Poster Review

Se Kwon Jang, MD
Hyun Seok Kang, M.D.
Chang-Gyu Hahn, MD PhD
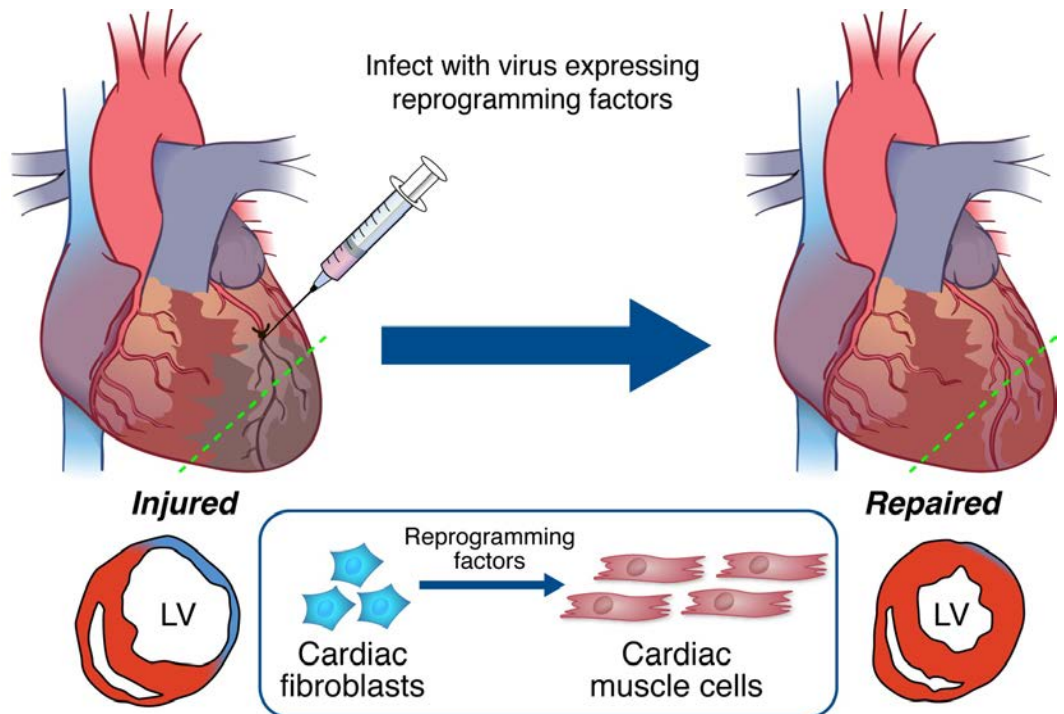Young Jae Nam, MD PhD
Jong Chul Park, M.D.
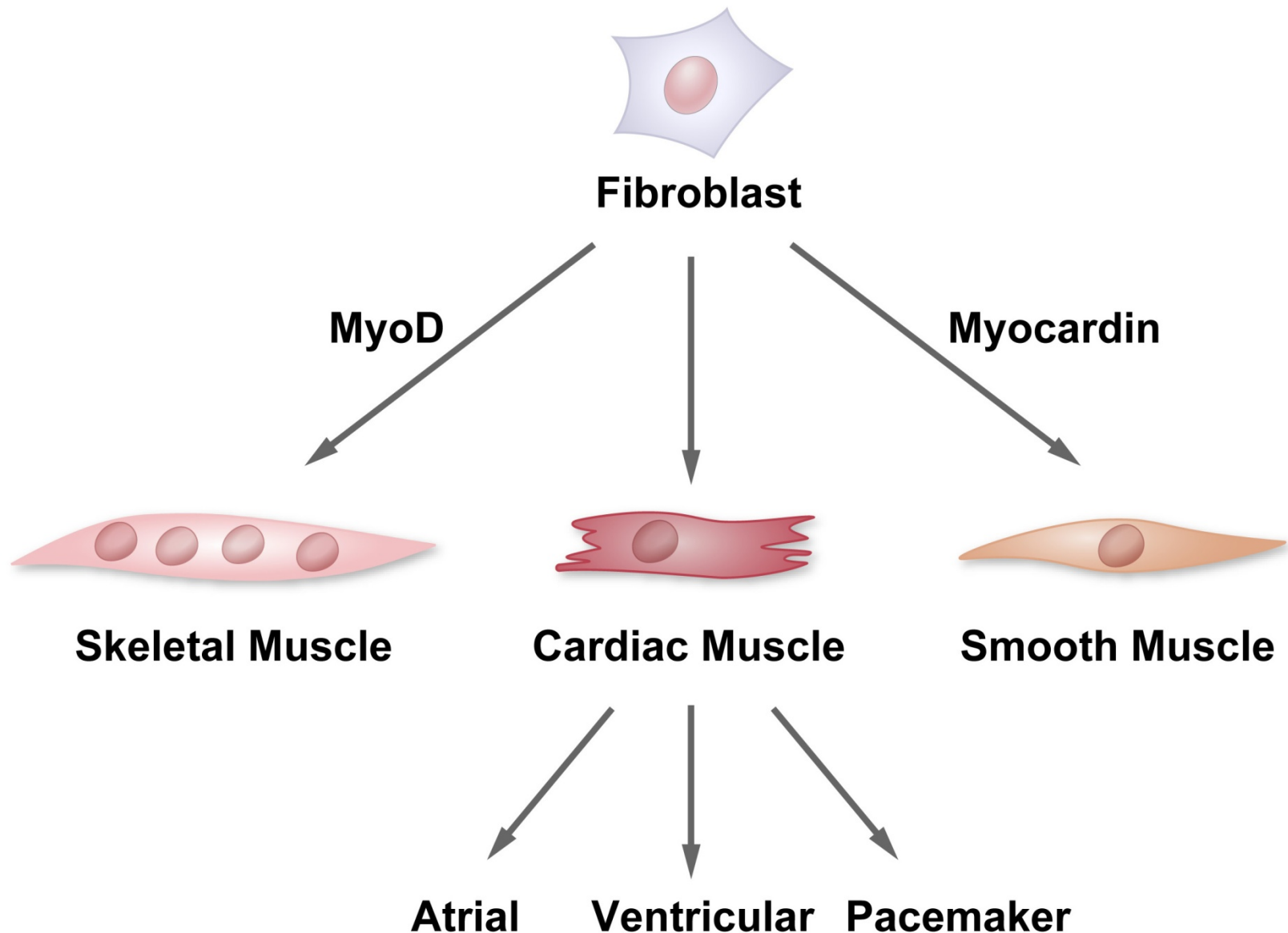
Heart Repair by Cardiomyocyte Reprogramming

