In Vivo Cell Tracking with MRI

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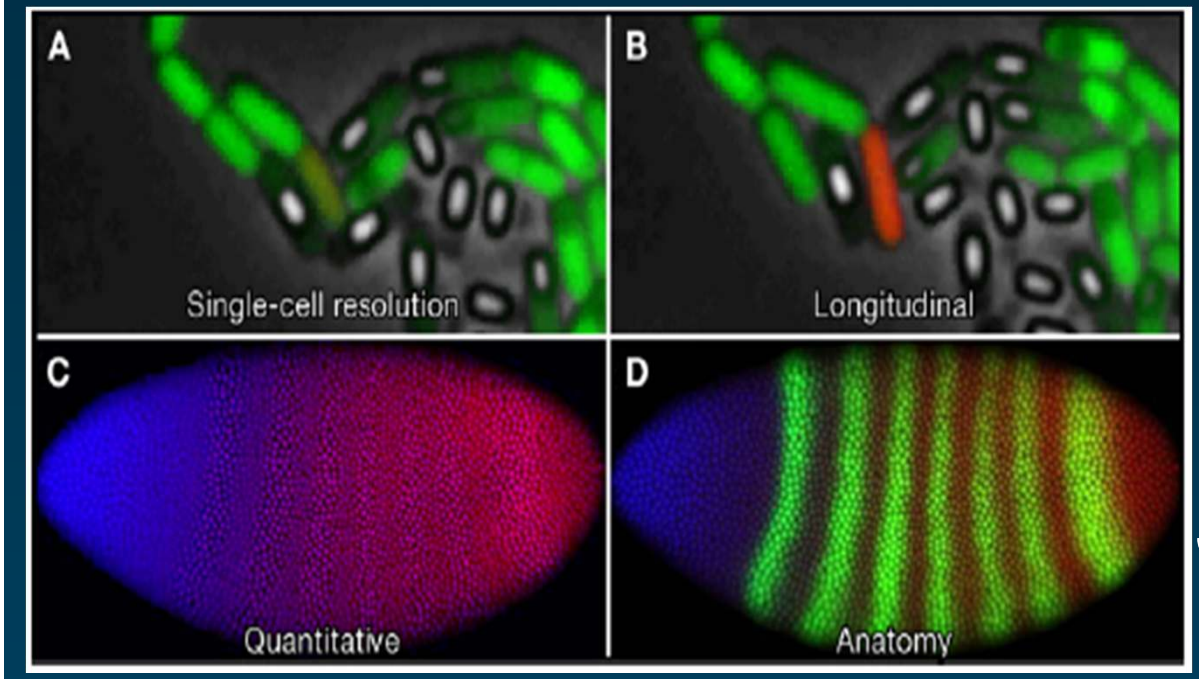
Advantages of imaging for systems biology



Single-Cell Resolution

Longitudinal Data

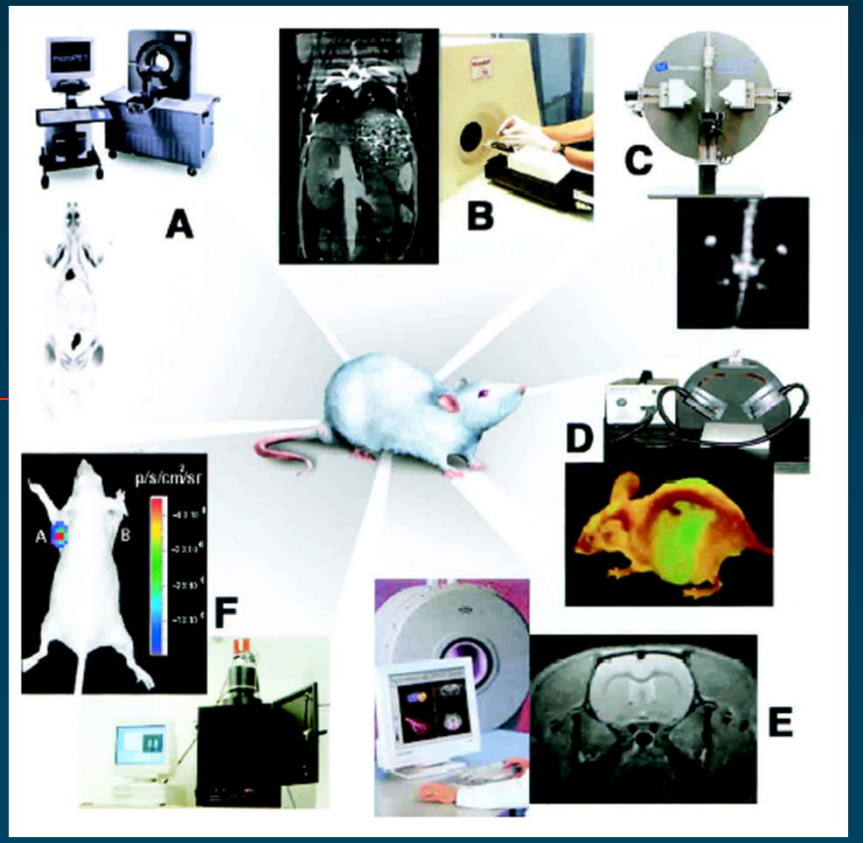
Quantitation

Biological Context

Current Imaging Technology for Molecular Imaging

Modality	Sensitivity	Resolution		
		Spatial	Temporal	Contrast
CT	+	++	+	++
MR imaging	++	+++	++	+++
Nuclear medicine	+++	+	+	++
Optical imaging	+++	+	+++	+++
US	++	+++	+++	++

Note.—+ = low resolution, ++ = intermediate resolution, +++ = high resolution.



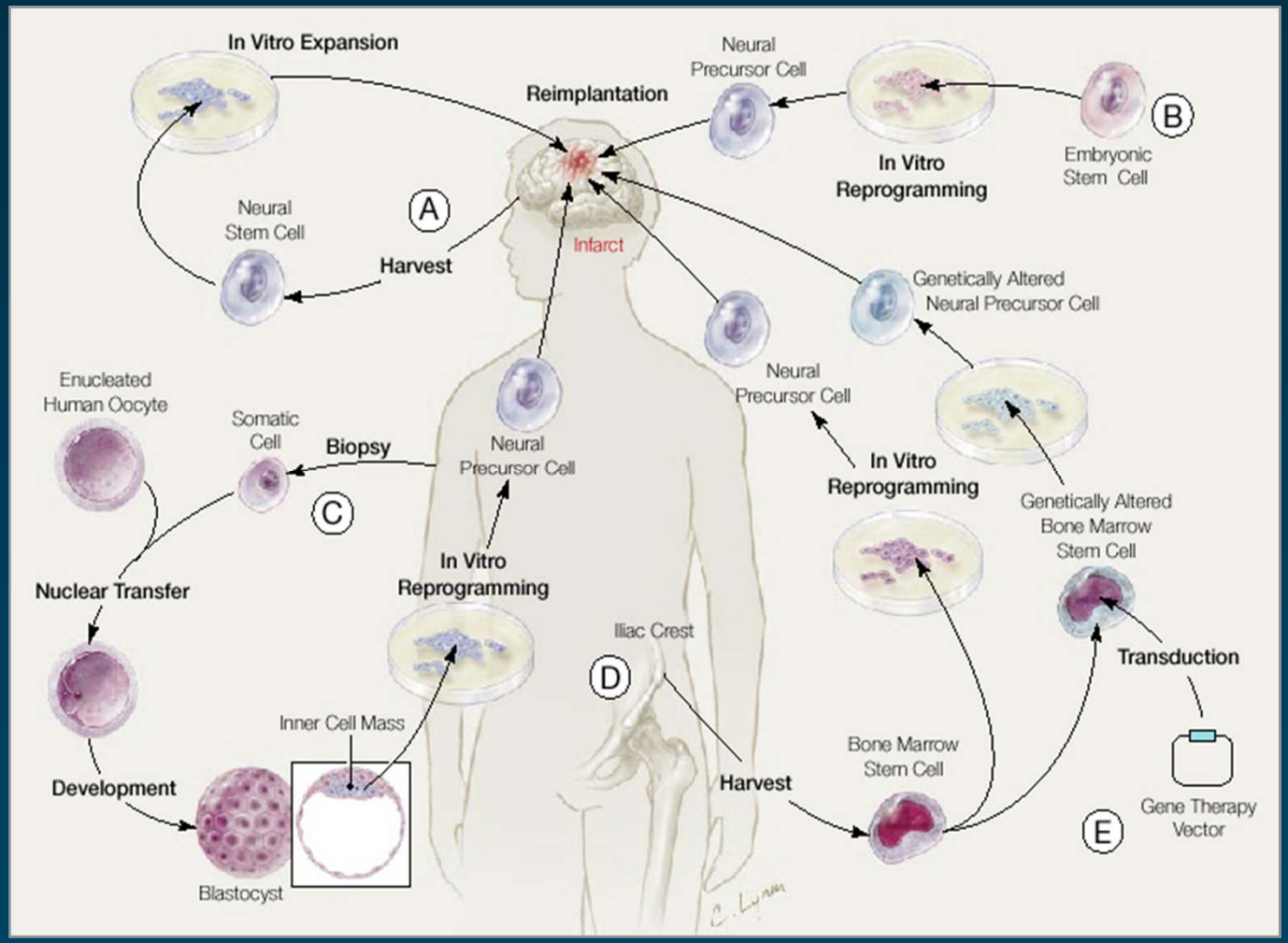
Acad Radiol 2001

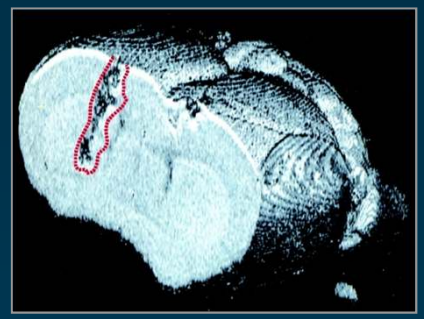
Strategy of Cell Trafficking Imaging

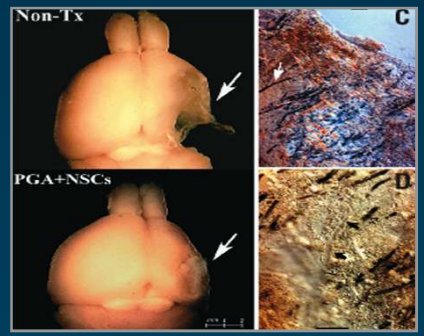
1. Direct cell labeling
   : fluorescence, radionuclide, magnetics

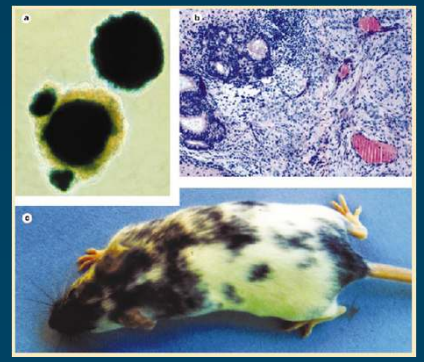
2. Imaging reporter gene
   : GFP, luciferase, TfR, ferritin, HSV1-tk

