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Supplemental Information

A Direct Comparison of IV and ICV Delivery Methods for Gene Replacement Therapy in a Mouse Model of SMARD1

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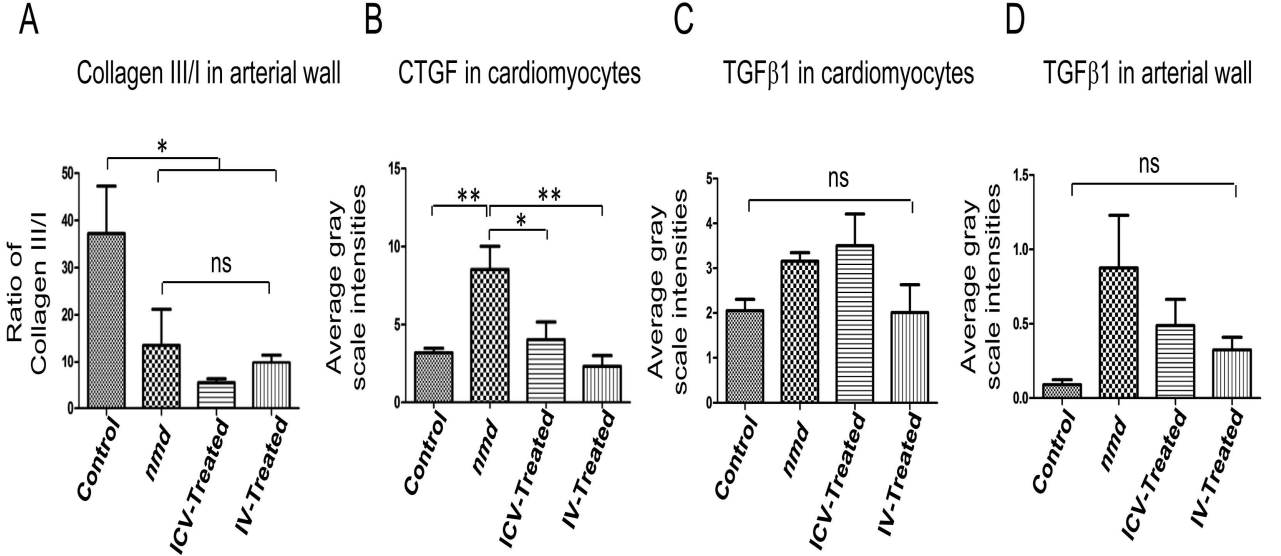
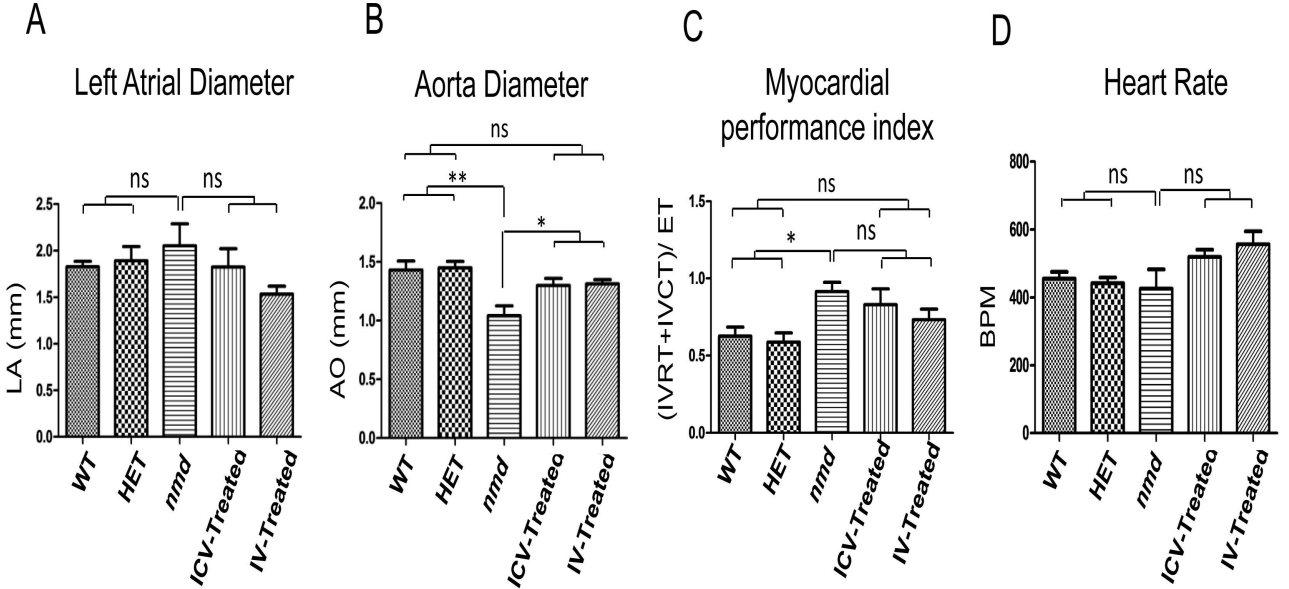