Young Jae Nam, MD PhD

Infect with virus expressing reprogramming factors

Injured

Repaired

Reprogramming factors

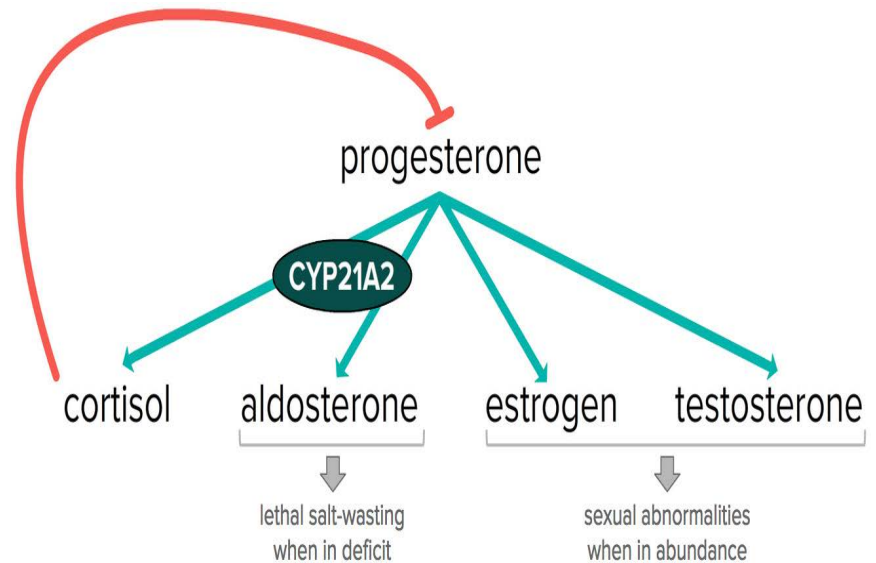Cardiac fibroblasts → Cardiac muscle cells