In Vivo Monitoring of Cell Therapy

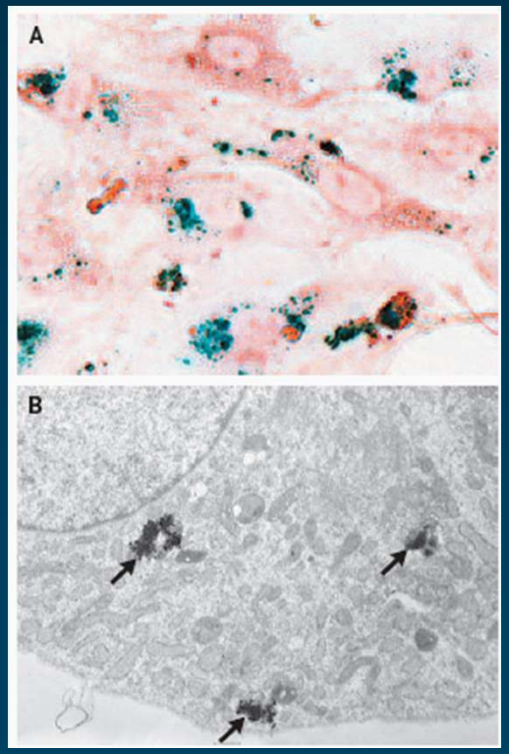




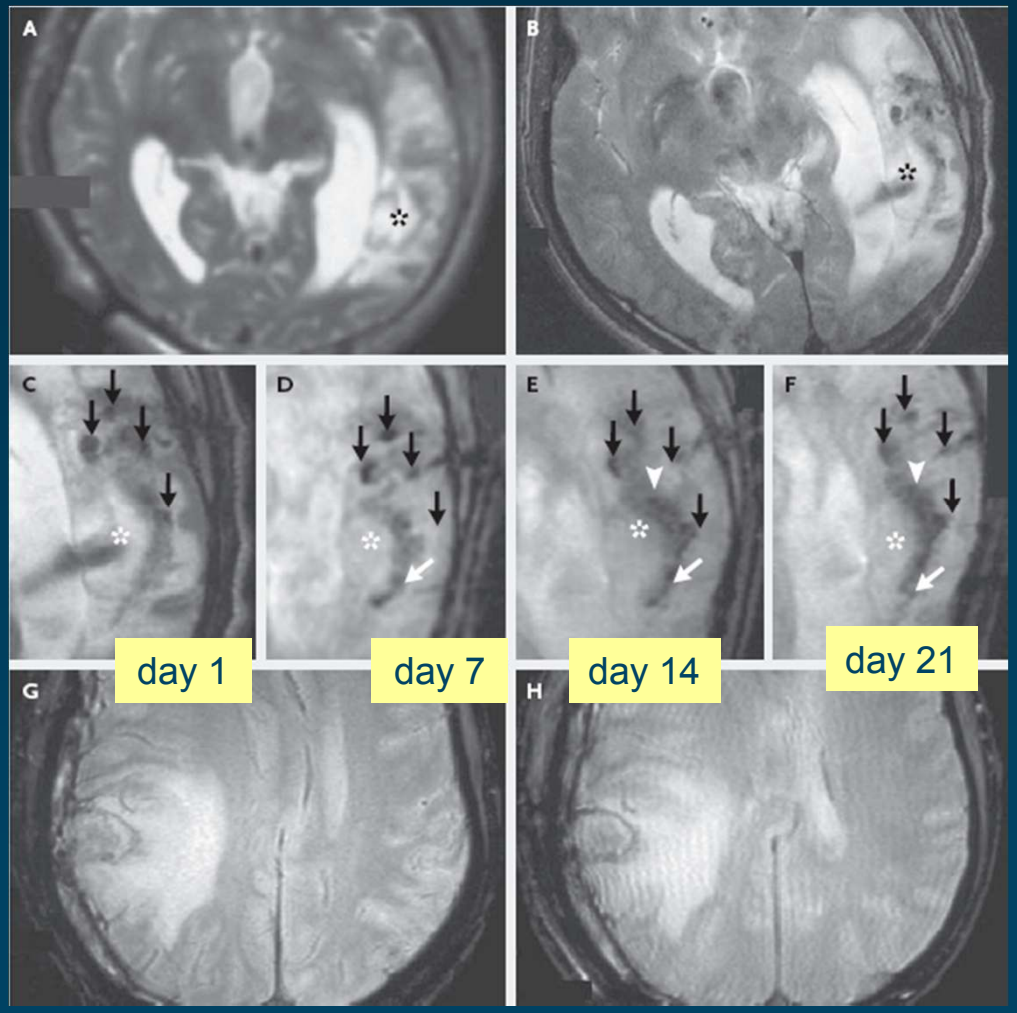




Tracking Neural Stem Cells in Patients with Brain Trauma

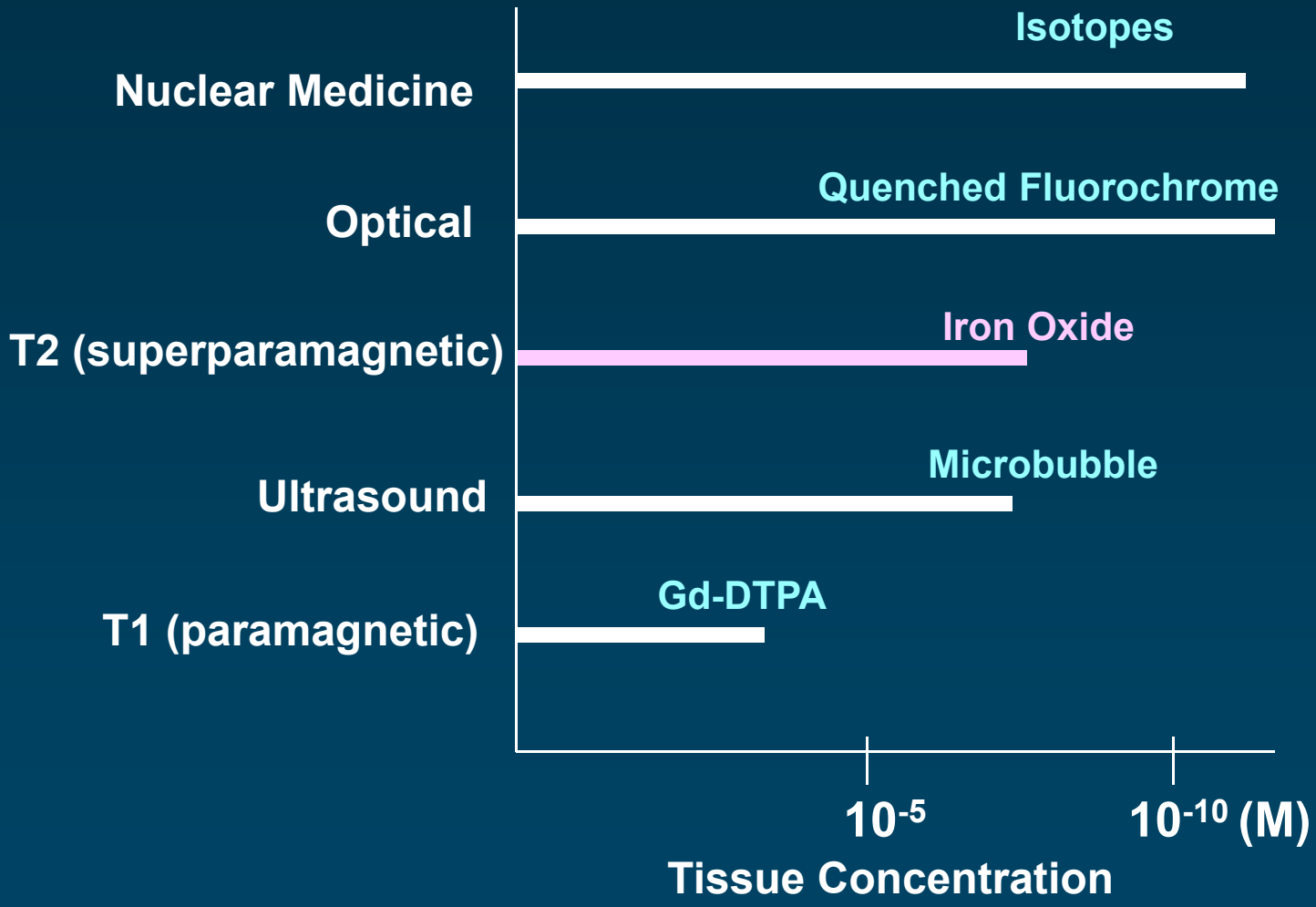


Feridex
(SPIO)



Zhu et al. NEJM 2006;355

Detection Level of Various Imaging Probes



SPIO: Feridex®

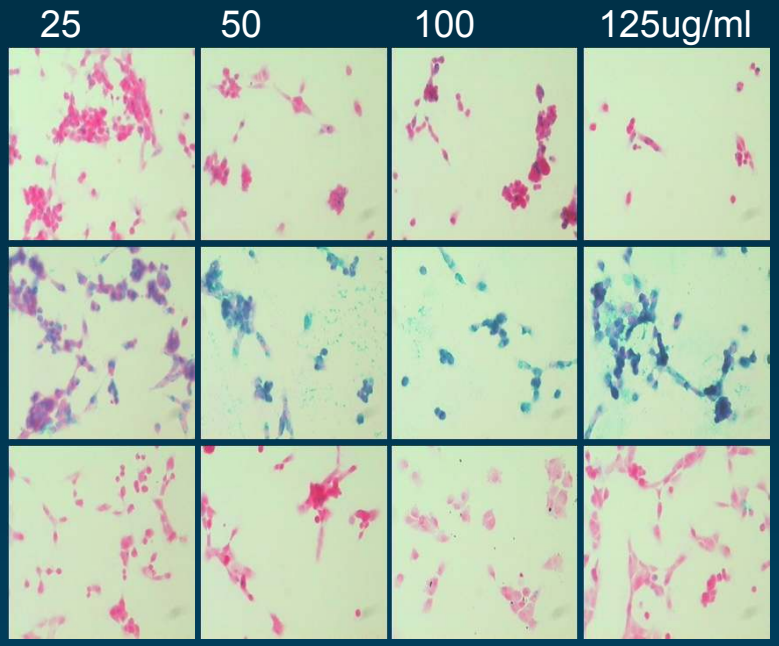
USPIO

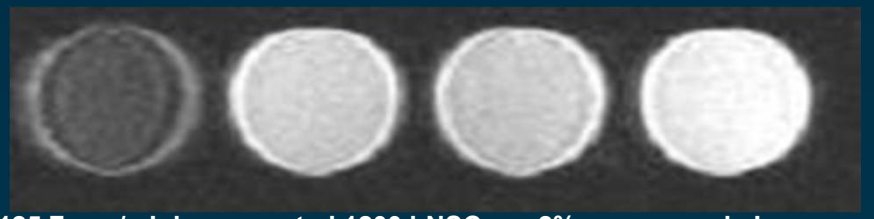
Monocrystaline iron oxide nanoparticles (MION-47)

Cross linked iron oxides with tat-peptide (tat-CLIO)

- To Compare the Capacity to Label hNSCs and MSCs for the in vivo MR Tracking using MR Imaging
- To Evaluate the Effect of Particle Size, Surface Modifications, Lipofection on Cell Labeling