A
Collagen III/I in arterial wall
Ratio of Collagen III/I
50
40
30
20
10
0
*
ns
Control
nmd
ICV-Treated
IV-Treated
B
CTGF in cardiomyocytes
Average gray scale intensities
15
10
5
0
**
**
*
Control
nmd
ICV-Treated
IV-Treated
C
TGFβ1 in cardiomyocytes
Average gray scale intensities
5
4
3
2
1
0
ns
Control
nmd
ICV-Treated
IV-Treated
D
TGFβ1 in arterial wall
Average gray scale intensities
1.5
1.0
0.5
0.0
ns
Control
nmd
ICV-Treated
IV-Treated


A
Left Atrial Diameter
LA (mm)
ns
ns
2.5
2.0
1.5
1.0
0.5
0.0
WT
HET
nmd
ICV-Treated
IV-Treated
B
Aorta Diameter
AO (mm)
ns
**
*
2.0
1.5
1.0
0.5
0.0
WT
HET
nmd
ICV-Treated
IV-Treated
C
Myocardial performance index
(IVRT+IVCT)/ ET
ns
*
ns
1.5
1.0
0.5
0.0
WT
HET
nmd
ICV-Treated
IV-Treated
D
Heart Rate
BPM
ns
ns
800
600
400
200
WT
HET
nmd
ICV-Treated
IV-Treated

