DENDRITIC CELLS

Helmut SINZINGER

Department of Nuclear Medicine, Medical University of Vienna, Austria

16th ISORBE, Pretoria, 21-23 March 2013

INTRODUCTION

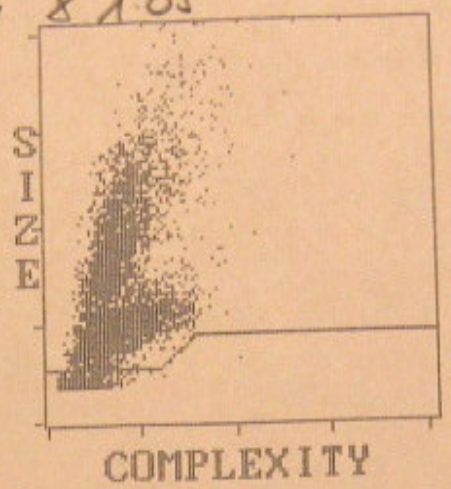
- DC are aimed to transport peripheral AG to lymph nodes
- Immunization with ex-vivo generated DC
- Optimal vaccine preparation
- Preferential site of injection and migration pattern largely unknown
- At present NM only non-invasive method for monitoring the fate of DC
- Promising area for DNM

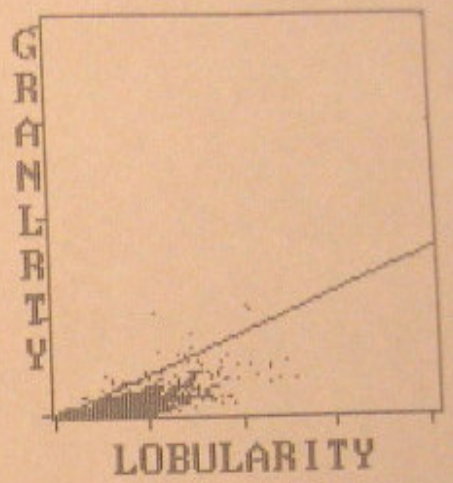
Specimen ID 012-2 60Mio DC
Patient
Sex DOB
Dr
Param: 1 Limits: 1 auffallend v 8.1.05

28 Sep 2005 09:24
Operator ID KRM
Sequence # 3082
Open Sampler

SUSPECT

WBC	4.50	G/L		(WOC)WBC
NEU	.011	.254	%N	
LYM	2.40	53.2	%L	VAR LYM
MONO	1.96	43.5	%M	NRBC/RRBC
EOS	.003	.076	%E	
BASO	.130	2.89	%B	DFLT(NLMEB)



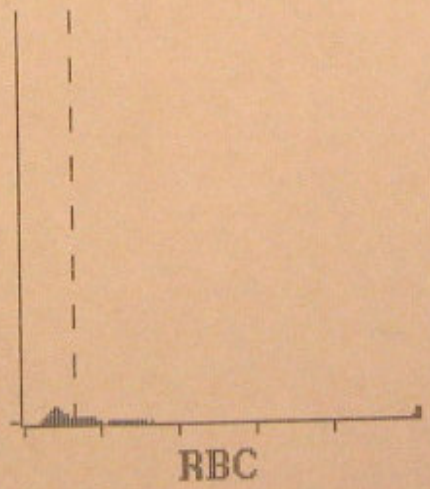


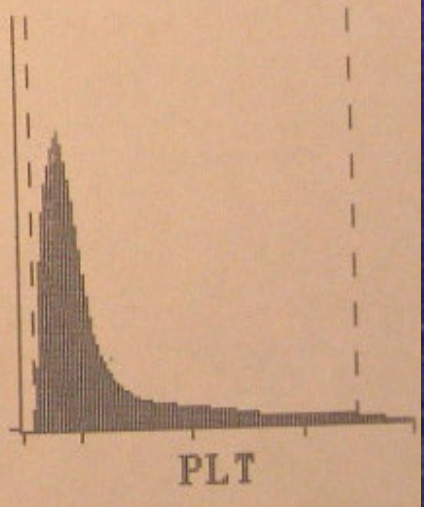
RBC	.024	T/L
HGB	.175	g/dL
HCT		%
MCV		fL
MCH		pg
MCHC		g/dL
RDW		%

SAMPLING ERR

PLT	96.8	G/L
MPV		fL

LRI





DENDRITIC CELLS (DC)

IMMUNOLOGICALLY EFFECTIVE AG-PRESENTING CELLS IN IMMUNE SYSTEM

ORIGINALLY DESCRIBED > 30 YEARS AGO

STAGES: PRECURSOR
IMMATURE
MATURE

CLASSES: MYELOID
PLASMACYTOID

TRANSPORT OF PERIPHERAL AG TO LYMPH NODE

RADIOISOTOPIC MONITORING OF DC IN HUMAN

M.A. MASSE, 1999,	immature DC
D. BLOCKLET, 2003,	immature/mature DC
I.J. DE VRIES, 2003,	mature DC
S. NAIR, 2003,	mature
P. LAVERMAN, 2006,	labeling of TU-assoc. AG peptides

MATURE DCs MORE COMMONLY TO SEVERAL LN, MIGRATION INCREASES 24 – 48 h

VISUALIZATION OF BIODISTRIBUTION AND FATE OF CELLS (OPTIMIZING WAY OF THERAPY) AND ANTIGEN PEPTIDES

METHODOLOGICAL BASIS

ISOLATION OF BM-DERIVED CD34 - CELLS

↓

EXPANSION OF DCs IN-VITRO

↓

AG-LOADING → APPLICATION

SCHEDULE (SINGLE, REPEATED, INTERVALS)

TUMOR SPECIFIC DIFFERENCES?

ROUTE OF INJECTION:

AFFERENT LYMPHATIC

LYMPH NODE

INTRADERMALLY (In)