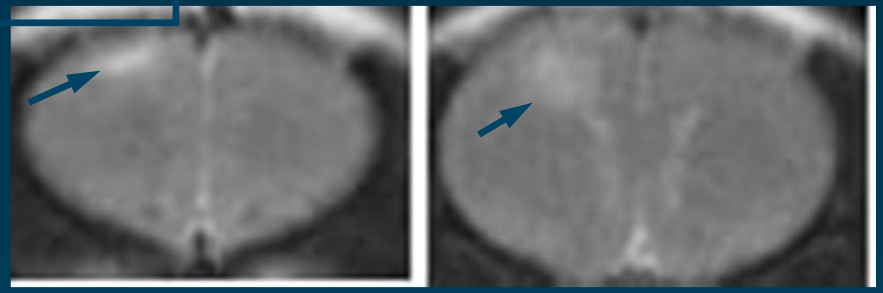
MR Trafficking of Human Stem Cells



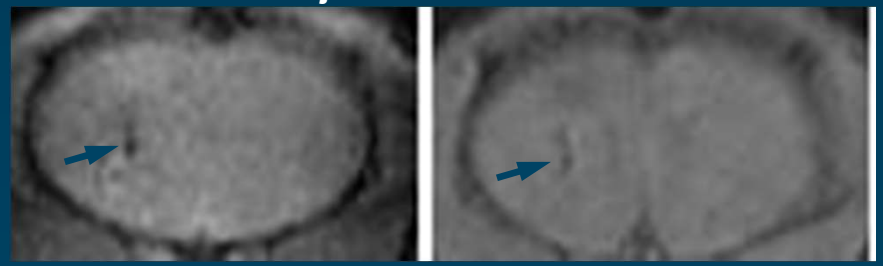


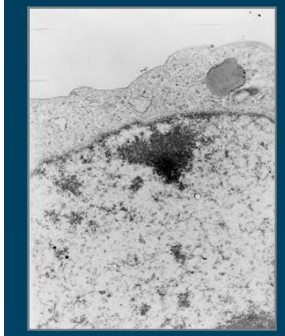
125 Fe μg/mL incorporated 1200 hNSC per 2% agarose gel μL

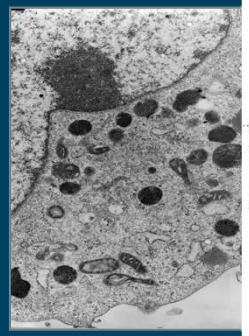
Control

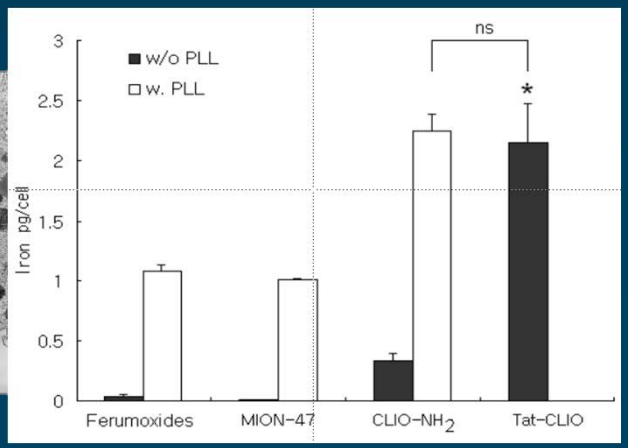


Rat with stem cell Injection









SONG M, Moon WK. KJR 2007;8:206

MRI in Diabetes

1. Imaging of β cell mass
2. Imaging of autoimmune attack
3. Imaging of islet vasculature
4. Imaging of islet transplantation

MRI of β Cell Mass and Function

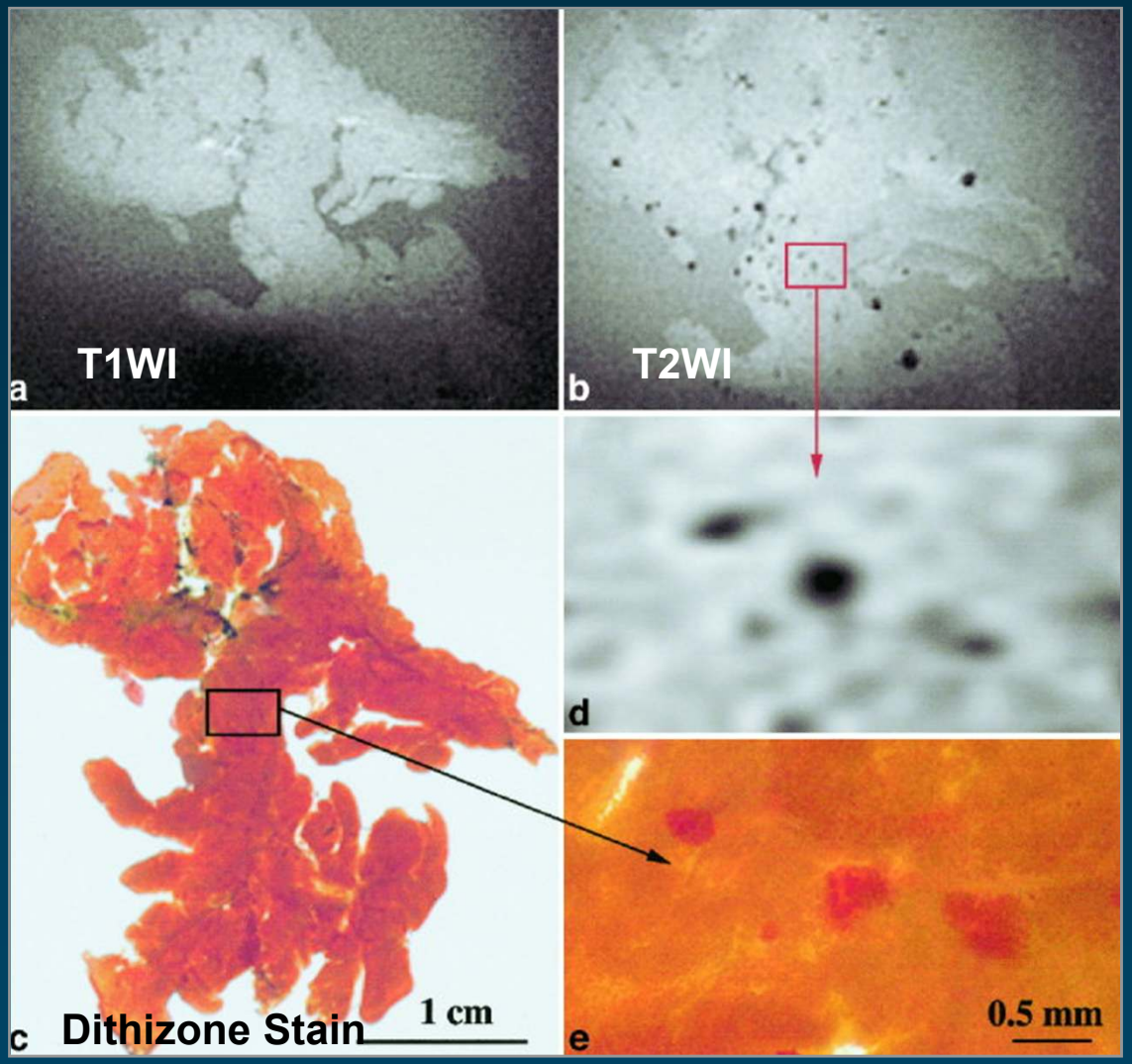
- β Cells are components of pancreatic islets and exist as part of micron-sized (-150 um) multifocal structures

- Designing β cell specific imaging agents

- Gd-G80BP for GLUT-2 receptor
- Manganese(Mn^{2+})
- Zn-sensitive probe

- Chemical exchange saturation transfer (CEST) , PARACEST
- Hyperpolarized, dynamic nuclear polarization (DNP) ^{129}Xe, ^{13}C

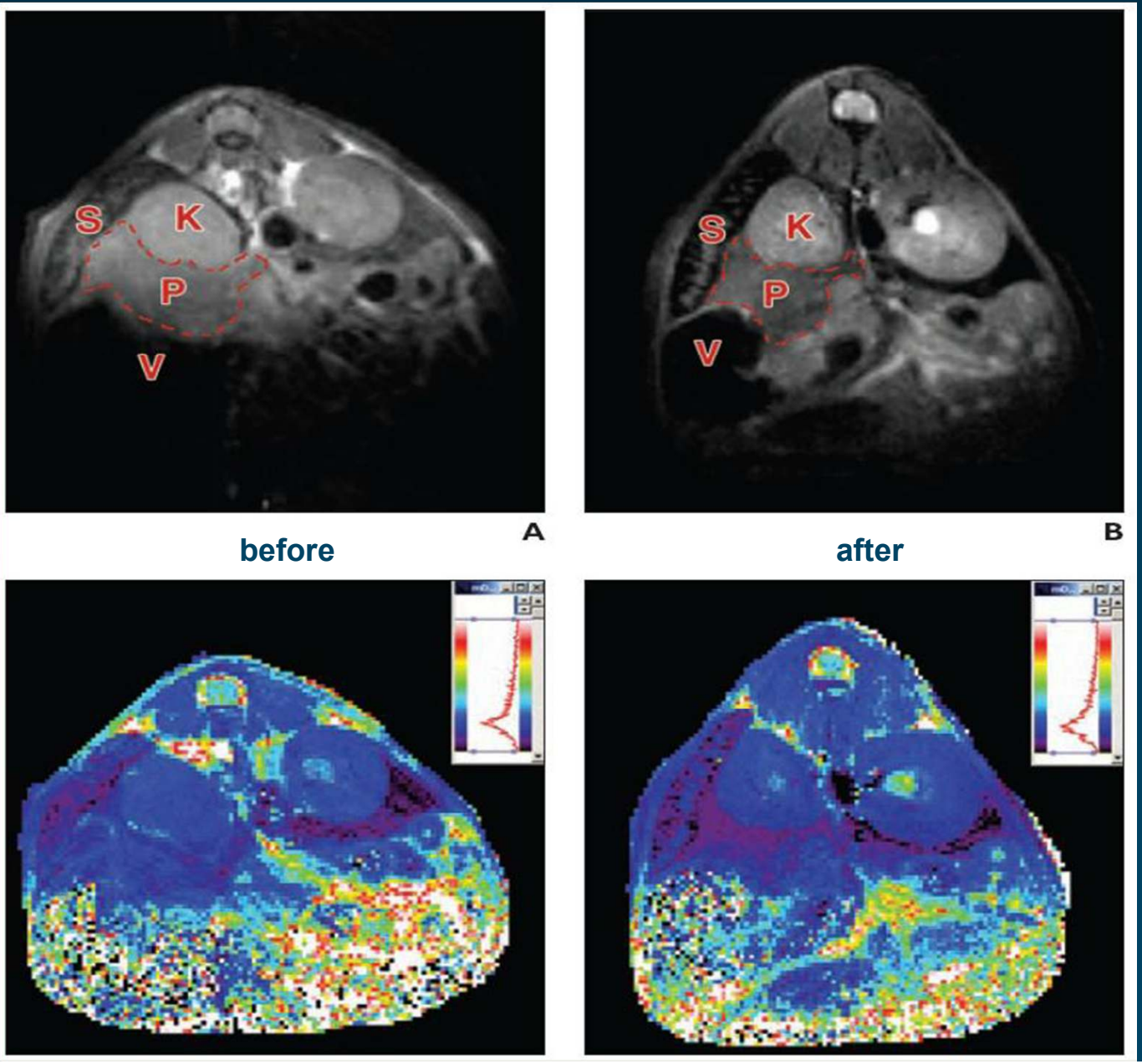
MRI of Insulitis in Autoimmune Diabetes



Pancreas after adoptive transfer of diabetic splenocytes labeled with CLIO-Tat into NOD.scid mice (1.5 T MRI)