LV

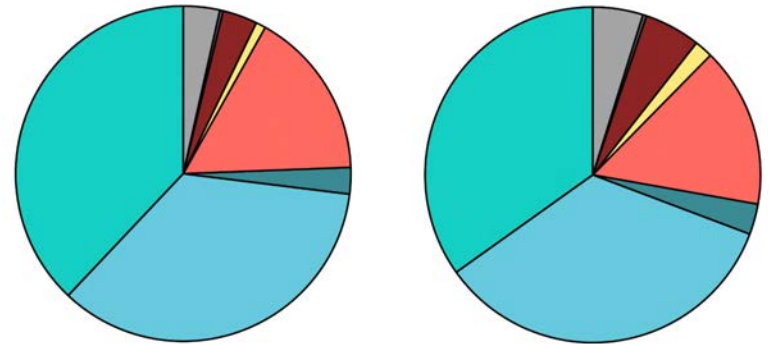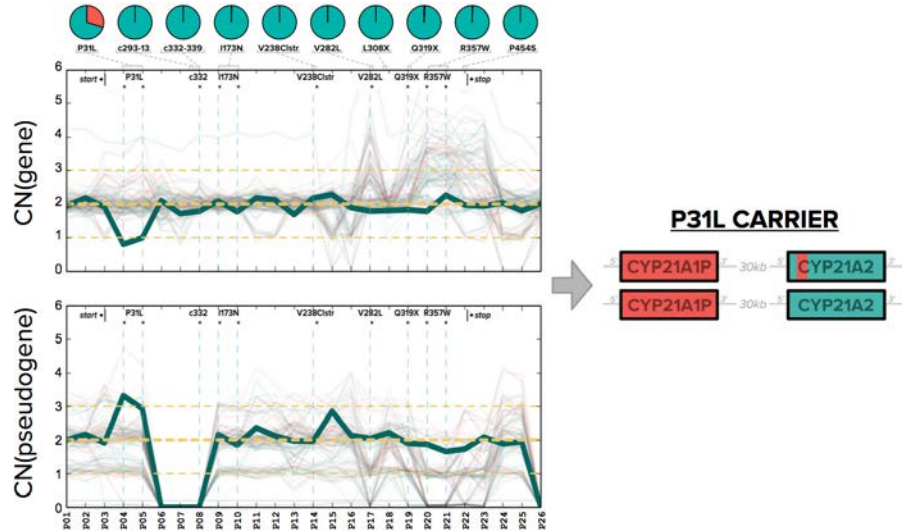# Reprogramming of Specific Cardiac Cell Fates

An NGS-based carrier screen for Congenital Adrenal Hyperplasia with 95% detection rate

Hyun Seok Kang, MD MS

An NGS-based carrier screen for Congenital Adrenal Hyperplasia with 95% detection rate

A RANDOMIZED PHASE 2 STUDY OF SIPULEUCEL-T WITH OR WITHOUT RADIUM-223 IN MEN WITH ASYMPTOMATIC OR MINIMALLY SYMPTOMATIC BONE-METASTATIC CASTRATE-RESISTANT PROSTATE CANCER
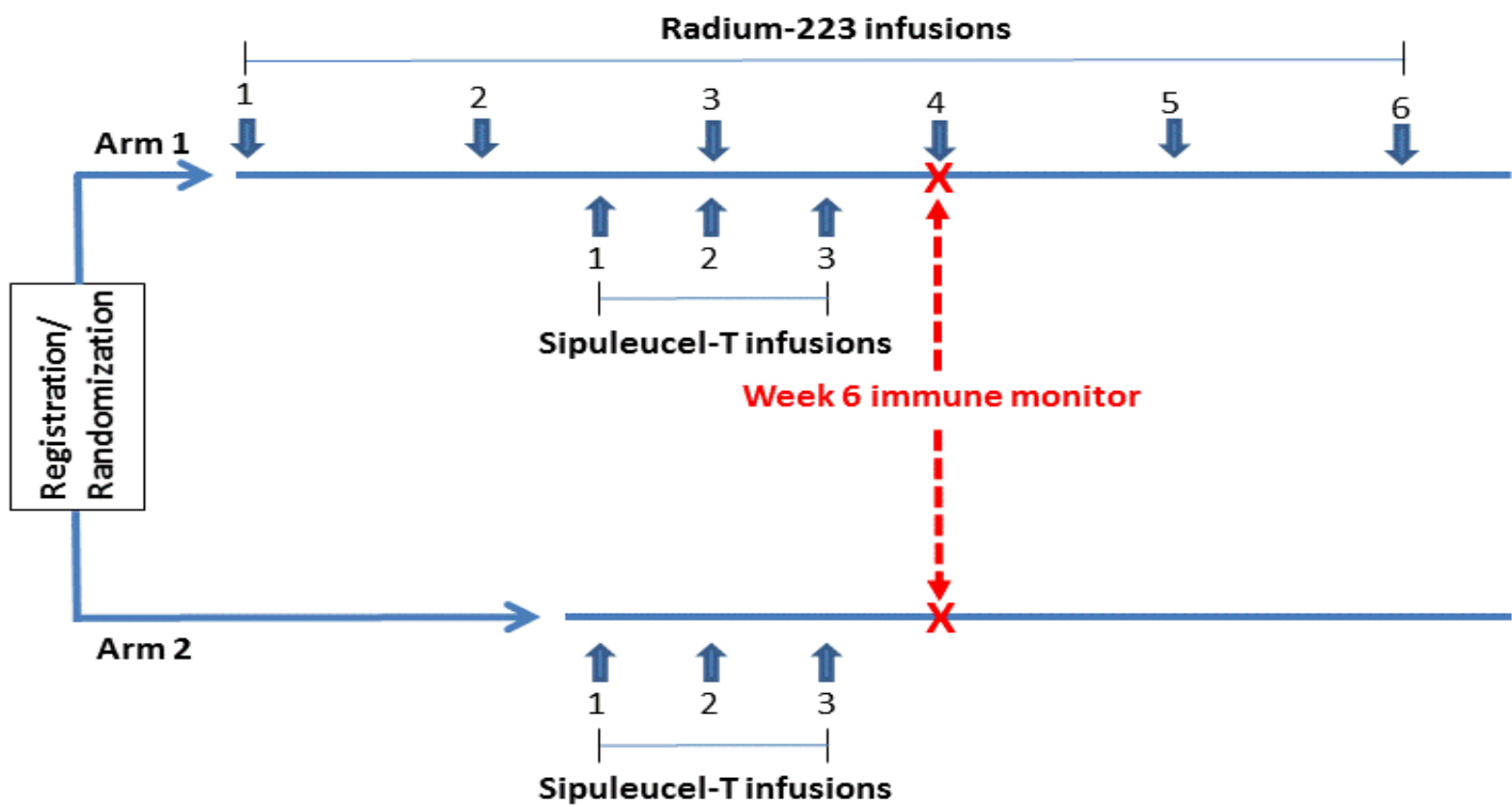
Jong Chul Park, MD