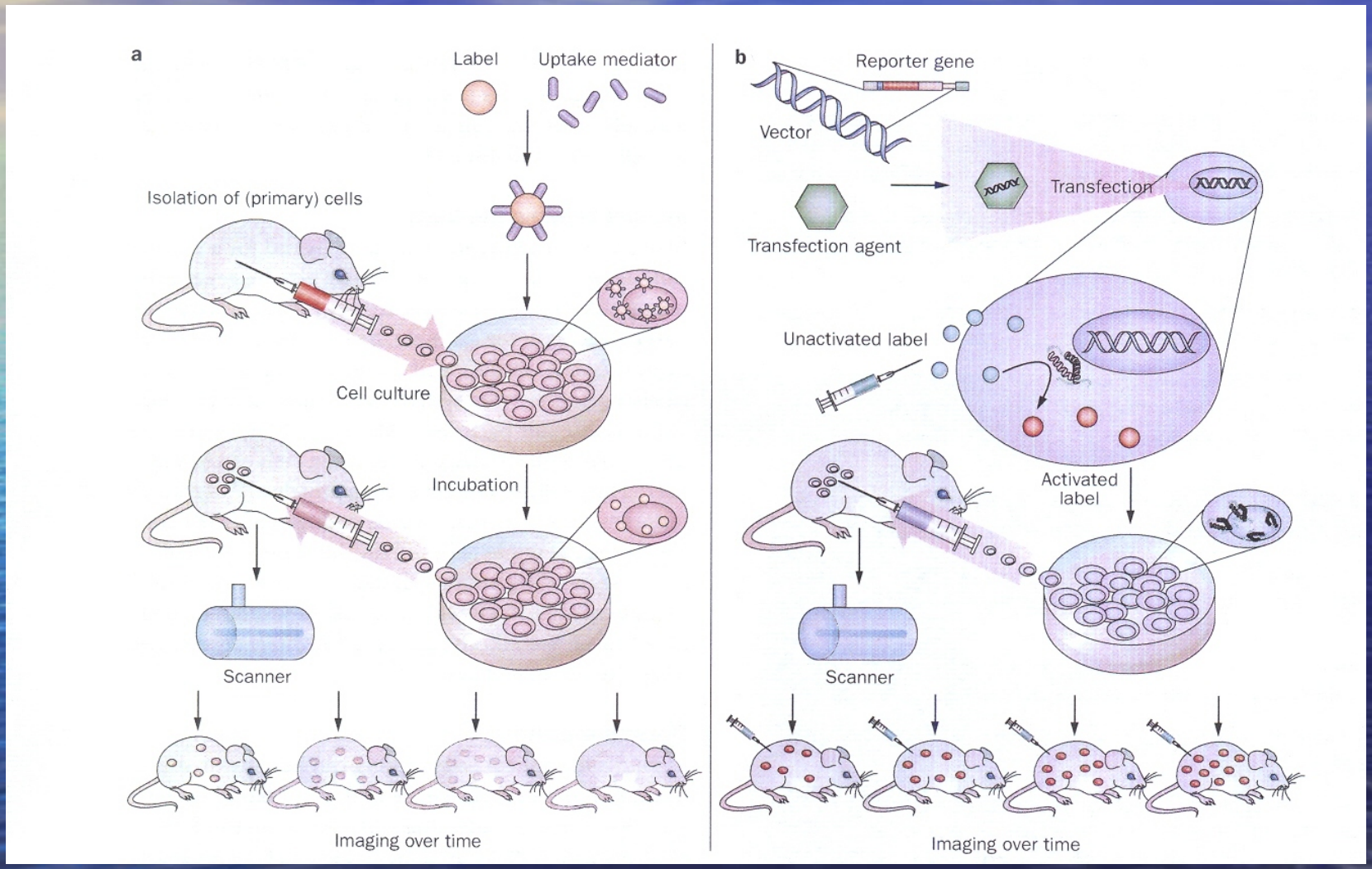
KEY QUESTIONS

- OPTIMAL TYPE OF DC
- OPTIMAL LABELING CONDITIONS
- RECOVERY, ELUTION, FUNCTIONAL BEHAVIOUR
- IMAGING/MONITORING

CELL LABELING

DIRECT

INDIRECT



DENDRITIC CELLS (LE)

t (min) / temp (°C)	5	15	30
22	82,96 ± 2,37	81,27 ± 2,80	82,00 ± 3,01
37	84,89 ± 1,36	84,07 ± 1,85	83,32 ± 1,93

x ± SD; values in %; n = 4 each; 1.10^6 cells/ml, 10 µCi/ml; ^{111}In-oxine

^{111}In-COMPLEXES

compl. / temp (°C)	OXINE	OXINE-SULPHATE	TROPOLONE
22	82,96 ± 2,37	83,27 ± 2,14	82,29 ± 2,07
37	84,89 ± 1,36	85,61 ± 2,42	83,05 ± 2,20

x ± SD; values in %; n = 4 each; 1.10^6 cells/ml, 10 µCi/ml

LE (^{99m}Tc vs. ^{111}In)

time / temp (°C)	^{111}In-OXINE	^{99m}Tc-HMPAO
12	82,96 ± 2,37	83,80 ± 3,12
37	84,89 ± 1,36	84,47 ± 4,16

x ± SD; values in %; n = 4 each; inc. time 5 min.

ELUTION AT 37°C

t (h) / temp (°C)	1	2	4	8	12	24
22	2±1	3±2	6±4	10±5	13±6	22±8
37	2±1	3±2	7±3	11±6	12±6	20±9

x ± SD; values in %; n = 6 each; ^{111}In-oxine

ELUTION
(^{111}In-oxine vs. ^{99m}Tc-HMPAO)

t (h) / tracer	1	2	4	8	12	24
^{111}In	2±1	3±2	7±3	11±6	12±6	20±9
^{99m}Tc	4±2	6±3	13±6	34±10	39±12	69±27

x ± SD; values in %; n = 6 each

SUMMARY

- DC SHOW A ROBUST LABELING BEHAVIOUR
- LE OF DC IS NOT TIME- AND TEMPERATURE-DEPENDENT
- IN-VITRO RELEASE OF ^{111}In AMOUNTS TO ABOUT 1 %/h, FOR ^{99m}Tc > 3 %/h, ^{18}F > 10 %/h
- SHORT-LIVED TRACERS (^{18}F, ^{99m}Tc), DISADVANTAGEOUS VS. ^{111}In
- ^{111}In-IDENTICAL LE AND REC, BUT LESS ELUTION AND LONGER FOLLOW-UP
- NO APPARENT INFLUENCE ON VIABILITY
- CRITICAL TRACER DOSIS: 15 μCi/10^6 CELLS/ml?
- COUPLING WITH TUMOR ASSOCIATED ANTIGEN PEPTIDES?