Moore et al. Mag Reson Med 2002

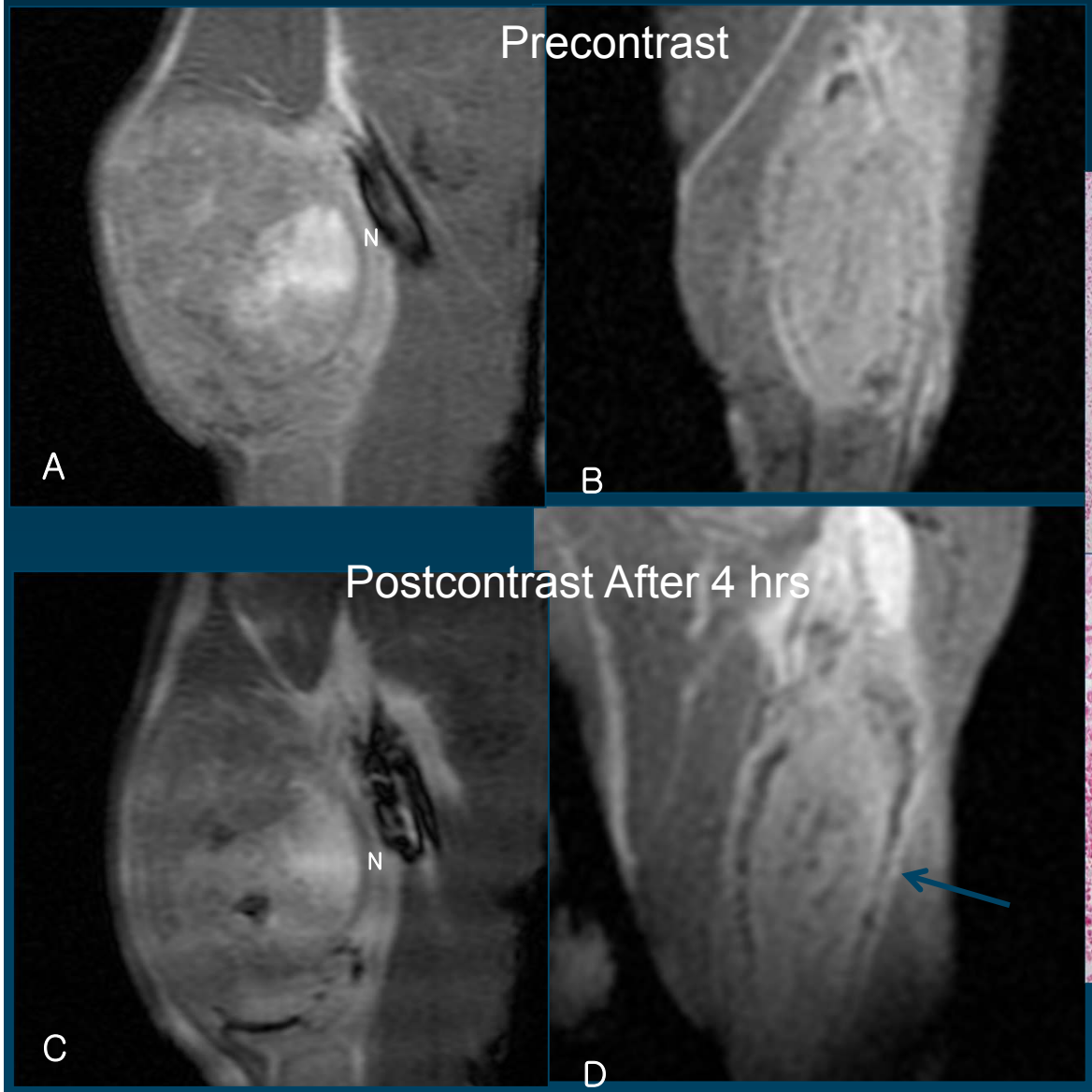
MRI of Lymphocyte Infiltration of Pancreas

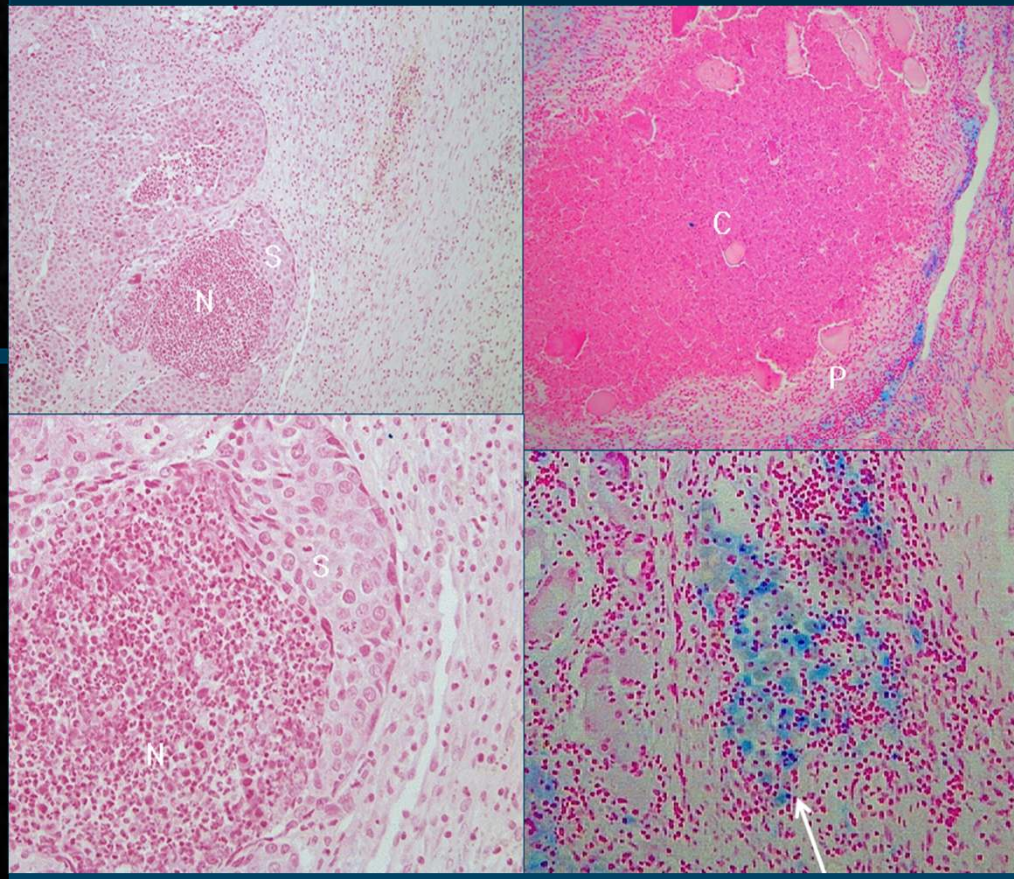


Iron oxide nanoparticles conjugated to peptide-specific diabetogenic (CD8+) T cells

