Tracking Transplanted Stem Cells

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Potential uses of Stem cells

- Stroke
- Traumatic brain injury
- Learning defects
- Alzheimer's disease
- Parkinson's disease
- Baldness
- Blindness
- Deafness
- Missing teeth
- Wound healing
- Bone marrow transplantation (currently established)
- Spinal cord injury
- Osteoarthritis
- Rheumatoid arthritis
- Amyotrophic lateral sclerosis
- Myocardial infarction
- Muscular dystrophy
- Diabetes
- Crohn's disease
- Multiple sites: Cancers
NeuroGeneration
Parkinson’s Treatment

1. Parkinson’s disease patient
2. Biopsy
3. Stem cell isolation
4. Stem cell amplification
5. Autologous transplant
6. Differentiation into dopaminergic and other neuronal population
Non-Invasive Whole Body Cell Tracking

1) Are stem cells being delivered/injected correctly?
2) How many stem cells have been correctly delivered/homed into the target organ?
3) For how long do stem cells survive?
4) Do stem cells replicate following administration including the formation of unwanted neoplasms/teratomas?
5) Do stem cells differentiate \textit{in vivo}, and if so, when does this occur?
Labeling Stem Cells with a “MAGNETIC “DYE”

Superparamagnetic Iron Oxide Particles (SPIO): Nanoscopic Magnets Disturb MRI Signal, Leading to Loss of Imaging Signal

Diameter: ~80 nm (size of a virus)
Labeling of Stem Cells with Superparamagnetic Iron Oxide (SPIO)
Routes of Stem Cell Delivery to the Brain

Intraparenchymal
Intraventricular
Intravenous
Intraarterial
Routes of Stem Cell Delivery to the Brain
MR Imaging of Magnetically Labeled Neural Stem Cells

P. Walczak et al. MRM 54, 769-774, 2005.
MR Imaging of Magnetically Labeled Neural Stem Cells

P. Walczak et al. Nanomedicine 2, 89-94, 2006
Intraventricular Routes of Stem Cell Delivery to the Brain
ICV-injected Feridex-labeled NSCs in perinatal hypoxic brain injury

M. Janowski, P. Walczak et al.
ICV-injected Feridex-labeled NSCs in perinatal hypoxic brain injury

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M. Janowski, P. Walczak et al.
Effect of Cell Size

GRPs – 15 µm

MSCs – 25 µm
Feraheme® Injection Compared to SPIO-MSC Injection

Feraheme®
(Perfusion agent)

SPIO-MSC
Feraheme® Injection Compared to SPIO-MSC Injection
MR Monitoring of Cell Delivery

Pterygopalatine artery
MR Monitoring of Cell Delivery

Can IA-Injected GRPs Extravasate?

3-day old ouabain stroke

Before transplantation

After transplantation

Red – transplanted cells
Green – vessels (vWF)

M. Janowski, P. Walczak et al.
As of today there are 8 published clinical MRI cell tracking trials

3. Callera et al. 2007 Stem Cells and Development. 16:461–466
5. Saudek et al. 2010 Transplantation. 90;12:1602-1606
Accidental Misinjection in 4 out of 8 Patients
(Injections performed under US guidance, not MR-Guided)

Routes of Stem Cell Delivery to the Brain

Intravenous
Suppression of inflammation

IV-injected SPIO-labeled MSCs localize in the occipital horns

Only FDA-approved cell tracker as of today: $^{111}$In-oxine (1980s)

Half-life = 2.8 days
$^{111}\text{In-Oxine Labeled MSCs following IV injection in a Canine Myocardial Infarct Model}$

Day 1

Day 2

Day 5

SPECT/CT

~30% of injections were unsuccessful using X-ray delivery

Kraitichman, Bulte et al.
MR-Guided, Real-Time Injection of Magnetically Labeled Canine MSCs in a Dog MI Model

Pericardial Access Using XFM

D.L. Kraitcman et. al.
Non-Invasive Whole Body Cellular Imaging

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American Firefly

Photinus pyralis
Bioluminescent Imaging of Cell Differentiation

CMV

Opalin

N. Rumpal et al.