DISADVANTAGES OF DIRECT LABELING

ELUTION OF LABEL

UNDERESTIMATION OF AMOUNT OF CELLS

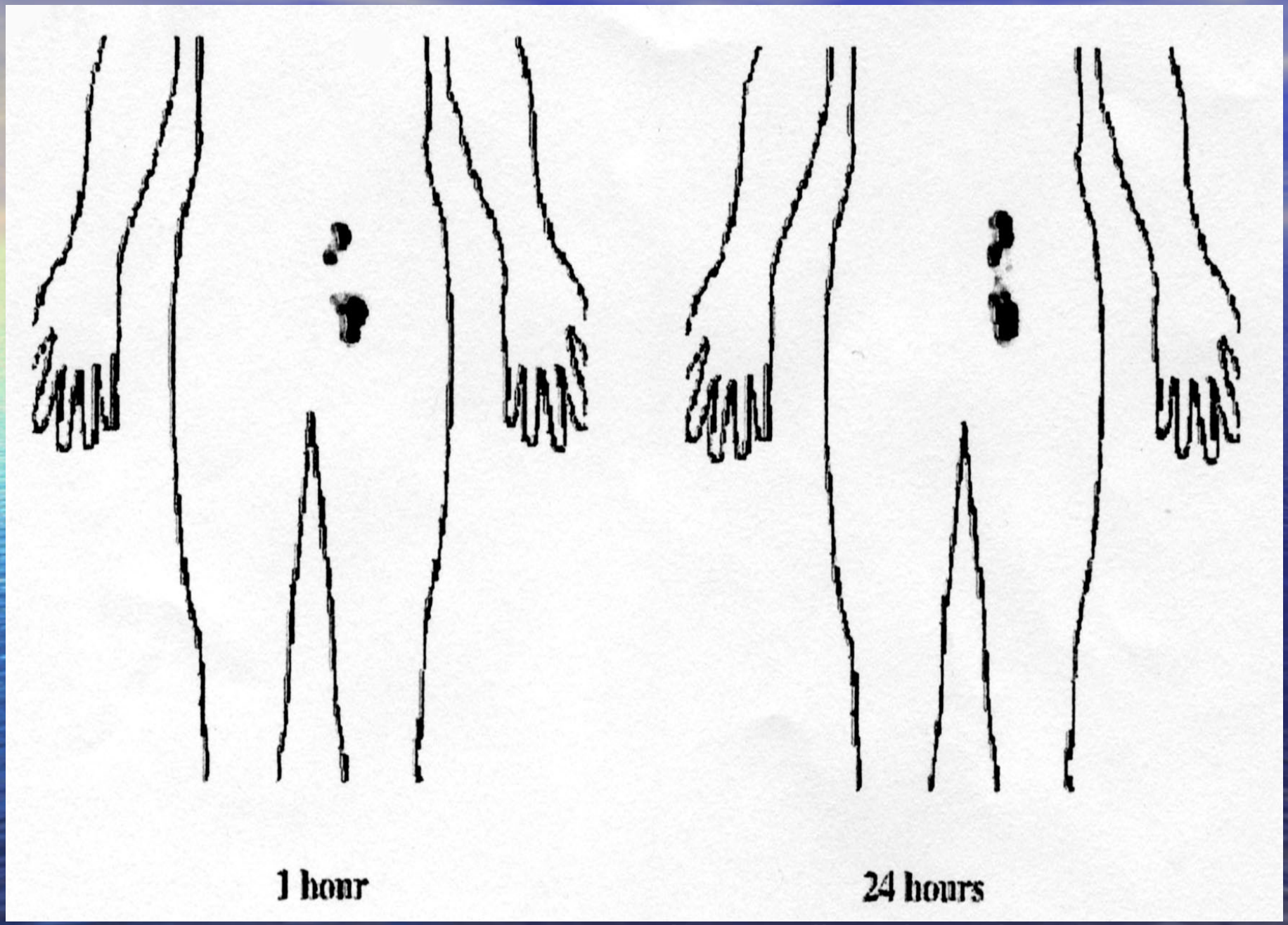
DISINTERPRETATION DUE TO ELUTED LABEL

REUTILIZATION

ASSESSING VIABILITY DIFFICULT

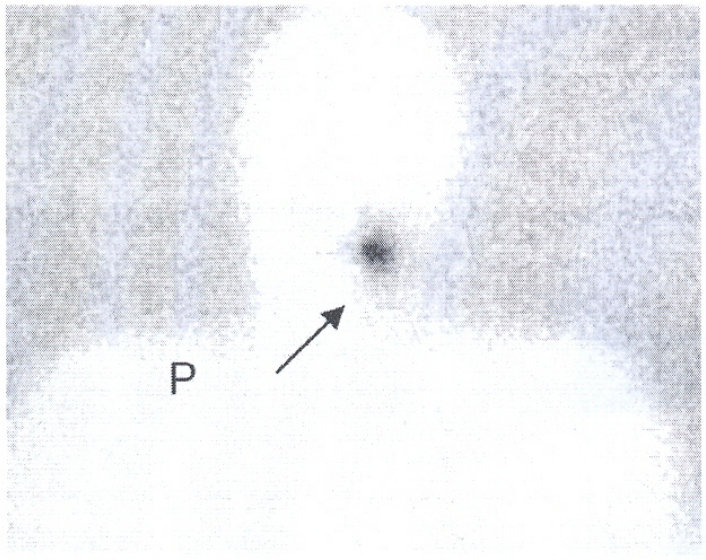
DILUTION WHEN CELLS DIVIDE

DC IN MELANOMA

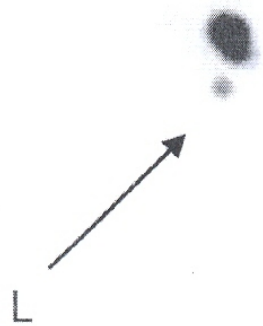


IN, 20.106 DC, LE 91% (from Quillian al 2005)

DC (IT) MIGRATE TO LN



Anterior co-57 403K



lateral 150K

3 vs. 24 hrs p.i.

DC GENERATED FROM CD14+ MONOCYTES

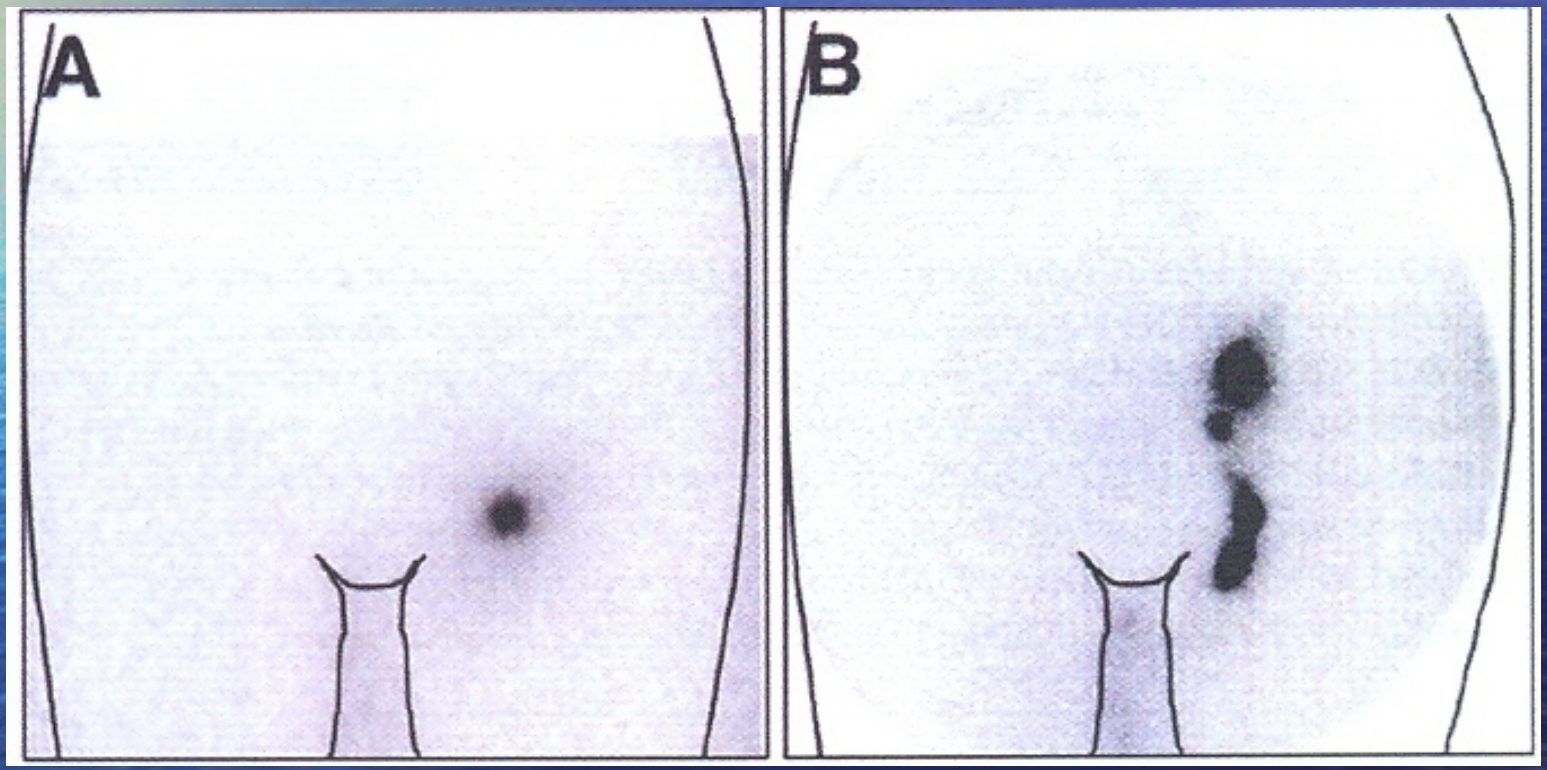
DC IMMUNOHISTOCHEMICALLY DOCUMENTED

Pandha al. 2012

111In-oxine DC (IL)