Moore et al. Mag Reson Med 2008

SPIO-Labeled MRI for Macrophage Tracking

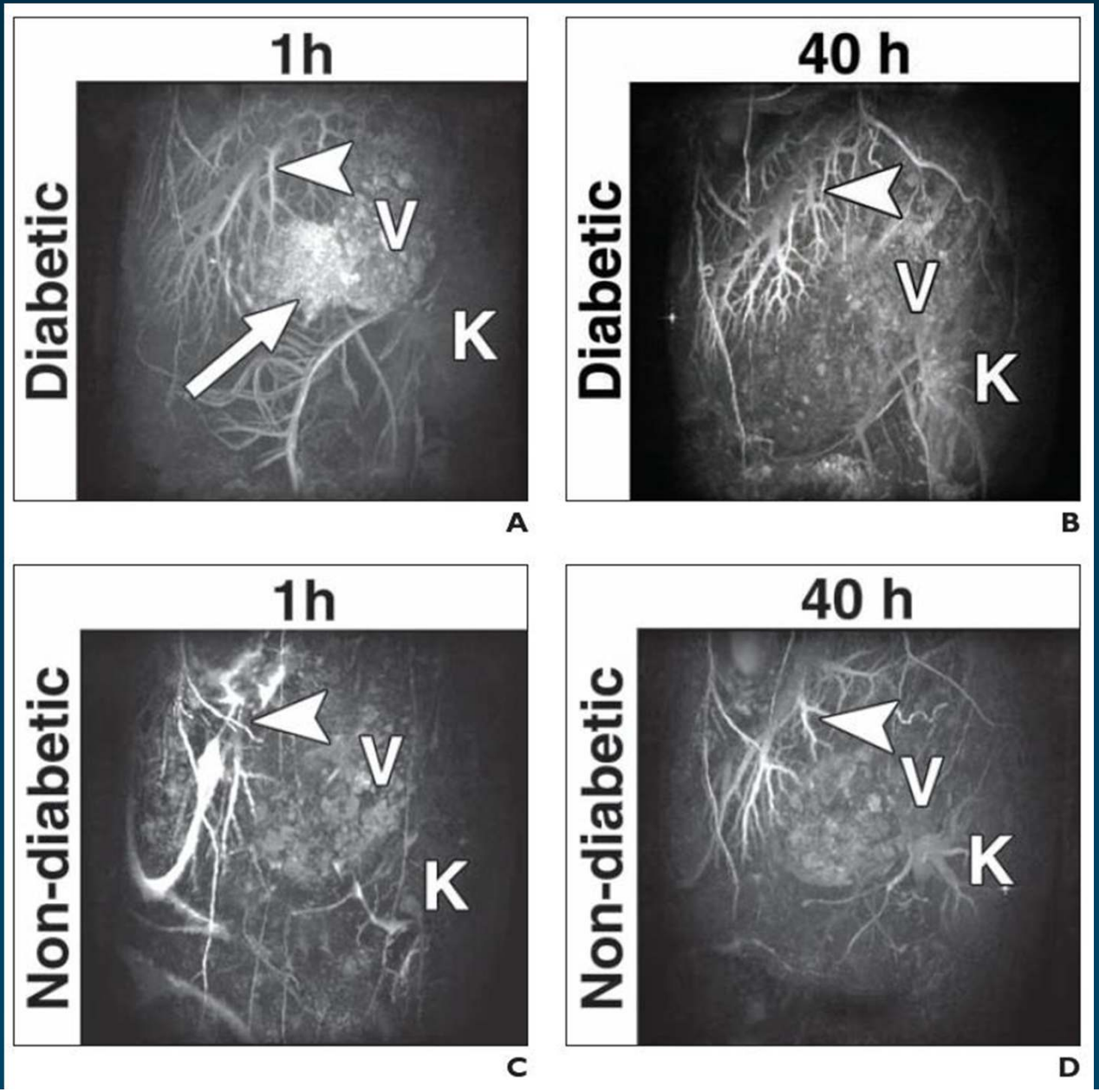




VX2 carcinoma **Abscess**

Kim SJ, et al. 2006 RSNA

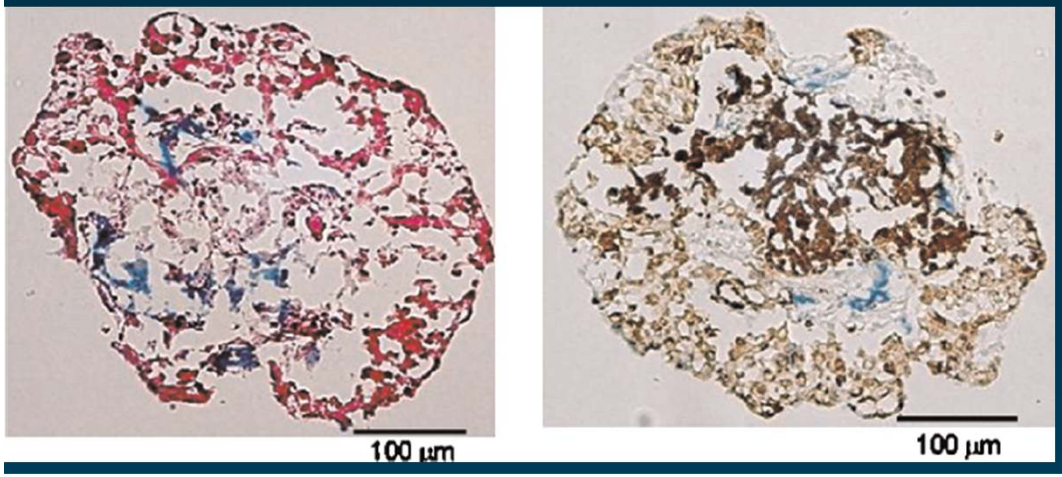
MRI of Islet Vasculature

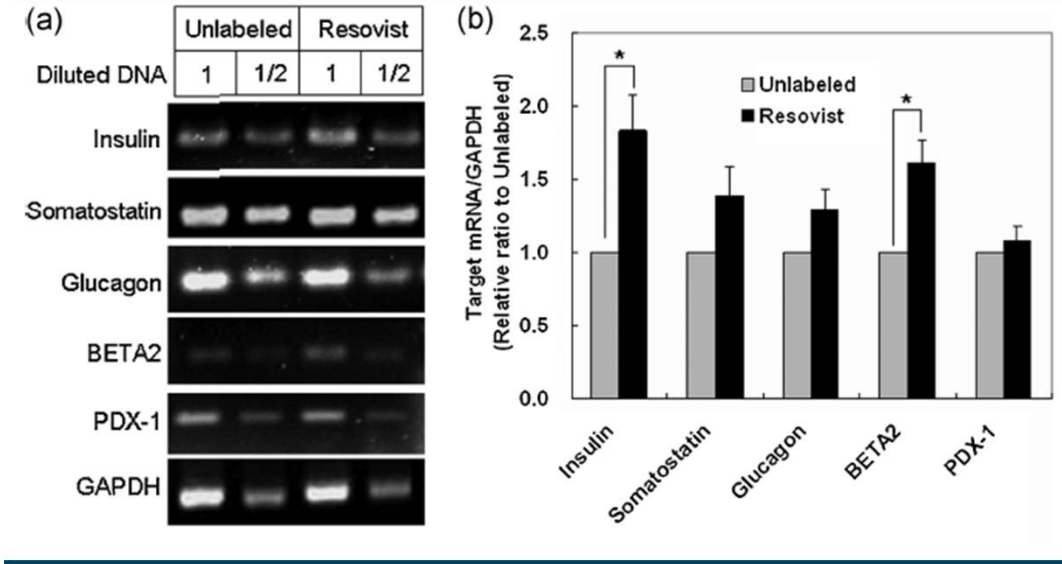


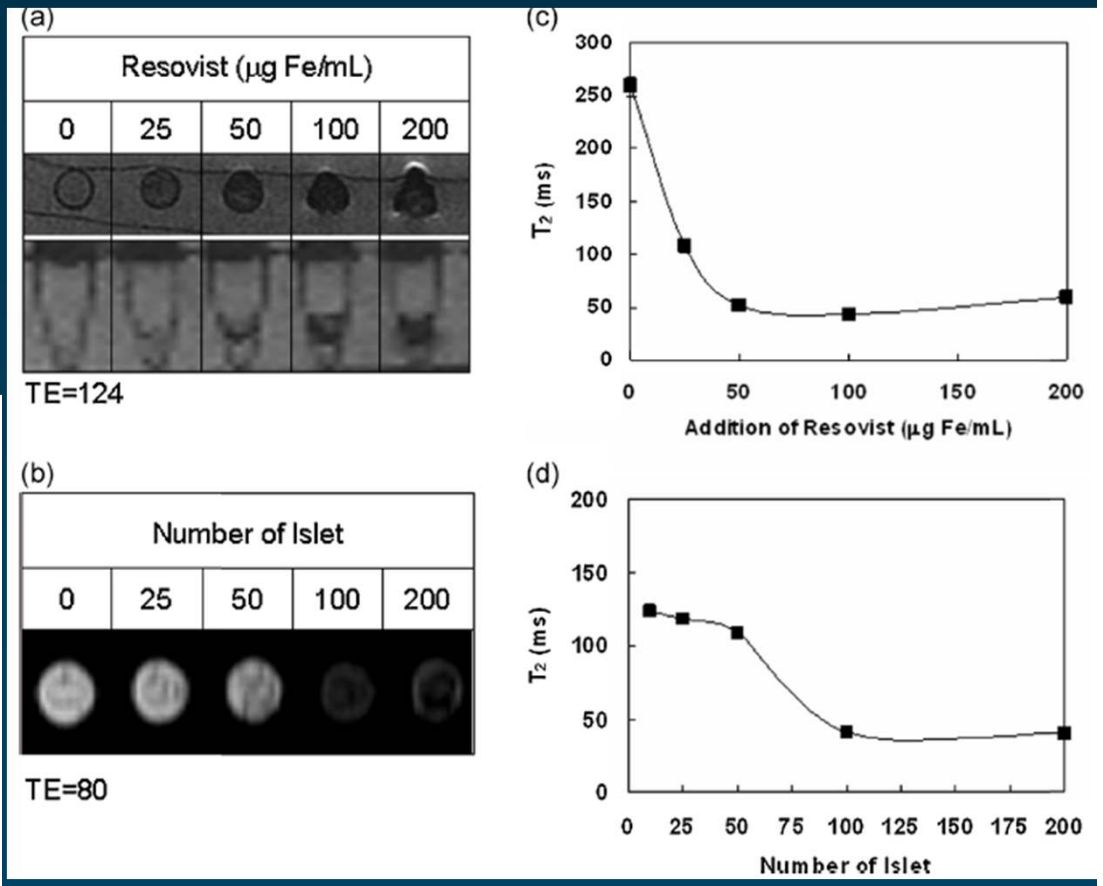
- PEG-GdDTPA
- 3D MR Angiography

Moore et al. Diabetes 2007

MRI and Biological Properties of Pancreatic Islets Labeled with Resovist



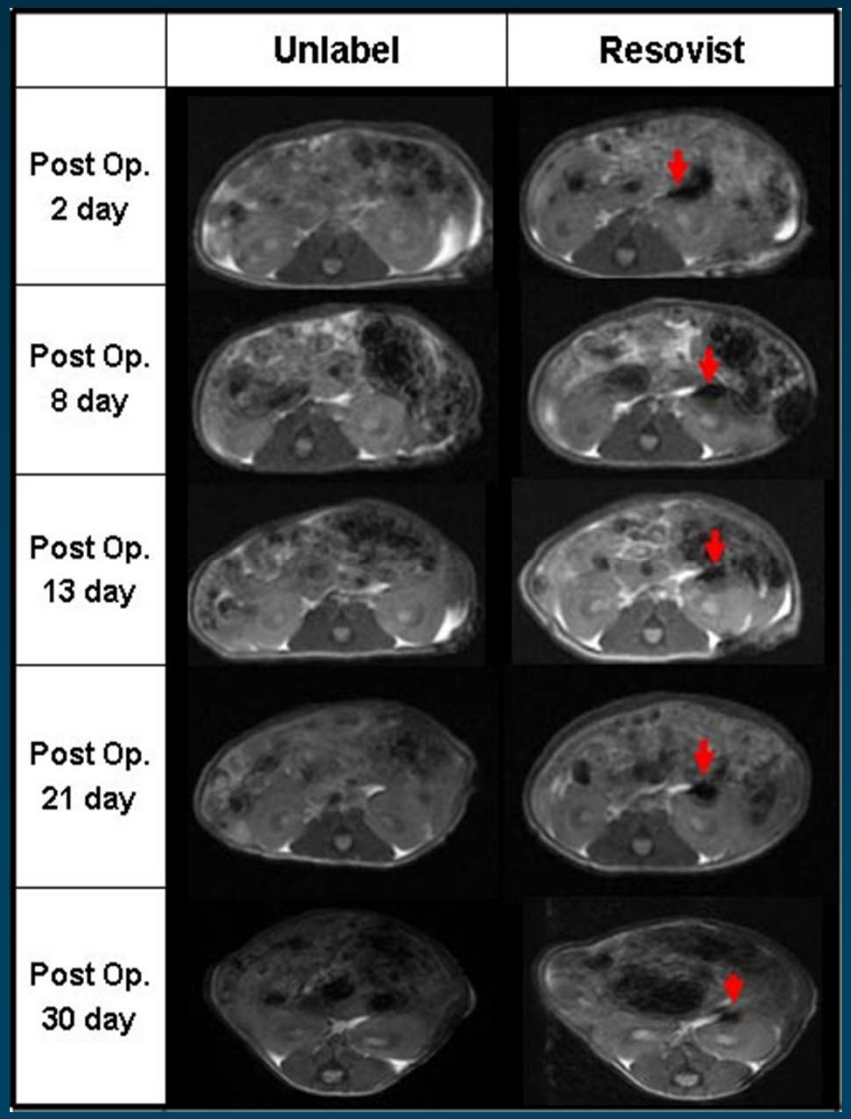


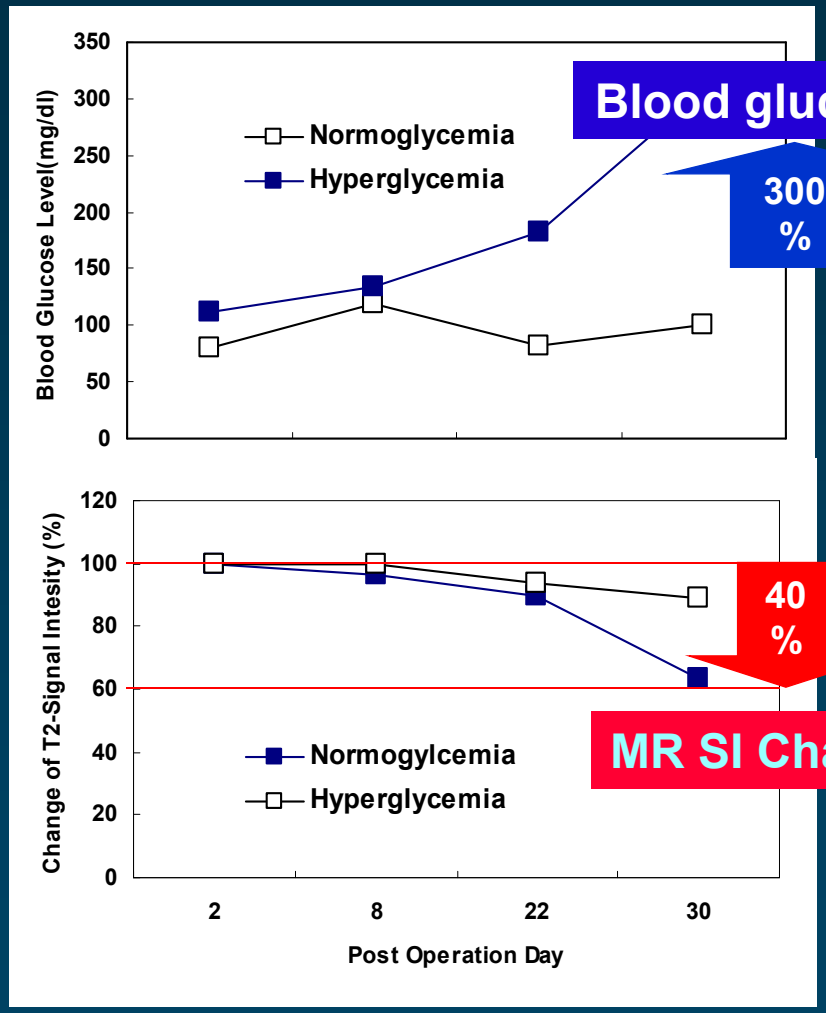


BETA2(beta–cell E-box trans-activator)

