was observed by confocal laser scanning microscopy. TEER measurements indicated no significant change in barrier function ($p > 0.05$) after 18

hours of NP exposure. E-cadherin and Zonula Occludens-1 junction proteins were found intact.

Conclusion
The transplacental drug delivery by IgG-modified NPs is a novel mechanism for prenatal therapies. The colocalization of the FcRn with IgG-modified NPs and the dose-dependent inhibition of IgG-modified NP transfer confirms that the maternal-fetal transfer of passive immunity is involved. Next, we intend to explore the biodistribution and pharmacokinetics in vivo.

Theme:
Basic Science

Do you have a table/figure to upload?
Yes

Untitled
Figure 1.pdf

Are you willing to participate in Goodbear's Den?
Yes

Presenter Status:
Non-Trainee

What was your role in the project?
All of the above.

Authors

Name	Email	Role	Profession
Andrew (Wai Hei) Tse	atse@chrim.ca	Presenting Author	Graduate
Sean Higgins	higginss@myumanitoba.ca	Co Author	Graduate
Malcolm Xing	malcolm.xing@umanitoba.ca	Co Author	Assitant Professor
Hagar Labouta	hagar.labouta@umanitoba.ca	Co Author	Associate Professor
Adrian West	adrian.west@umanitoba.ca	Co Author	Assitant Professor
Richard Keijzer	richard.keijzer@umanitoba.ca	Co Author	Full Professor

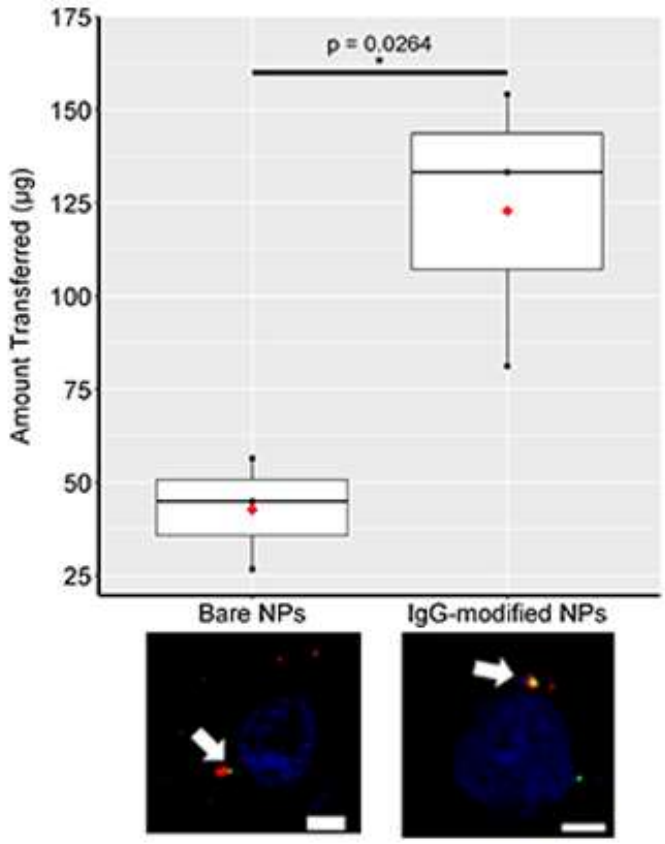

Figure 1. Neonatal Fc receptor (FcRn) mediated transplacental transport of IgG-modified nanoparticles (NPs). FITC-tagged bare and IgG-modified NPs were administered to human placental epithelial cells (BeWo). Transplacental transport of IgG-modified NPs in the transwell model was significantly increased by 2.8 times compared to bare NPs ($p = 0.0264$). The interaction between FcRn (red) expressed in BeWo cells counterstained with DAPI (blue) and FITC-tagged NPs (green) was determined by confocal laser scanning microscopy. The colocalization (yellow) of IgG-modified NPs with the FcRn indicates the maternal-fetal transfer of passive immunity is involved in the transplacental transport of IgG-modified NPs.