- **Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. Sipuleucel-T has shown survival benefit in patients with asymptomatic or minimally symptomatic mCRPC in phase III trials.[1]**
- **Recent analysis of immune responses in men treated with sipuleucel-T showed that antigen-specific immune responses to sipuleucel-T were correlated with improved survival, confirming the immune-based mechanism of action and suggesting the possibility that producing a stronger immune response may lead to the better clinical outcomes.[2]**
- **Radiopharmaceutical agents have been shown to enhance immune modulation through a variety of mechanisms including enhanced display of tumor-associated antigens.[3]**

A RANDOMIZED PHASE 2 STUDY OF SIPULEUCEL-T WITH OR WITHOUT RADIUM-223 IN MEN WITH ASYMPTOMATIC OR MINIMALLY SYMPTOMATIC BONE-METASTATIC CASTRATE-RESISTANT PROSTATE CANCER

- Based on the immune-modulatory effects of radiopharmaceutical agents, we hypothesized that combined use of radium-223 and sipuleucel-T may enhance the sipuleucel-T-induced immune response, translating into improved clinical outcomes.
- Since majority of patients with mCRPC have bone metastases, this approach can be widely applied to early stage of mCRPC when patients are asymptomatic or minimally symptomatic when the greatest clinical benefit can be obtained with immune-based therapies.

Radium-223 infusions

Arm 1

1 2 3 4 5 6

Registration/Randomization

Sipuleucel-T infusions

1 2 3

Week 6 immune monitor

Arm 2

1 2 3

Sipuleucel-T infusions

Cardiovascular Toxicity After Antiangiogenic Therapy in Persons Older Than 65 Years With Advanced Renal Cell Carcinoma

Se Kown Jajng, MD

VEGF inhibitor for RCCA
Therapeutic efficacy via the target
On – target adverse effects?

NIH contract
Medical records via insurance

TABLE 4. Incidence Rates of Cardiovascular Events Between the Start of Drug Use and 60 Days After the Last Dose Among Users of Sunitinib and/or Sorafenib

Event	Sunitinib or Sorafenib (n = 670)		Sunitinib Only (n = 396)		Sorafenib Only (n = 163)		Sunitinib and Sorafenib (n = 111)	
	No.	Event Rate[a]	No.	Event Rate[a]	No.	Event Rate[a]	No.	Event Rate[a]
CHF/CM	146	0.87 (0.74-1.03)	90	1.11 (0.90-1.37)	33	0.97 (0.66-1.36)	23	0.44 (0.28-0.66)
AMI	23	0.14 (0.09-0.21)	11	0.14 (0.07-0.24)	—	—	—	—
Stroke	24	0.14 (0.09-0.21)	13	0.16 (0.09-0.28)	—	—	—	—
CV death	—	—	—	—	—	—	—	—
Any event	171	1.02 (0.88-1.19)	103	1.27 (1.04-1.55)	39	1.14 (0.81-1.56)	29	0.55 (0.37-0.80)

Abbreviations: AMI, acute myocardial infarction; CHF/CM, congestive heart failure and cardiomyopathy; CV, cardiovascular-related.
Counts less than 11 were suppressed because of Surveillance, Epidemiology, and End Results-Medicare reporting policies.
[a] Incidence per 1000 person-days.