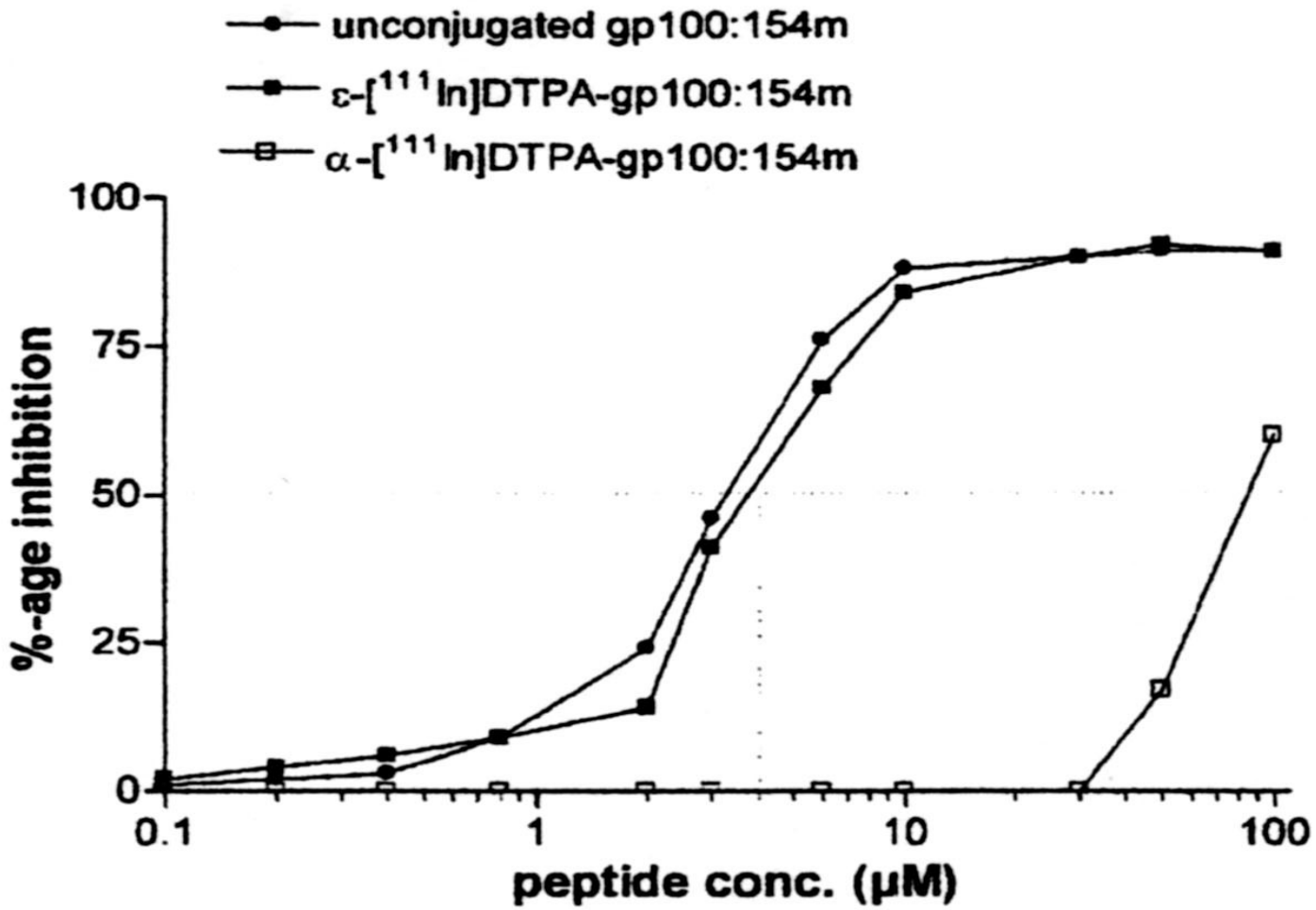
INJECTION

48 HRS

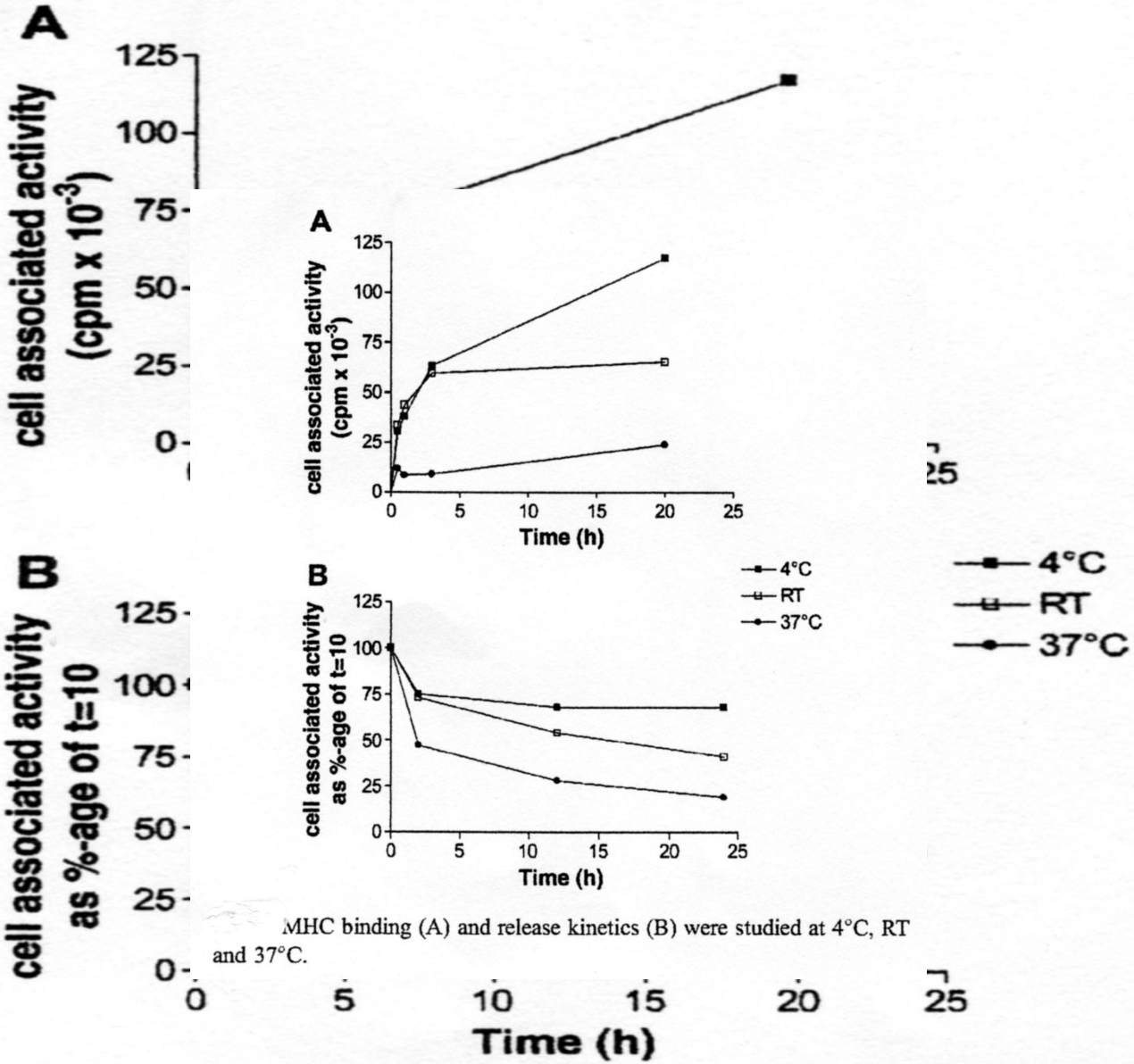


INDIRECT LABELING WITH REPORTER GENE

- TRANSCRIPTION INTO A PROTEIN
- REQUIRES VIABLE CELL
- GENETIC MANIPULATION UNITS USE TO SPECIALIZED CENTERS
- GENE TRANSFER BY VIRAL- AND NON-VIRAL METHODS



Competitive HLA-A2.1 peptide binding assay as analyzed by FACS. HLA-A2.1^{+}JY cells were incubated with fluorescein-conjugated reference peptide (HBC 18-27: FLPSDC$_{[fluorescein]}$FPSV) and with a serial dilution of competitor peptide (gp100:154m, α-[^{111}In]DTPA-gp100:154m and ε-[^{111}In]DTPA-gp100:154m).



MHC binding (A) and release kinetics (B) were studied at 4°C, RT and 37°C.

MHC binding (A) and release kinetics (B) were studied at 4°C, RT and 37°C.

TRACKING OF

TUMOR ASSOCIATED ANTIGEN PEPTIDES
- BINDING AFFINITY
- VIABILITY
- OPTIMAL CONDITIONS (CONC., COMPLEX, TEMPERATURE)

COUPLING TO DENDRITIC CELLS

DOUBLE LABELING ?