HS Kim, Moon WK. NMR Biomed 2009

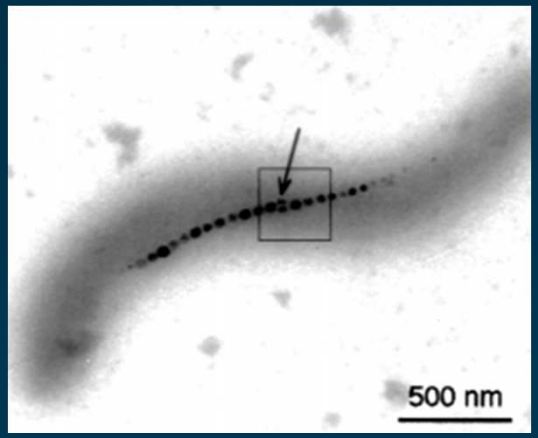
Porcine Islets Transplanted in the Kidney Capsules of Diabetic Mice



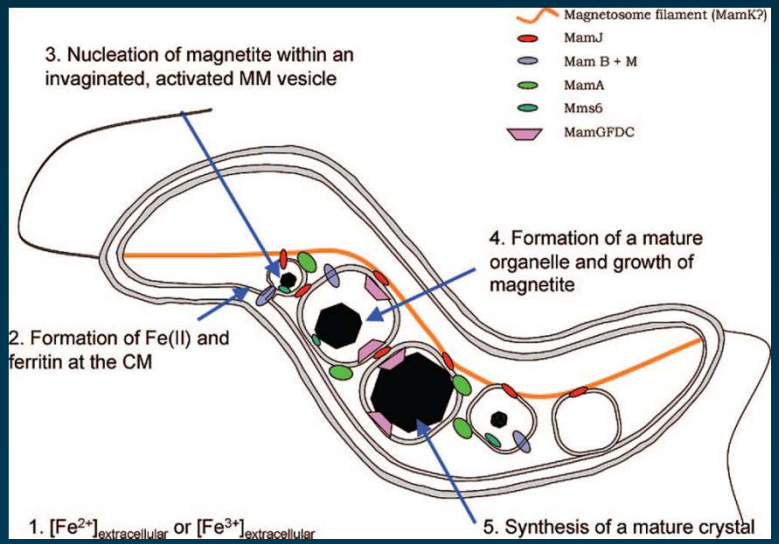


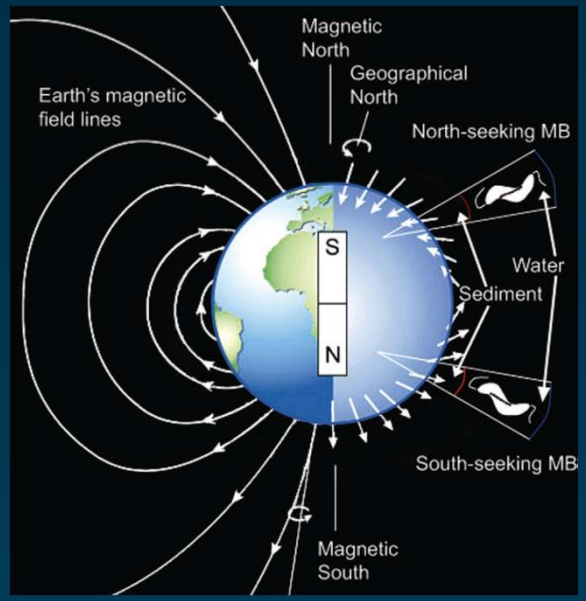
Korean J Radiol. 2010;11 Nov.