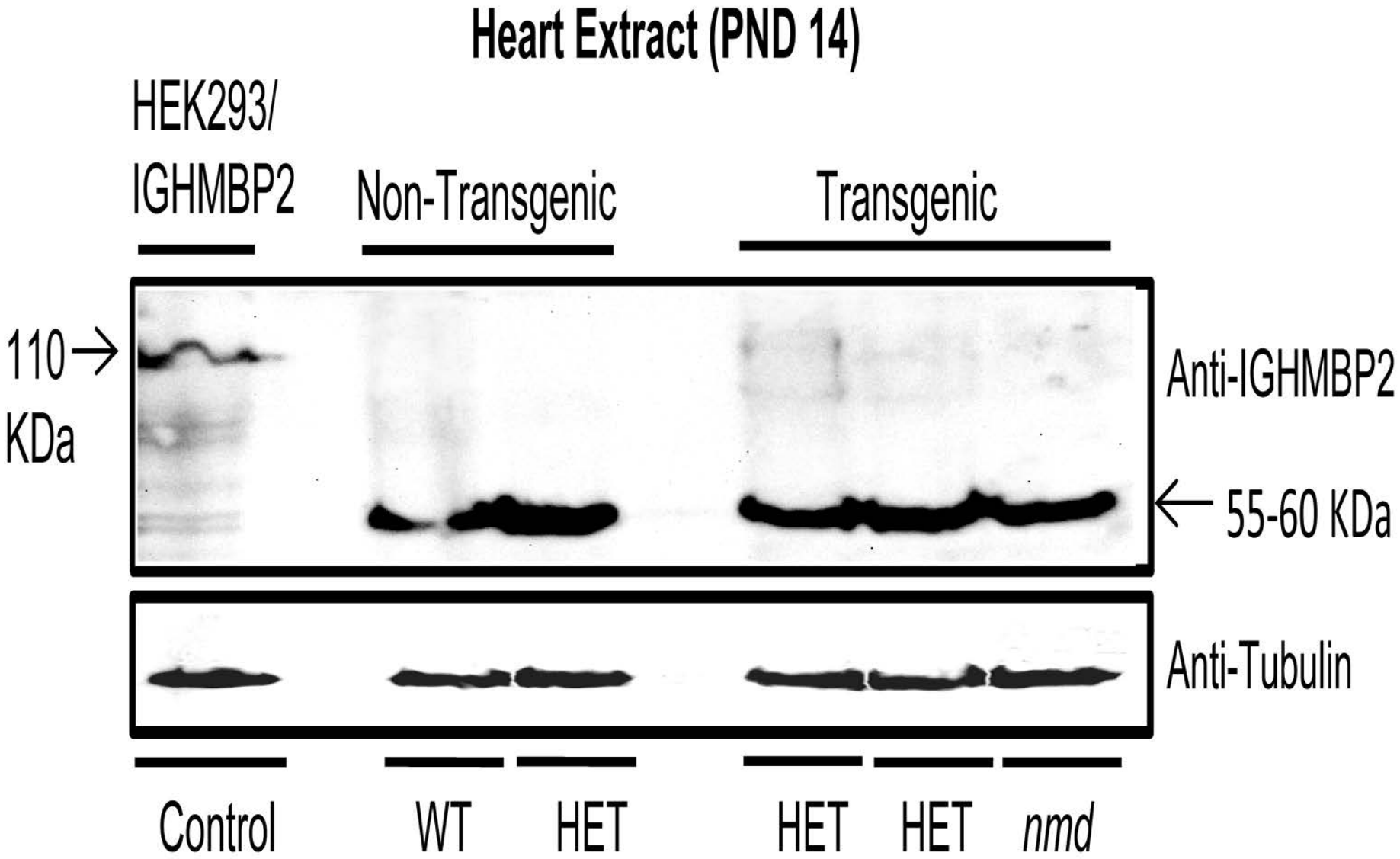

Heart Extract (PND 14)
HEK293/
IGHMBP2
Non-Transgenic
Transgenic
110→
KDa
Anti-IGHMBP2
← 55-60 KDa
Anti-Tubulin
Control
WT
HET
HET
HET
nmd

Figure S1. Expression levels of ECM proteins and growth factors in Cardiomyocytes and arteries of *nmd* heart. (**A**) Ratio of collagen III/I in arteries (one-way ANOVA unaffected control vs. *nmd*, IV, and ICV treated, $P< 0.05$); (**B**) Expression of CTGF in cardiomyocytes (one-way ANOVA IV-treated vs. *nmd*, $P<0.01$; ICV-treated vs. *nmd*, $P<0.05$) (**C**, **D**) expression of TGFβ in cardiomyocytes (**C**) and arteries (**D**). The levels of TGFβ are not significantly different between the cohorts.

Figure S2. Functional parameters of *nmd* heart. (**A**) Left atrial diameter; (**B**) Aorta diameter; (**C**) Myocardial performance index (one-way ANOVA controls vs. *nmd*, $P<0.05$); (**D**) Heart rate. BPM (beat per minute).

Figure S3. **Expression level of IGHMBP2 in cardiac rescue transgenic *nmd*.** Western blot with the heart extracts of non-transgenic and cardiac rescue transgenic *nmd* detects a low expression of IGHMBP2 in transgenic heart. HEK 293 cells transfected with IGHMBP2 construct was used as size control and anti-tubulin was used as loading control.