VIABILITY (QUALITY CONTROL)

- MATURATION AND MIGRATORY PROPERTIES (UNCHANGED?)
- DIFFERENT METHODS / INCONSISTENT RESULTS
- HARM TO DC IMMUNOLOGICAL FUNCTION
- (TYPE OF CELLS?)
- FREE ^{111}In → TRANSFERRIN, OR BONE MARROW + LIVER?
- DOES REUTILIZATION FROM DYING CELLS INFLUENCE THE DATA?
- ^{18}F NO EFFECT ON VIABILITY (HIGH SPATIAL RESOLUTION – 2 cm – 3D IMAGING, ALLOWING QUANTIFICATION)

FUTURE

RADIOISOTOPIC MONITORING OF DC MIGHT BECOME A KEY TOOL TO EXPLORE THIS FASCINATING NEW THERAPEUTIC APPROACH

RADIOISOTOPES USED

- ^{111}IN-OXINE[1] (LOWER ACTIVITY, LONGER FOLLOW-UP MONITORING, LESS RELEASE)
- ^{99m}Tc-HMPAO (HIGHER ACTIVITY, THEORET. ADVANTAGE OF BETTER SENSITIVITY)
- ^{64}Cu-PTSM
- (^{18}F-FDG HIGH SPATIAL RESOLUTION)

NO FUNCTIONAL IMPAIRMENT EXCEPT [1]MONTEIRO et al. 2009: HEMATOPOIETIC PROGENITOR CELLS

I.V. INFUSED DCs, TRANSIENT LUNG UPTAKE (MACKENSEN et al. 1989)

KEY REQUIREMENT OF LONG TERM MONITORING EXCLUDES USE OF SHORT-LIVED TRACER (^{99m}Tc, ^{18}F)

NON-INVASIVE CELL TRACKING

- MONITOR DISTRIBUTION, MIGRATION OF BIOLOGICALLY ACTIVE CELLS
- CELL BASED THERAPY WITH NATURAL OR GENETICALLY ENGINEERED CELLS
  - T-CELLS
  - DENDRITIC CELLS
  - STEM CELLS

BIODISTRIBUTION OF RADIOLABELED DC

Reference	Source	Activation status	Culture conditions	Antigen loading	Radioisotope	Route of injection	No of cells (×10.6)	No of patients	Migration to LN, no pos/no total (range %)
[87]	Monocyte	Immature		Pulsing tumor lysate	^{111}In-oxine	i.d.	6	1	0.42
[87]	Monocyte	Immature		Pulsing tumor lysate	^{99}Tc-HMPAO	i.d.	6–9	3	3/3, 0.05–0.22
[88]	Monocyte	Immature		Electroporated RNA	^{111}In-oxine	i.d.	12.5	6	0
[88]	Monocyte	Immature		Electroporated RNA	^{111}In-oxine	i.d.	12.5	2	0.54
[23]	Monocyte	Immature		Pulsing tumor antigen	^{99}Tc-HMPAO	i.d.	10	3	1/3, 0.07
[15]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	i.d.	10	8	0.2–0.4
[76]	Monocyte	Immature		Lipid transfected RNA	^{111}In-oxyquinoline	i.d.	1	4	Max 0.41
[89]	Monocyte	Immature		Pulsing tumor antigen	^{99}Tc-HMPAO	i.d.	1–7	5	"+"
[29]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	i.d.	n/a	3	2/3, 0.48
[23]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	i.d.	10	3	0/3
[76]	Monocyte	Immature		Lipid transfected RNA	^{111}In-oxyquinoline	s.c.	1	4	0/4
[29]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	s.c.	n/a	3	1/3
[23]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	s.c.	10	3	0/3
[23]	Monocyte	Immature		Pulsing tumor antigen	^{99}Tc-HMPAO	s.c.	10	3	0/3
[15]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	i.n.	10	7	0.5–30
[76]	Monocyte	Immature		Lipid transfected RNA	^{111}In-oxyquinoline	i.v.	100	3	0/3
[29]	Monocyte	Immature		Pulsing tumor antigen	^{111}In-oxine	i.v.	33–^{18}0	3	0/3
[29]	Monocyte	Immature		Pulsing tumor antigen	^{18}F-FDG	i.v.	130–150	2	0/2
[23]	Monocyte	Mature	MPL	Pulsing tumor antigen	^{111}In-oxine	i.d.	10	3	1/3, 0.25
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{64}Cu-PTSM	i.d.	15.3–21.3	2	2/2, 0.06, 0.10
[88]	Monocyte	Mature	IL-1b, TNF-a, IL-6, PGE2	Electroporated RNA	^{111}In-oxine	i.d.	12.5	8	0.5–2.0
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{111}In-oxine	i.d.	n/a/	3	2/3, 1.08, 1.29
[23]	Monocyte	Mature	MPL	Pulsing tumor antigen	^{99}Tc-HMPAO	i.d.	10	3	0/3
[15]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor antigen	^{111}In-oxine	i.d.	10	10	10/10, 0.5–3.9
[28]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor antigen	^{111}In-oxine	i.d.	15	12	12/12, 0.1–3.7
[90]	Monocyte	Mature	IFNg, Ribomunyl	Pulsing tumor antigen	^{111}In-oxine	i.d.	8–34	6	2/6, 0–1.8
	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor lysate	^{111}In-oxine	i.d.	6.7–7	2	2/2, 0.95–3.14
	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor lysate	^{99}Tc-HMPAO	i.d.	4–12	5	5/5, 0.39–1.75
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{111}In-oxine	s.c.	n/a	3	3/3, 1.3, 0.73
[23]	Monocyte	Mature	MPL	Pulsing tumor antigen	^{111}In-oxine	s.c.	10	3	1/3, 0.25
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{64}Cu-PTSM	s.c.	17.6	2	1/2, 0.04
[23]	Monocyte	Mature	MPL	Pulsing tumor antigen	^{99}Tc-HMPAO	s.c.	10	3	0/3
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{64}Cu-PTSM	i.n.	n/a	2	0/2

Reference	Source	Activation status	Culture conditions	Antigen loading	Radioisotope	Route of injection	No of cells (×10.6)	No of patients	Migration to LN, no pos/no total (range %)
[13]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor antigen	^{111}In-oxine	i.n.	15	9	4/9, 1.7–17
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{111}In-oxine	i.n.	n/a	3	1/3
[15]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor antigen	^{111}In-oxine	i.n.	10	7	0.4–84
[28]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	Pulsing tumor antigen	^{111}In-oxine	i.n.	15	15	9/15, 0–56
[91]	Monocyte	Mature	IL-1b, IL-6, TNF-a, PGE2	RNA electroporated	^{111}In-oxine	i.n.	15	8	6/8, 0–65
[90]	Monocyte	Mature	IFNg, Ribomunyl	Pulsing tumor antigen		i.n.	7–25	5	2/5, 0–26
[92]	CD34+ proge	Mature	TNF-a	Pulsing tumor antigen	^{111}In-oxine	i.v.	16–17	2	0/2
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{64}Cu-PTSM	i.v.	140–160	2	0/2
[29]	Monocyte	Mature	IFN-g, Imukin, FMKp	Pulsing tumor antigen	^{111}In-oxine	i.v.	110–250	3	0/3
[92]	CD34+ proge	Mature	TNF-a	Pulsing tumor antigen	^{99}Tc-HMPAO	i.l.	10–13	3	"+"
[90]	Monocyte	Mature	IFNg, Ribomunyl	Pulsing tumor antigen	^{111}In-oxine	i.l.	33–50	4	4/4, "80"