Cardiovascular Toxicity After Antiangiogenic Therapy in Persons Older Than 65 Years With Advanced Renal Cell Carcinoma

TABLE 5. HRs for Cardiovascular Events Associated With the Use of Sunitinib and Sorafenib Among Patients With Advanced Renal Cell Carcinoma

Event	Unadjusted HR (95% CI)[a]			
	Sunitinib or Sorafenib (n = 670)	Sunitinib Only (n = 396)	Sorafenib Only (n = 163)	Sunitinib and Sorafenib (n = 111)
CHF/CM	0.95 (0.61-1.49)	1.19 (0.71-2.00)	0.89 (0.32-2.42)	0.48 (0.13-1.34)
AMI	1.28 (0.57-2.88)	0.80 (0.24-2.67)	1.40 (0.33-5.98)	1.35 (0.39-4.62)
Stroke	2.68 (1.15-6.29)[b]	1.45 (0.42-5.09)	7.84 (2.70-22.75)[c]	0.86 (0.11-6.83)
CV death	0.63 (0.22-1.83)	0.59 (0.08-4.35)	1.32 (0.31-5.61)	—
Any event	1.16 (0.80-1.68)	0.52 (0.12-2.21)	1.39 (0.68-2.87)	0.58 (0.25-1.34)

Event	Adjusted HR (95% CI)[d]			
	Sunitinib or Sorafenib (n = 670)	Sunitinib Only (n = 396)	Sorafenib Only (n = 163)	Sunitinib and Sorafenib (n = 111)
CHF/CM	1.24 (0.88-1.75)	1.53 (1.01-2.33)[b]	1.36 (0.67-2.75)	0.57 (0.24-1.33)
AMI	1.65 (0.92-2.94)	1.06 (0.46-2.45)	2.40 (0.87-6.61)	1.66 (0.60-4.56)
Stroke	2.84 (1.52-5.31)[e]	2.28 (1.00-5.22)	5.30 (1.80-15.61)[e]	2.03 (0.62-6.66)
CV death	1.55 (0.71-3.40)	1.31 (0.50-3.45)	1.88 (0.56-6.33)	—
Any event	1.38 (1.02-1.87)[b]	1.48 (1.01-2.15)[b]	1.60 (0.88-2.92)	0.74 (0.38-1.45)

