MR Imaging of Human Neural Progenitor Stem Cells: an in vivo Longitudinal Model
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Introduction and Aims

- Human pluripotent stem cell derived neural progenitor cells (hNP1, ArunA Biomedical) provide a meaningful representation of neural development.
- In vitro assays employing high-throughput screenings with hNP1 and differentiated hN2 cells have provided for sensitive measures of developmental neural toxicity (DNT)

Using these same cells in complimentary in vivo studies can be used to uncover additional key elements of adverse outcome pathways in humans.
- Our overall goal is to link key elements of in vitro toxicological findings to whole organism systems in the chick using non-invasive stem cell tracking.
- Specifically, our aim here is to determine whether hNP1 cells can maintain viability, function and can be tracked using MR imaging

MR Imaging and Stem Cell Tracking

- A Varian Magnex 7 Tesla magnet facilitates MR imaging of anatomical structures at a high level of resolution.
- Optimized pulse sequences provide excellent contrast for tracking SPIO-labeled hNP1 cells.

![Image of MR Imaging of Stem Cells](image)

Methods

- Label hNP1 cells with SPIO
- Transplant to Chicken Embryo
- MR imaging Through Development

Results: SPIO Labeling of Human Neural Progenitor Stem Cells

- The SPIO Moland1 Rhodamine B (MIRB) was readily taken up by hNP1 cells
- SPIO-labeled hNP1 cells retained normal progenitor marker expression
- SPIO-labeled hNP1 cells undergo in vitro neural differentiation similar to unlabeled hNP1 cells

Results: Transplantation and MR tracking of Human Neural Progenitor Cells

- Transplanted hNP1 cells were successfully tracked through 11 days of development with MR imaging.
- Colocalization of MIRB (Red) and GFP reporter introduced into the hNP1 cells.
- Hypointense regions of T2 and T2* weighted anatomy MR images co-localizes MIRB (Red) and GFP in later chick stages (D3 & D6).
- Clear anatomical contrast in between tissues. (D9 and D11)

Future Direction

- Optimize longitudinal imaging of treated hNP1 (Table 1) in a single chick embryo, monitoring cell survival and migration throughout development
- Volumetrically characterize development of central nervous system and normal hNP cells migration and integration within the chick embryo post toxicant exposure (Fig 4; Table 1)

Conclusion

- hNP1 cells can be efficiently labeled with SPIO without harming the biological integrity of stem cells
- SPIO-labeled hNP1 cells can be tracked throughout development after transplantation to the chicken embryo.
- Experimental design is easily scaled up for toxicological studies
- Foundation for a novel method of in vivo toxicology modeling

Acknowledgments and Funding

![Image of Acknowledgments and Funding](image)

Table 1. Suspected EAC Selected for DNT Testing

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Neurotoxicity Evidence</th>
<th>Endocrine Activity</th>
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<tbody>
<tr>
<td>BPA</td>
<td>Yes, central dopaminergic system</td>
<td>Contradictory evidence, leads to thyroid hormone receptor</td>
</tr>
<tr>
<td>Depublated</td>
<td>Yes, reduced ovular nerve innovation</td>
<td>Yes, female reproductive loss</td>
</tr>
<tr>
<td>Polychlorinated Biphenyls</td>
<td></td>
<td></td>
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<tr>
<td>PCB 153 – non-</td>
<td>Yes, affects neurotransmitter, brain development</td>
<td>Suggestive in humans, rats develop</td>
</tr>
<tr>
<td>PCB 126 –</td>
<td>Yes, brain development in males</td>
<td>Yes, affects thyroid hormones, indeed estrogen receptor (2-stage)</td>
</tr>
<tr>
<td>Non-steroid positive controls</td>
<td></td>
<td></td>
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