A

Passage 3-5 (n = 3)

Culture medium

Culture medium + daily 1 μM H_2O_2 (3 days)

mRNA analysis after 3 days (80% confluence)

Relative mRNA expression

55
45
35
7
6
4
2
0

Bmi1 Hif1α p16^{ink4a} p19^{inkb} Gata4 Duox1 Lpo Noxa Pouf5f1 Sox2 C-myc αSMA cd146 Myh6 Tnnt2 Tnnt3

Bmi1 targets | Stemness | Differentiation

- H_2O_2
+ H_2O_2

** * ** * ** ** ** * * * ** **

B

TM

-8 +0 +5

RT-qPCR (+5)

Relative Bmi1 mRNA
4
2
0

Non-myocyte IR non-myocyte CM IR CM Control

WB (+5)

BMI1 (37 kDa)
Tubulin (50 kDa)

C

Bmi1$^{GFP/+}$ mice

WT

Tomato

GFP

Homeostasis
9Gy
20Gy

GFP-gated population (%)
14
12
10
8
6
4
2
0

Homeo 20Gy 9Gy Homeo 9Gy

5 days | 4 months

** *

D

IPA predicted pathways affected (BMI1)

Top Canonical Pathways

Name	p-value	Overlap	
cAMP-mediated signaling	1.33E-05	11.2 %	24/214
G-Protein Coupled Receptor Signaling	2.44E-05	10.2 %	27/266
nNOS Signaling in Skeletal Muscle Cells	1.94E-04	35.7 %	5/14
Amyotrophic Lateral Sclerosis Signaling	2.00E-04	12.8 %	14/109
Melatonin Signaling	5.41E-04	14.7 %	10/68

IPA predicted pathways affected (H2Aub)

Top Canonical Pathways

Name	p-value	Overlap	
Axonal Guidance Signaling	6.73E-07	7.3 %	32/438
Leukocyte Extravasation Signaling	5.70E-05	8.3 %	17/204
Protein Kinase A Signaling	1.11E-04	6.5 %	24/370
Gap Junction Signaling	2.09E-04	8.5 %	14/165
G12/13 Signaling	2.17E-04	9.4 %	12/127

E

DAPI DHE

Bmi1$^{-/+}$

Bmi1$^{-/+}$ G6PD^{tg}

Fluorescence intensity [RU]
1
0

Bmi1$^{+/-}$ Bmi1$^{+/-}$ G6PD^{tg}

*