Abbreviations: AMI, acute myocardial infarction; CHF/CM, congestive heart failure and cardiomyopathy; CI, confidence interval; CV, cardiovascular-related; HR, hazard ratio.
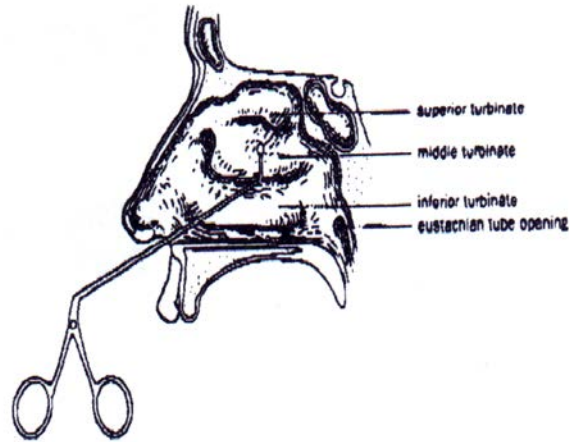[a] Censored cases on the 61st day after the last dose of the drug without adjustments.
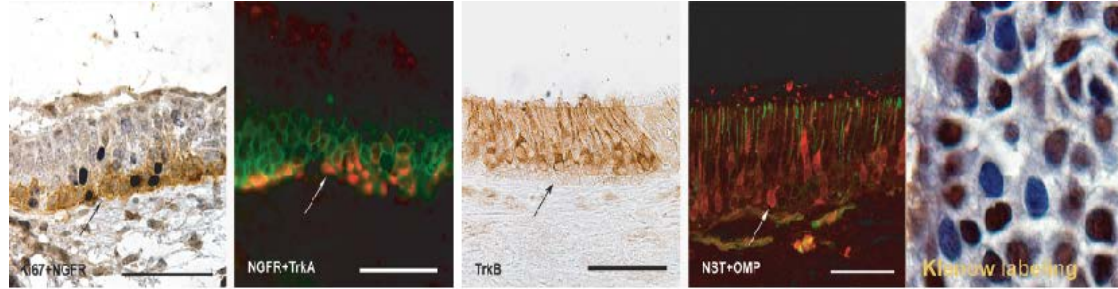[b] P <.05.
[c] P <.001.
[d] Censored cases on the 61st day after the last dose of the drug with adjustments for sex, age at diagnosis, baseline comorbidity, and use of other chemotherapy.
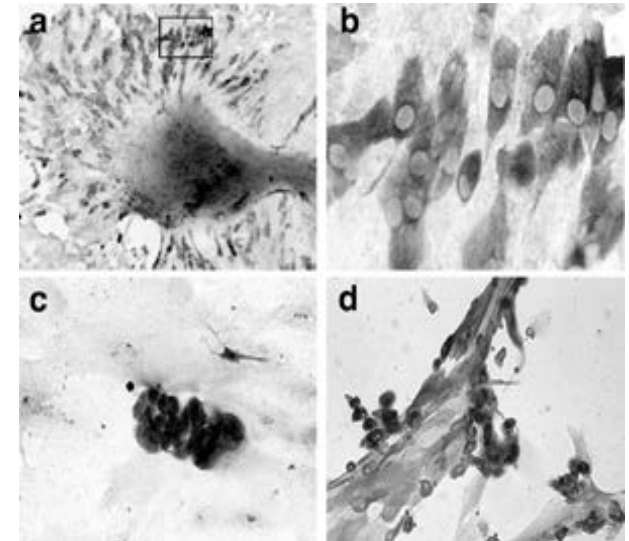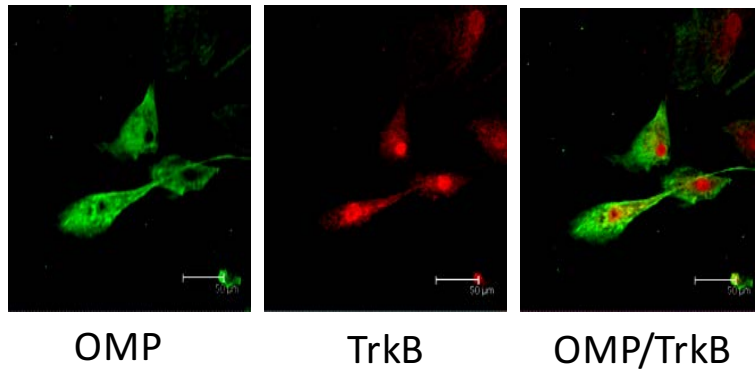[e] P <.01.

Human olfactory epithelial biopsy

superior turbinate
middle turbinate
inferior turbinate
eustachian tube opening

Tissue sections for histological examination

Ki67+NGFR   NGFR+TrkA   TrkB   N3T+OMP   Klenow labeling
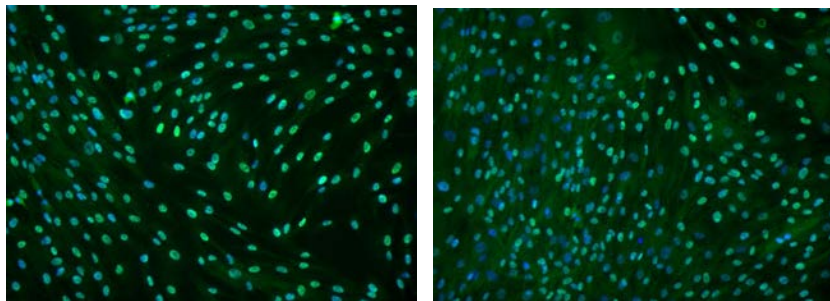
Ex-vivo tissues permit direct examination of patient-derived neurons in culture
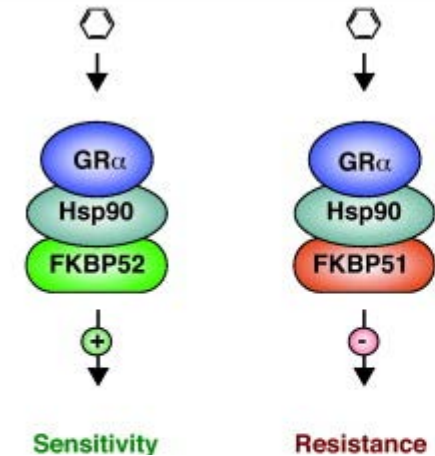