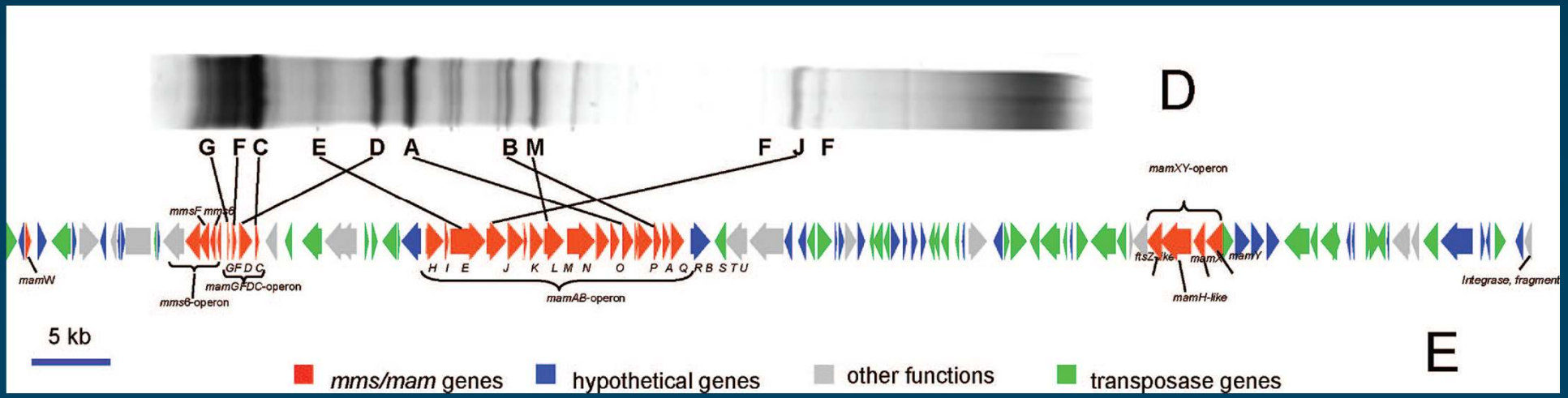
Magnetotactic Bacteria and Magnetosomes



Magnetospirillum magnetotacticum

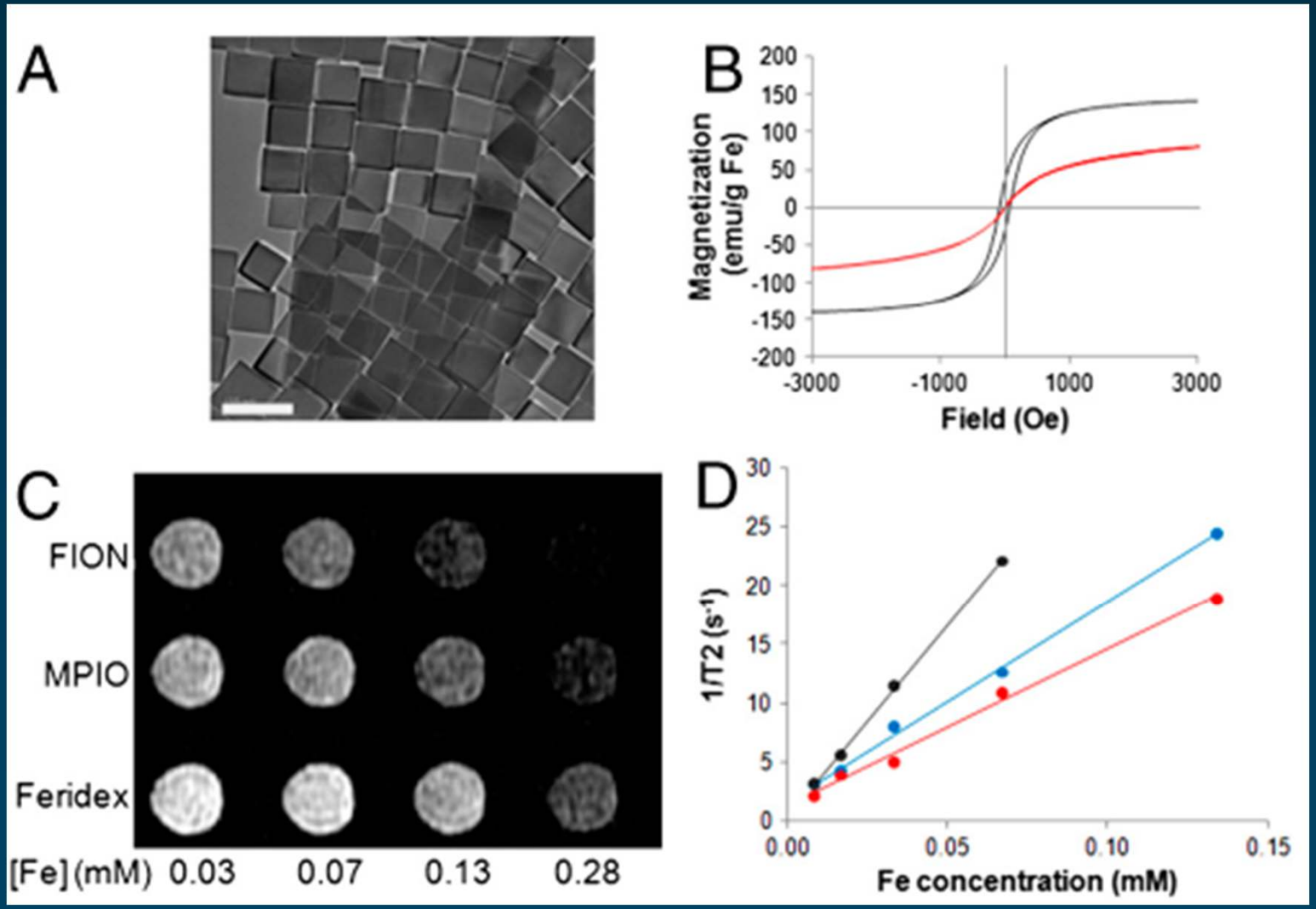






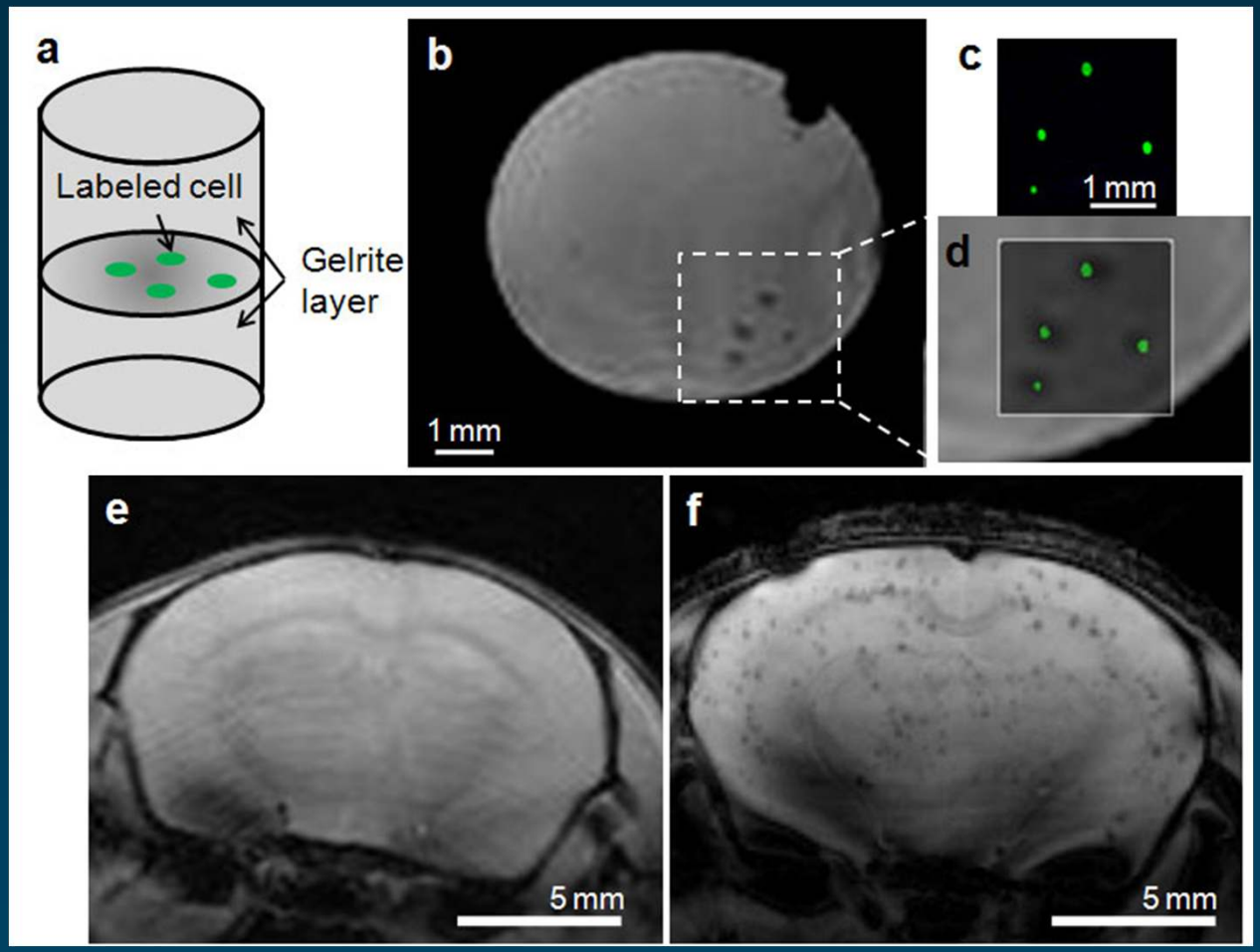
Chemical Reviews, 2008

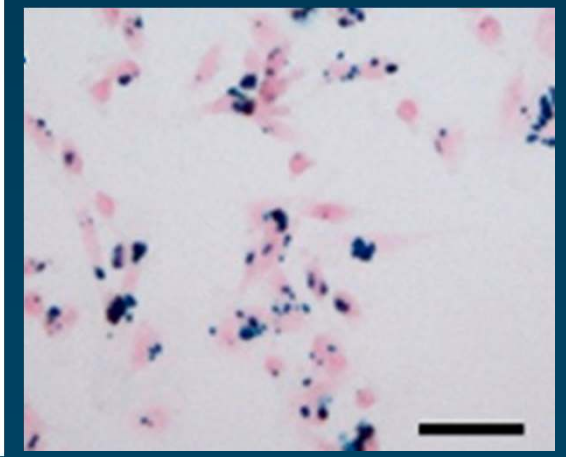
Magnetosome-like ferrimagnetic iron oxide nonocubes (FION)



Collaboration with Dr. Hyeon T

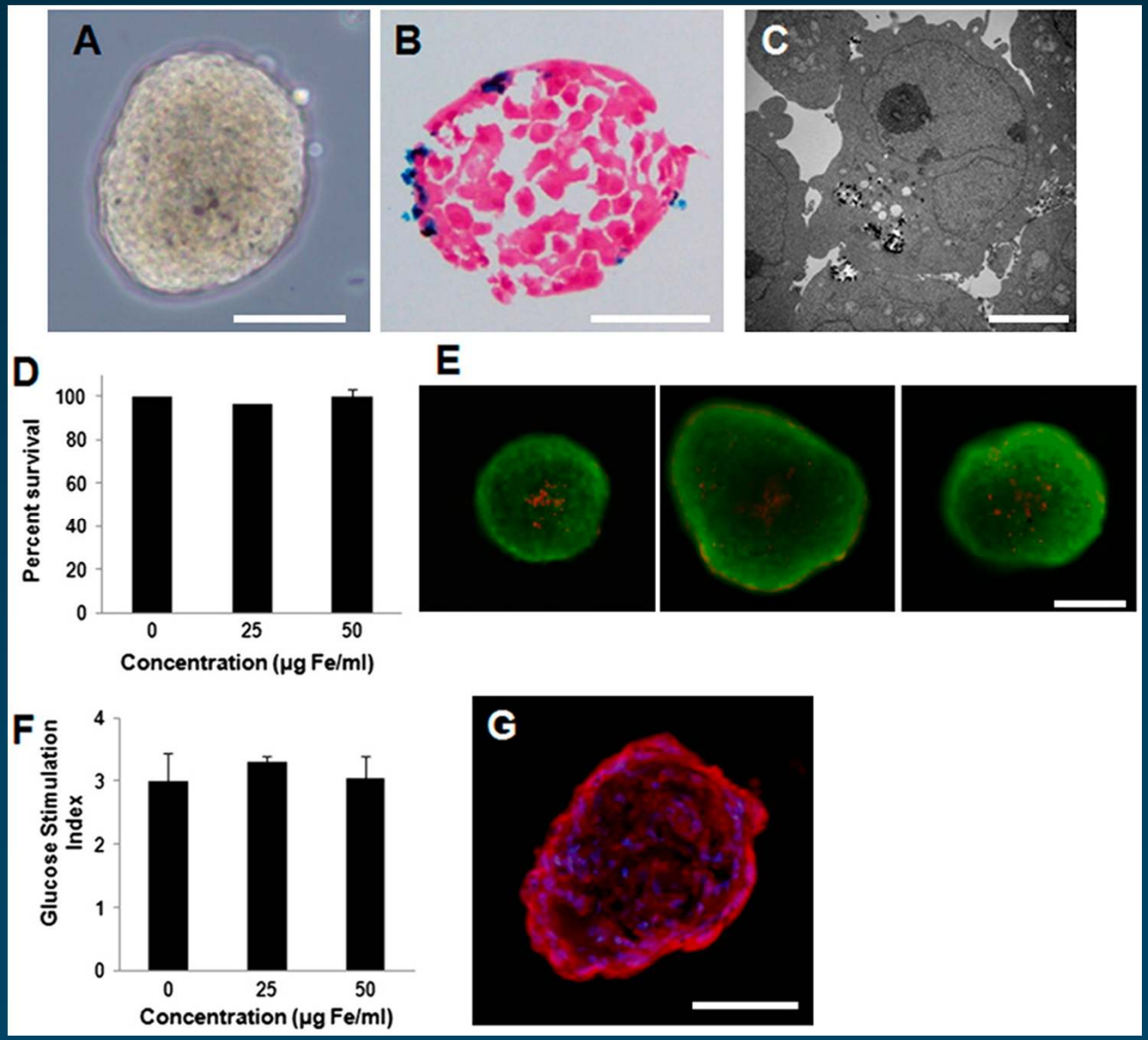
Single Cell Imaging using FION and 9.4T MRI