DC APPLICATION, TRACKING AND OUTCOME

Patient ID	Type of DC	Route	No. DCs†	Labeling Method	Nodal Tracking Observed?	Comment on Tracking	Immunologic Assays: ELISpot	Immunologic Assays: Antibody Response
Pt001	nmDC	IV	1.6×10^8	^{111}In-oxine	No	Uptake in liver, spleen, lung	Weak baseline positive with no subsequent change	Nil
		ID/SC/IN	6.7×10^7	^{111}In-oxine	Nodal uptake with ID			
		IV	1.3×10^8	^{18}F-FDG*	No	Washout of FDG from cells		
		ID/SC/IN	6.6×10^7	^{18}F-FDG*	No	No uptake		
Pt002	nmDC	IV	3.3×10^7	^{111}In-oxine	No	Uptake in liver, spleen, lung	Nil	Nil
		ID+SC+IN	1.1×10^8	^{111}In-oxine	Nodal uptake with SC			
		IV	1.5×10^8	^{18}F-FDG*	—	Washout of ^{18}F-FDG from cells		
		ID+SC+IN	8.7×10^7	^{18}F-FDG*	—	^{18}F-FDG tracking discontinued		
Pt003	nmDC	ID+SC+IN	3.9×10^7	^{111}In-oxine	Nodal uptake with ID		Moderate baseline positive with no subsequent change	Weak transient antibody response
		IV	1.8×10^8	^{111}In-oxine	No	Uptake in liver, spleen, lung		
		ID+SC+IN	4.7×10^7	—	—	—		
		IV	1.2×10^8	—	—	—		
Pt004	mDC	ID+SC+IN	6.7×10^7	^{111}In-oxine	Nodal uptake with SC		Moderate baseline positive with loss at week 5	Nil
		IV	2.5×10^8	^{111}In-oxine	No	Uptake in liver, spleen, lung		
		ID+SC+IN	7.7×10^7	—	—	—		
Pt005	mDC	ID+SC+IN	5.0×10^7	^{111}In-oxine	Nodal uptake with SC, ID		Not tested	Not tested
		IV	1.1×10^8	^{111}In-oxine	No	Uptake in liver, spleen, lung		
Pt006	mDC	ID+SC+IN	6.4×10^7	^{111}In-oxine	Nodal uptake with SC, ID, IN		Moderate baseline positive with loss at week 5 and recurrence at week 16.	Nil
		IV	1.6×10^8	^{111}In-oxine	No	Uptake in liver, spleen, lung		
		ID+SC+IN	5.9×10^7		—	—		
		IV	1.2×10^8		—	—		
Pt003(R)/ Pt003(R2)	mDC	ID+SC+IN	4.6×10^7	^{64}Cu-PTSM	No	False-positive with early nodal appearance	Not tested	Not tested
		IV	1.6×10^8	^{64}Cu-PTSM	No	Comparison with In tracking studies		
		ID+SC+IN	5.3×10^7	^{64}Cu-PTSM	Nodal uptake with SC, ID			
		IV	1.1×10^8		—	—		
Pt006(R)	mDC	ID+SC+IN	6.1×10^7	^{64}Cu-PTSM	Nodal uptake with ID		Not tested	Not tested
		IV	1.4×10^8	^{64}Cu-PTSM	No	Lung uptake		
		ID+SC+IN	8.8×10^7		—	—		
		IV	1.6×10^8		—	—		

Shaded areas indicate infusions associated with cell tracking available for analysis.

*Protocol was later modified after patient 2, cohort 1, to remove ^{18}F-FDG-PET imaging after the observation that FDG-PET was not a suitable label for tracking (see text). For consistency across cohorts, patients in subsequent cohorts still received injections at week 5 and 7 although no labeling and tracking was performed.

†For IN, ID, SC, this dose is divided into 3 equal aliquots with some cells used for quantitative and qualitative assessment of DC.

R, Re-enrolled into later cohort.