In-vitro neuroepithelial culture cells

OMP   TrkB   OMP/TrkB

Hahn 2005, Borgmann-Winter, 2009

GR translocation is impaired in MDD patients

1 µM dex 15 min

Ctrl   MDD

Sensitivity   Resistance

GR Translocation

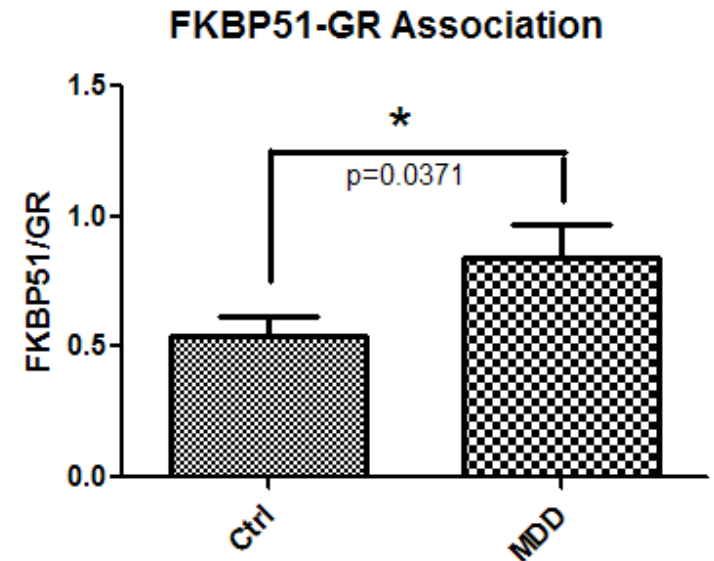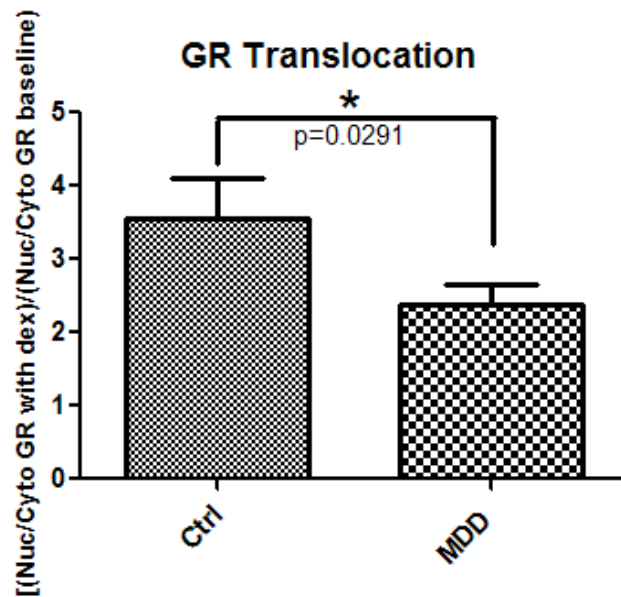FKBP51-GR Association

Nose as a Translational Bridge

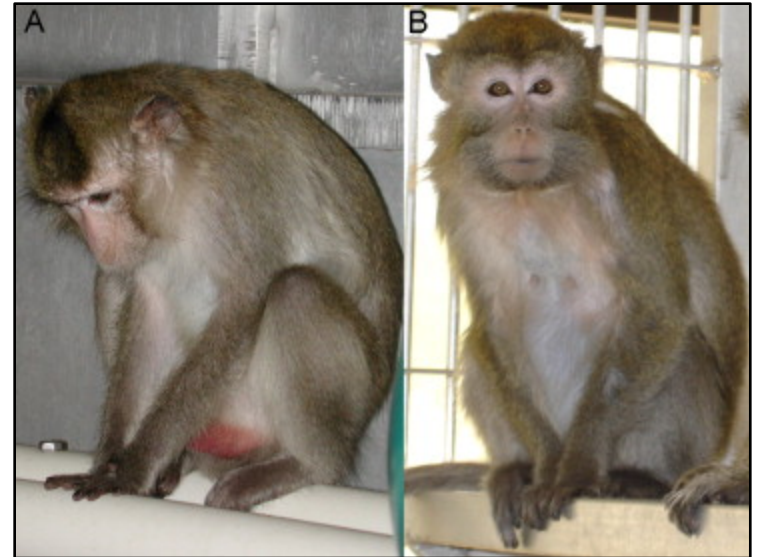Nose   →   Brain

Molecules   ->   Behaviors

Behavioral Depression

- Some adult female monkeys display behavior like human depression

- **Behavioral Depression**: Defined as a slumped/ collapsed body posture with eyes open and unresponsive to environmental stimuli (Suomi et al., 1975)