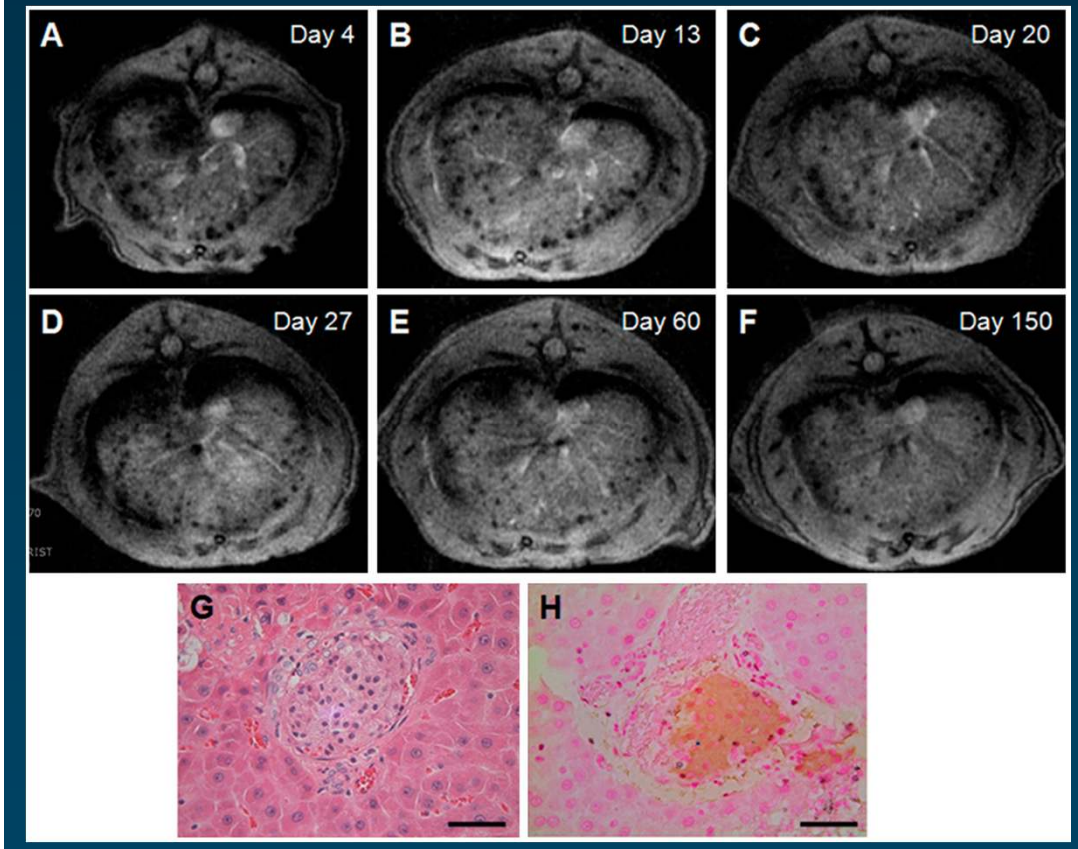
PNAS 2011 Feb 1

Labeling of pancreatic islets with FIONs

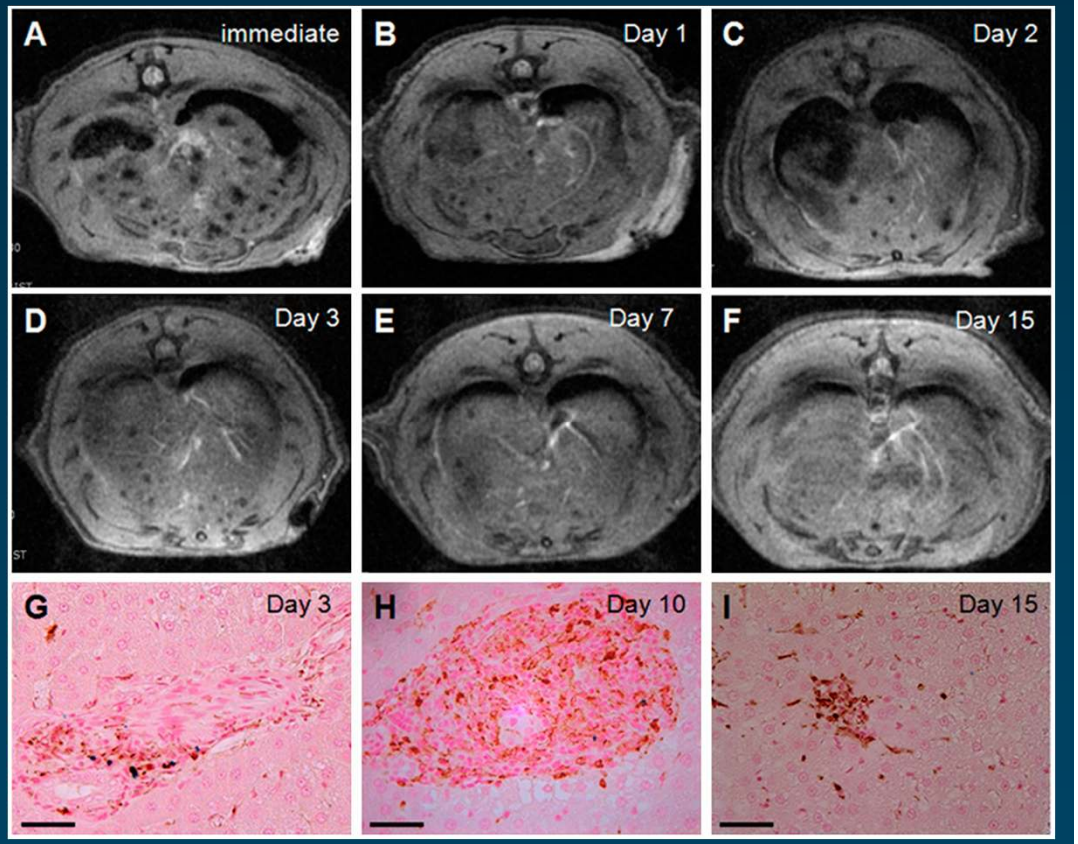


Transplanted pancreatic islets

Rat models

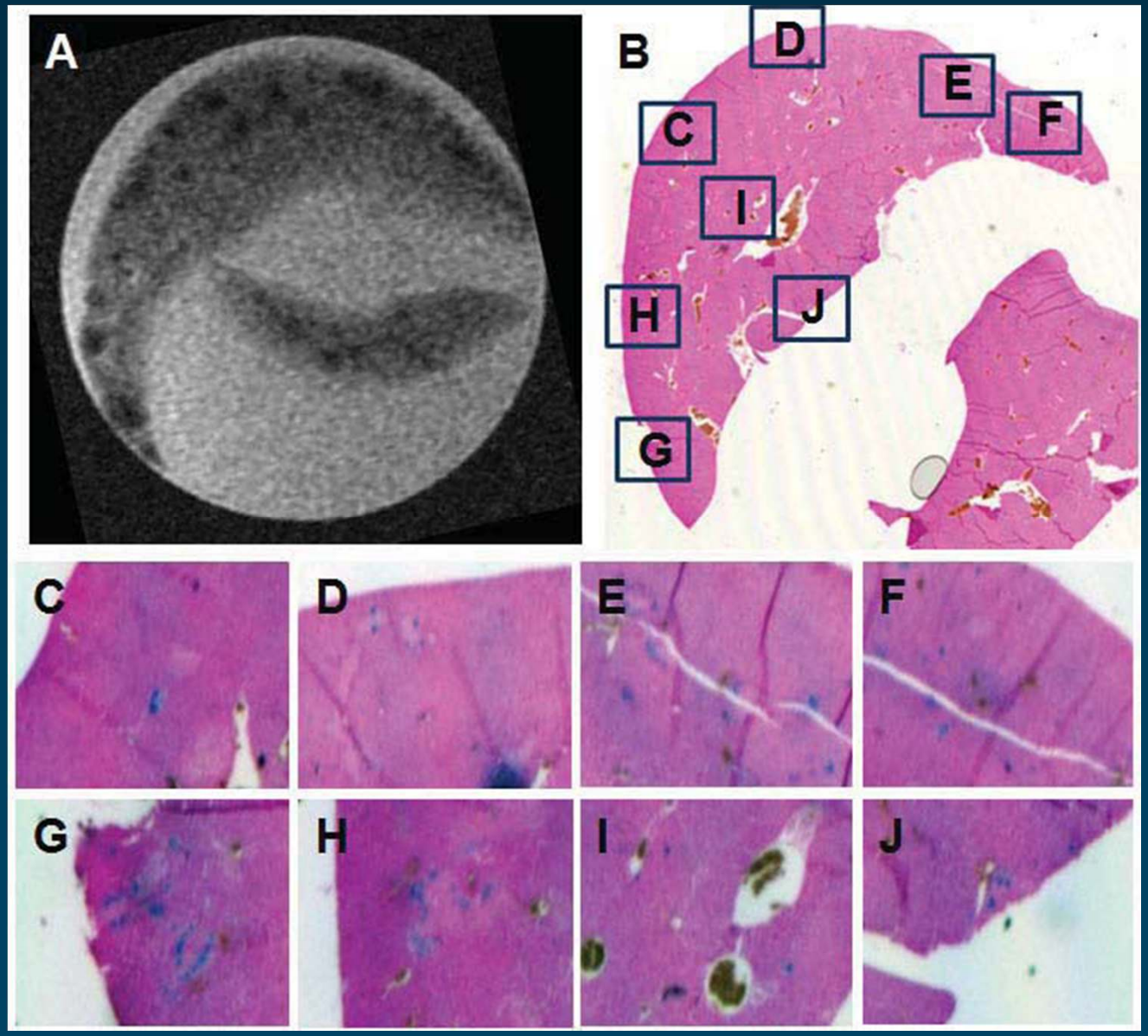


syngeneic islets



allogeneic islets

Transplanted pancreatic islets



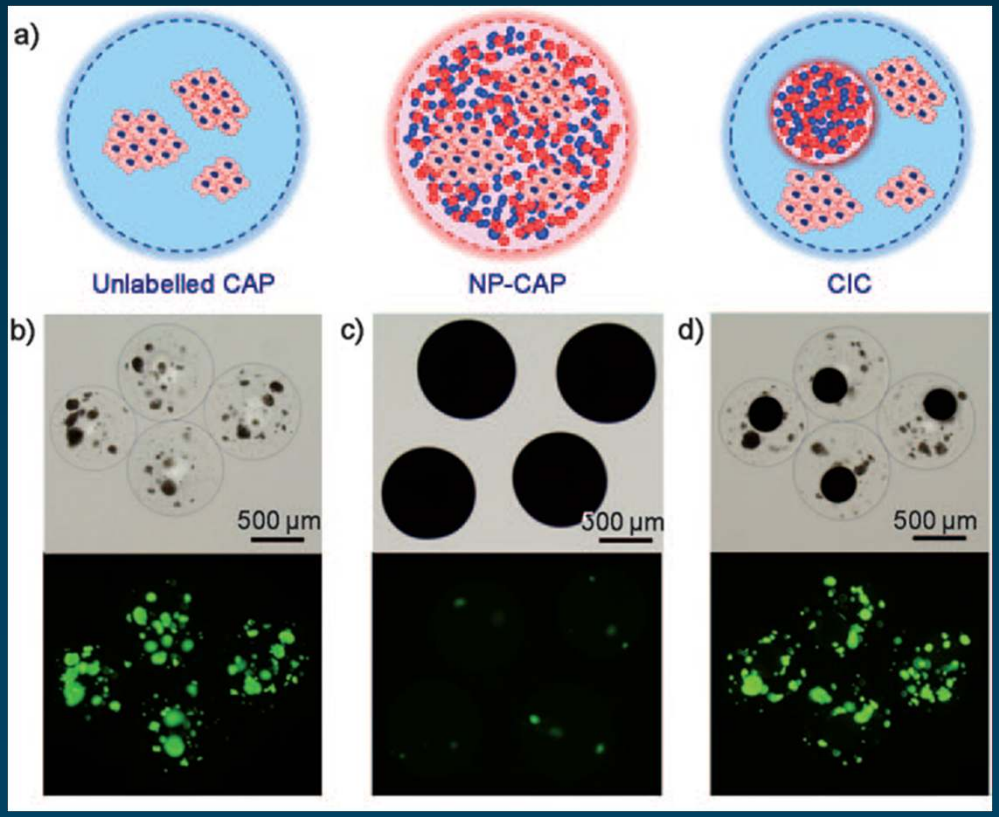
PNAS 2011 Feb 1

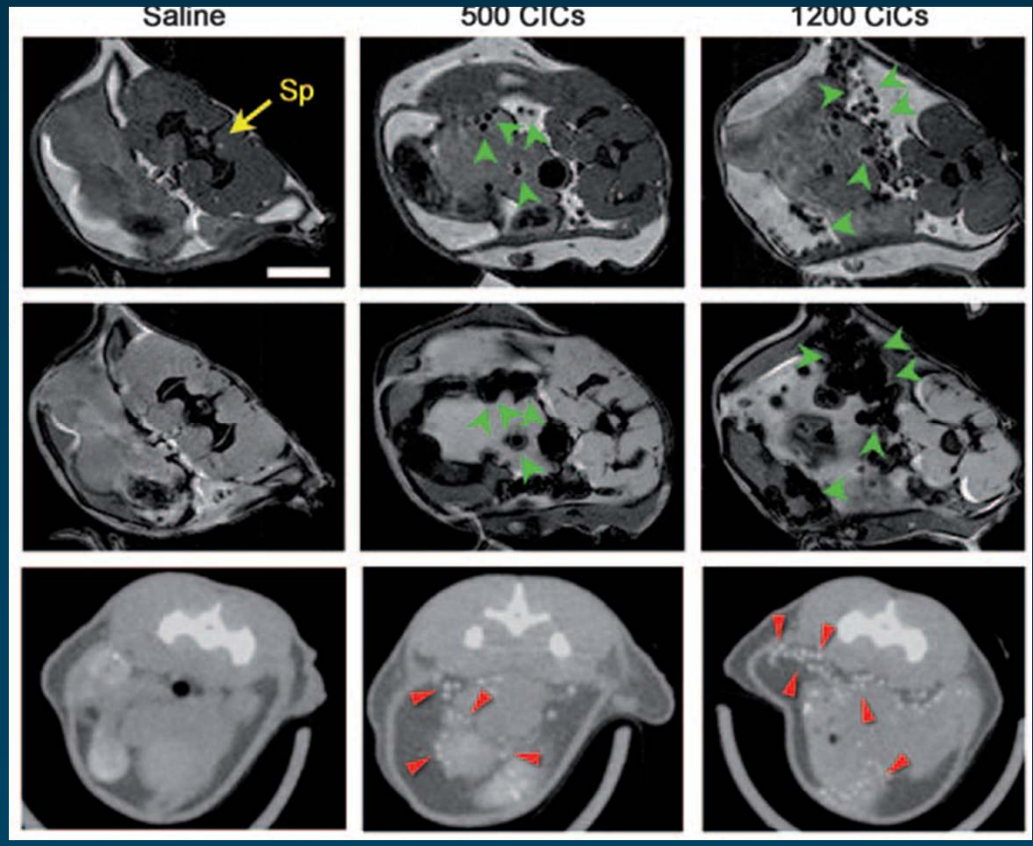
Transplanted pancreatic islets

Swine models

PNAS 2011 Feb 1

Multifunctional capsule-in-capsules for immunoprotection and trimodal imaging





현택환 . Agewante Chemie 2011

Limitation of cell labeling with SPIO

- It is not possible to discriminate live from dead cells.
- The SPIO label quickly is divided among daughter cells to undetectable levels when cells divide rapidly after transplantation.
- MRI cell tracking is difficult to perform in cases of traumatic injury in which hemorrhage is present or when hypointensity areas obscure the normal anatomic features of underlying tissue.

Conclusion

1. MRI is a powerful technique capable of detecting small micron-size objects such as pancreatic islets.
2. 나노입자 세포 표지와 MRI를 이용하여 이식 췌도의 생존 및 기능 등 치료효과를 비침습적 평가할 수 있음.
3. Reporter gene methods offer several advantages over direct labeling techniques but are not as established.

감사드립니다.

- 박경수, 정혜승
- 김회숙, 전련희, 김형수