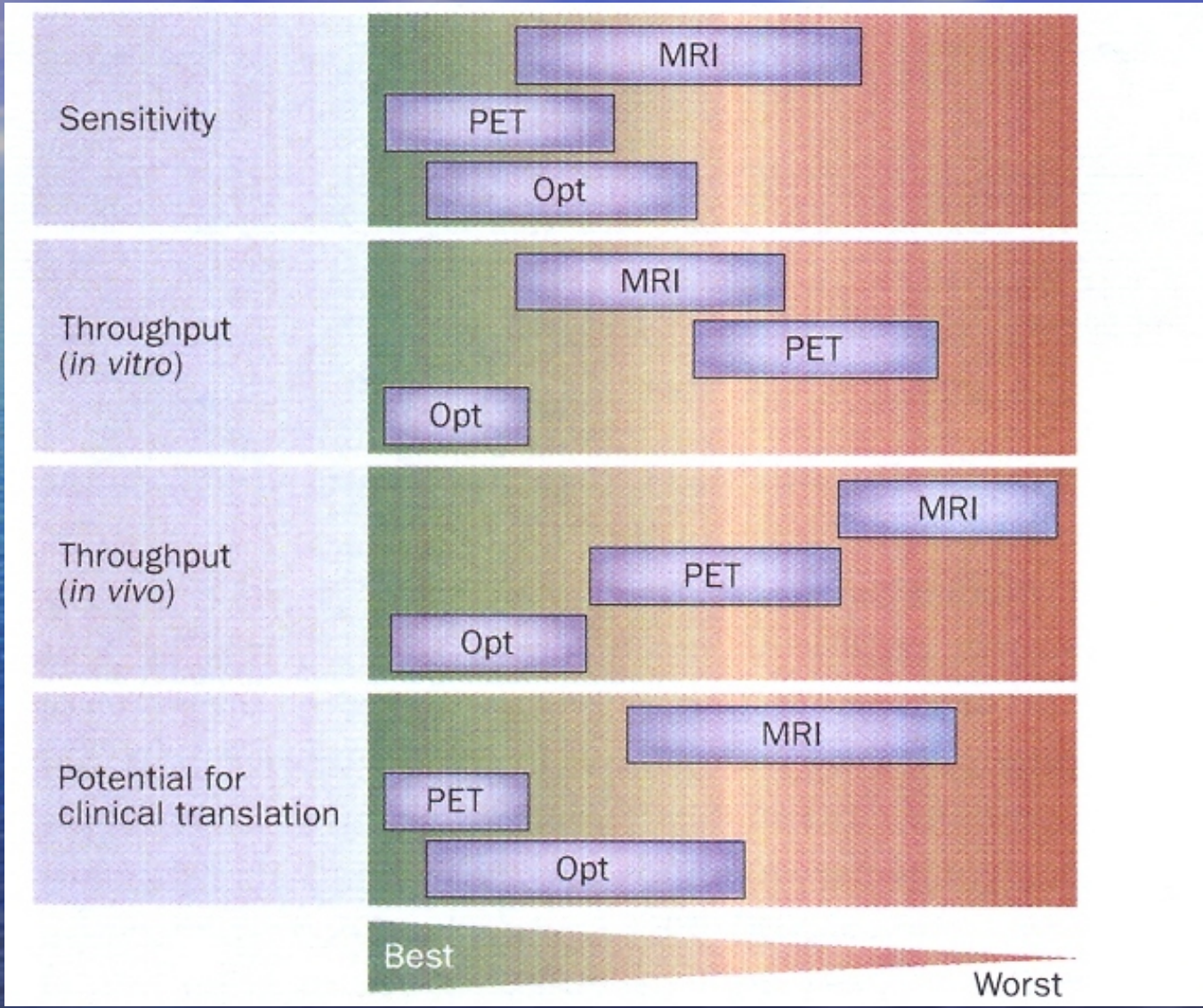
Prince et al 2008

TRACKING APPROACHES

References	DC Production Method	Tracking Method	Route	mDC Success	mDC % Tracked to Nodes	nmDC Success	nmDC % Tracked to Nodes
This report	GM-CSF + IL13 Mo-DC	^{111}In-oxine	SC	3/3	0.73-1.3	1/3	NA
			ID	2/3		2/3	0.48
			IN	1/3	NA	0/3	NA
This report	GM-CSF + IL13 Mo-DC	^{64}Cu-PTSM	SC	1/2	0.14-0.3	—	—
			ID	2/2		—	—
			IN	0/2	NA	—	—
Quillien et al[36]	GM-CSF + IL13 Mo-DC	^{111}In-oxine	Lymphatic	4/4	80	—	—
			IN	2/5	4-26	—	—
			ID	2/6	1.4-1.8	—	—
Blocklet et al[44]	GM-CSF + IL4 Mo-DC Matured with MPL	^{111}In-oxine	ID/SC	1/3	0.25	NS	0.0
		^{99}mTc-HMPAO	ID/SC	1/3	0.0	NS	0.07
Ridolfi et al[45]	GM-CSF Mo-DC Matured with cytokine cocktail	^{111}In-oxine	ID	2/2	1.88-3.14	—	—
				1/1	—	NS	0.42
		^{99}mTc-HMPAO	ID	5/5	0.39-1.75	—	—
				3/3	—	NS	0.05-0.22
De Vries et al[46]	GM-CSF + IL-4 M0-DC Matured with PGE_2 + TNFα	^{111}In-oxine	ID	NS	1.8 ± 1.1	NS	0.3 ± 1
			IN	NS	0.4-84	NS	0.5-30
Barratt-Boyes et al[62] Chimpanzee studies	GM-CSF + IL4 Mo-DC Matured with CD40L	$DiIC_{18}$ + flow cytometry	ID	5/5	0.07-0.12 (regardless of the in vitro DC maturation state)		

$DiIC_{18}$: 1.1′dioctadecyl-3,3,3′,3′-tetramethyllindodicarbocyanine perchlorate; Mo-DC, monocyte-derived dendritic cells; MPL, monophospholipid; NA, not assessed; NS, not stated; PGE, prostaglandin; TNF, tumor necrosis factor.

VALUE OF CELL TRACKING MODALITIES



Thank you for your attention!

BIODISTRIBUTION OF RADIOLABELED DC

Reference	Disease stage	Source of cells	Label	Site of transfer	No. of patients	Distribution in myocardium, <2 h (%)	Distribution in myocardium, 24 h (%)
[93]	5–10 days after stent for AMI	Bone marrow cells, unselected	^{18}F-FDG	Intracoronary, infarct related artery	6	1.3–5.3	n/a
[93]	5–10 days after stent for AMI	CD34+ bone marrow cells	^{18}F-FDG	Intracoronary, infarct related artery	3	14–39	n/a
[94]	3–300 days after AMI	Peripheral HSC	^{18}F-FDG	Intracoronary artery	17	0.2–3.3	Myocardial localization in one patient
[95]	Congestive heart failure	Bone marrow MNC	^{99}Tc	Intracoronary artery	6	5.4 ± 1.7	2.3 ± 0.6
[96]	18–22 months after AMI	CD34+	^{18}F-FDG	Intracoronary artery	7	1.2–5	n/a
[97]	AMI	Bone marrow MNC	^{99}Tc-HMPAO	Intracoronary artery	12	16.14 ± 7.06	10.29 ± 6.88
[98]	5 days to 17 years after AMI	Proangiogenic progenitor	^{111}In-oxine	Intracoronary	17	1–19	1–3
[99]	>12 months after AMI	CD133+ peripheral blood stem cells	^{111}In-oxine	Intracoronary	2	6.9–8 2	2.3–3.2
[100]	9–81 months after AMI	CD133+ / CD34+ bone marrow progenitor cells	^{99}Tc-HMPAO	Intracoronary, infarct related artery	8	9.2 ± 3.6	6.8 ± 2.4
[101]	7–21 days after AMI	Peripheral blood CD34+	^{18}F-FDG	Intracoronary	6	4–7	n/a
[97]	AMI	Bone marrow MNC	^{99}Tc-HMPAO	Intracoronary vein	6	4.62 ± 1.40	3.13 ± 0.99
[94]	3–300 days after AMI	Peripheral HSC	^{18}F-FDG	Intravenous	3	0	n/a
[93]	5–10 days after stent for AMI	Bone marrow cells, unselected	^{18}F-FDG	Intravenous	3	0	n/a

DC AND ATHEROSCLEROSIS

- DC ACCUMULATED IN LESIONS
- DC MIGRATION ↓ WITH HLP
- RESTORED AFTER HDL-ADDITION
- STATINS INCREASE DC-MIGRATION
- ROLE ALSO IN TUMOR PATIENTS

LE OF DENDRITIC CELLS

t	5	10	20	30
20°C	57.3 ± 5.8	60.4 ± 6.1	62.8 ± 4.1	67.8 ± 6.3
37°C	82.7 ± 5.6	87.3 ± 4.0	86.4 ± 2.9	88.4 ± 3.2

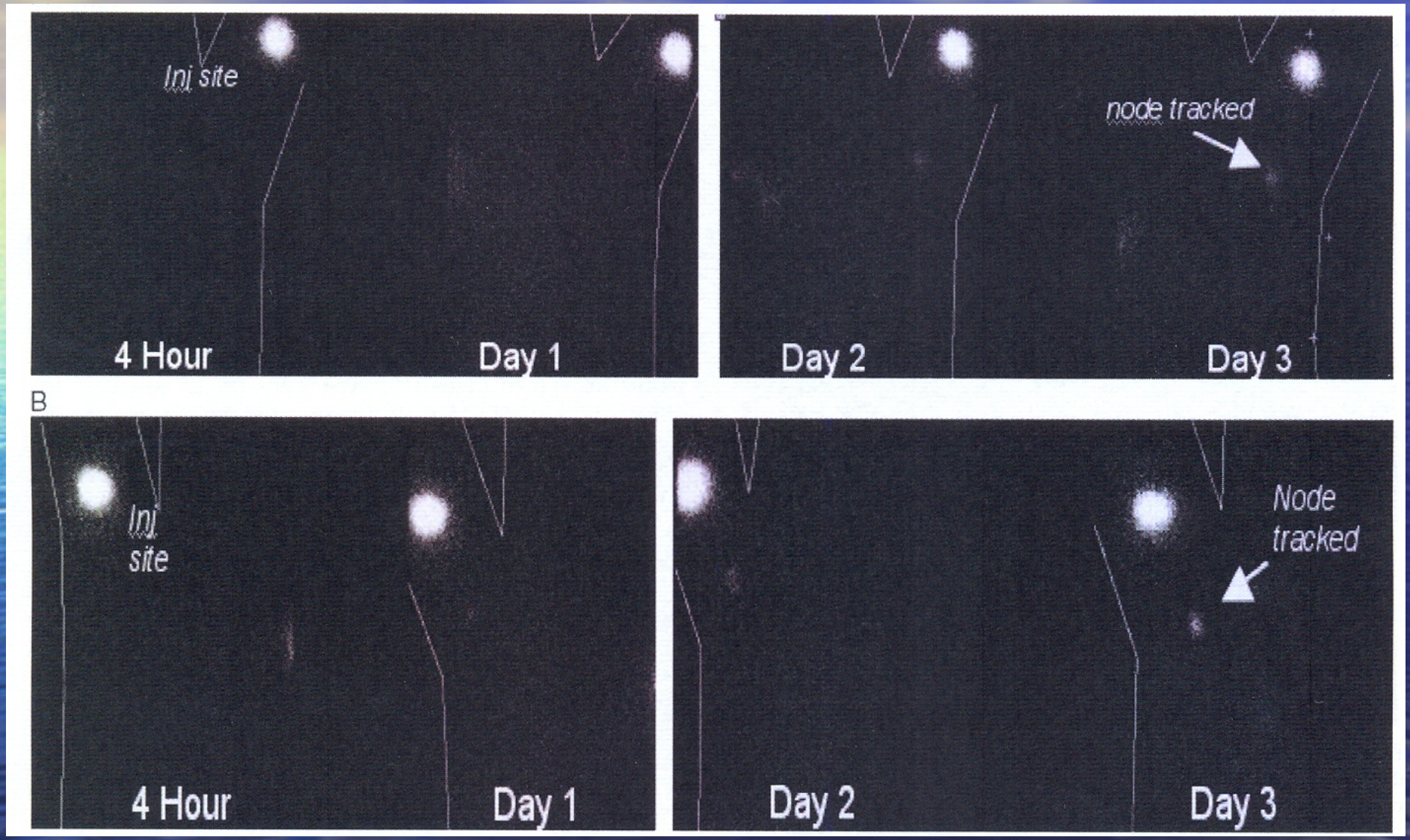
% values in x ± SD; n = 6 each;
labeling in 1 ml RPMI-1640; 1.10^6 cells/ml