A. Depressed monkey; **B**. Alert monkey
Figure 1, Willard et al., 2009

Shively et al., 1997; 2002; 2005; 2006; 2009; 2011; Willard & Shively 2011
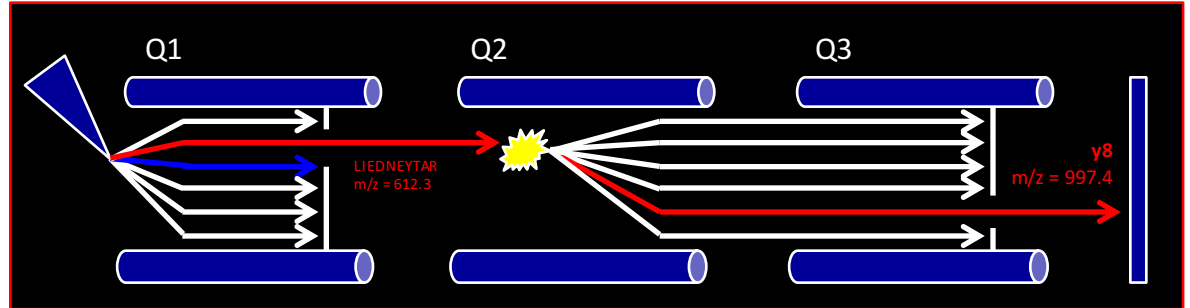
LC-SRM / MS

Practical application

src

MGSNKSKPKD ASQRRRSLEP SENVHGAGGA FPASQTPSKP ASADGHRGPS AAFVPPAAEP
KLFGGFNSSD TVTSPQRAGP LAGGVTTFVA LYDYESRTET DLSFKKGERL QIVNNTRKVD
VREGDW WLAH SLSTGQTGYI PSNYVAPSDS IQAEEW YFGK ITRRESERLL LNAENPRGTF
LVRESETTKG AYCLSVSDFD NAKGLNVKHY KIRKLDSGGF YITSRTQFNS LQQLVAYYSK
HADGLCHRLT TVCPTSKPQT QGLAKDAW EI PRESLRLEVK LGQGCFGEVW MGTWNGTTRV
AIKTLKPGTM SPEAFLQEAQ VMKKLRHEKL VQLYAVVSEE PIYIVTEYMN KGSLLDFLKG
ETGKYLRLPQ LVDMSAQIAS GMAYVERMNY VHRDLRAANI LVGENLVCKV ADFGLAR**LIE
DNEYTAR**QGA KFPIKW TAPE AALYGRFTIK SDVW SFGILL TELTTKGRVP YPGMVNREVL
DQVERGYRMP CPPECPESLH DLMCQCW RKE PEERPTFEYL QAFLEDYFTS TEPQYQPGEN

Peptide
database

LIEDNEYTAR

LC-SRM / MS

Practical application

src

MGSNKSKPKD ASQRRRSLEP SENVHGAGGA FPASQTPSKP ASADGHRGPS AAFVPPAAEP
KLFGGFNSSD TVTSPQRAGP LAGGVTTFVA LYDYESRTET DLSFKKGERL QIVNNTRKVD
VREGDWWLAH SLSTGQTGYI PSNYVAPSDS IQAEEWYFGK ITRRESERLL LNAENPRGTF
LVRESETTKG AYCLSVSDFD NAKGLNVKHY KIRKLDSGGF YITSRTQFNS LQQLVAYYSK
HADGLCHRLT TVCPTSKPQT QGLAKDAWEI PRESLRLEVK LGQGCFGEVW MGTWNGTTRV
AIKTLKPGTM SPEAFLQEAQ VMKKLRHEKL VQLYAVVSEE PIYIVTEYMN KGSLLDFLKG
ETGKYLRLPQ LVDMSAQIAS GMAYVERMNY VHRDLRAANI LVGENLVCKV ADFGLAR**LIE
DNEYTAR**QGA KFPIKWTAPE AALYGRFTIK SDVWSFGILL TELTTKGRVP YPGMVNREVL
DQVERGYRMP CPPECPESLH DLMCQCWRKE PEERPTFEYL QAFLEDYFTS TEPQYQPGEN

Peptide database

LIEDNEYTAR

ITMS + c NSI Full ms2 612.30@cid25.00

100

MH-H2O+2

50

B7-2H2O-NH3

y1
a1 b2 y2
v3
b3 b4 y8+2 b ;
y4 y9-NH3+2
y8;
b6;
y6
y7
b7
b8 b9 y9

0

400   **m/z**   800   1200

Relative Abundance

Q1   Q2   Q3

LIEDNEYTAR
m/z = 612.3

y8
m/z = 997.4

LIEDNEYTAR