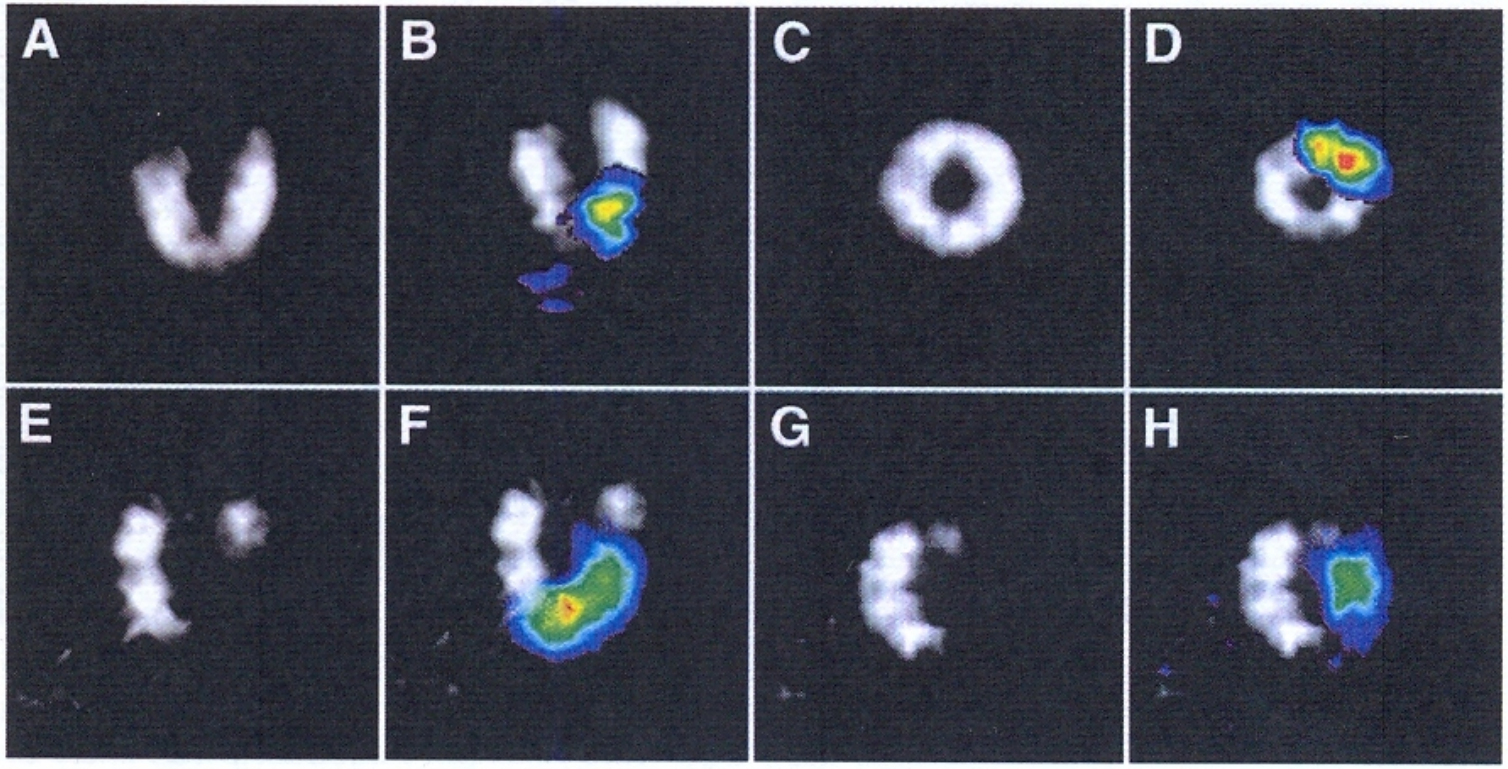
ELUTION OF DENDRITIC CELLS

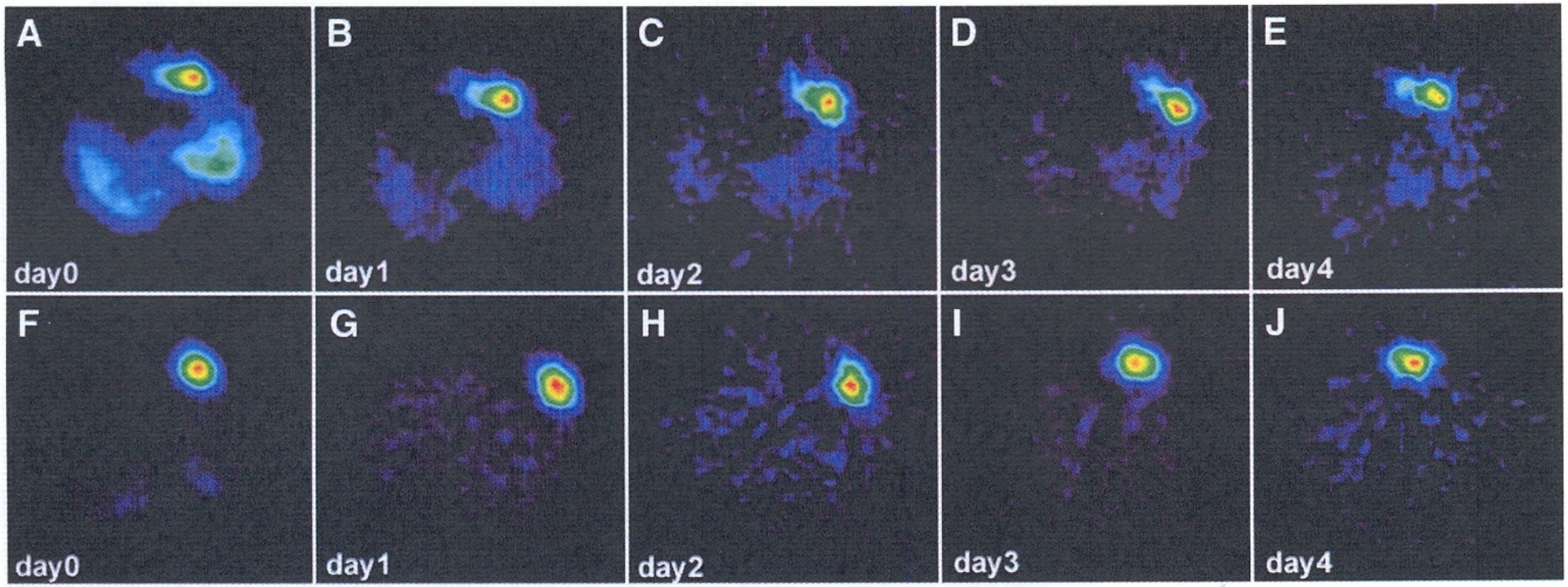
t (h)	^{111}IN-OXINE	^{99m}Tc-HMPAO
1	1.7 ± 0.9	3.2 ± 1.8
2	2.2 ± 1.0	6.7 ± 3.2
4	3.4 ± 1.3	12.9 ± 6.6
6	5.6 ± 2.2	17.4 ± 7.8
12	9.6 ± 2.8	35.8 ± 9.6
24	19.6 ± 3.9	51.3 ± 14.2

% values in x ± SD; n = 6 each

NODE TRACKING




A
B
C
D
E
F
G
H


A
day0
B
day1
C
day2
D
day3
E
day4
F
day0
G
day1
H
day2
I
day3
J
day4