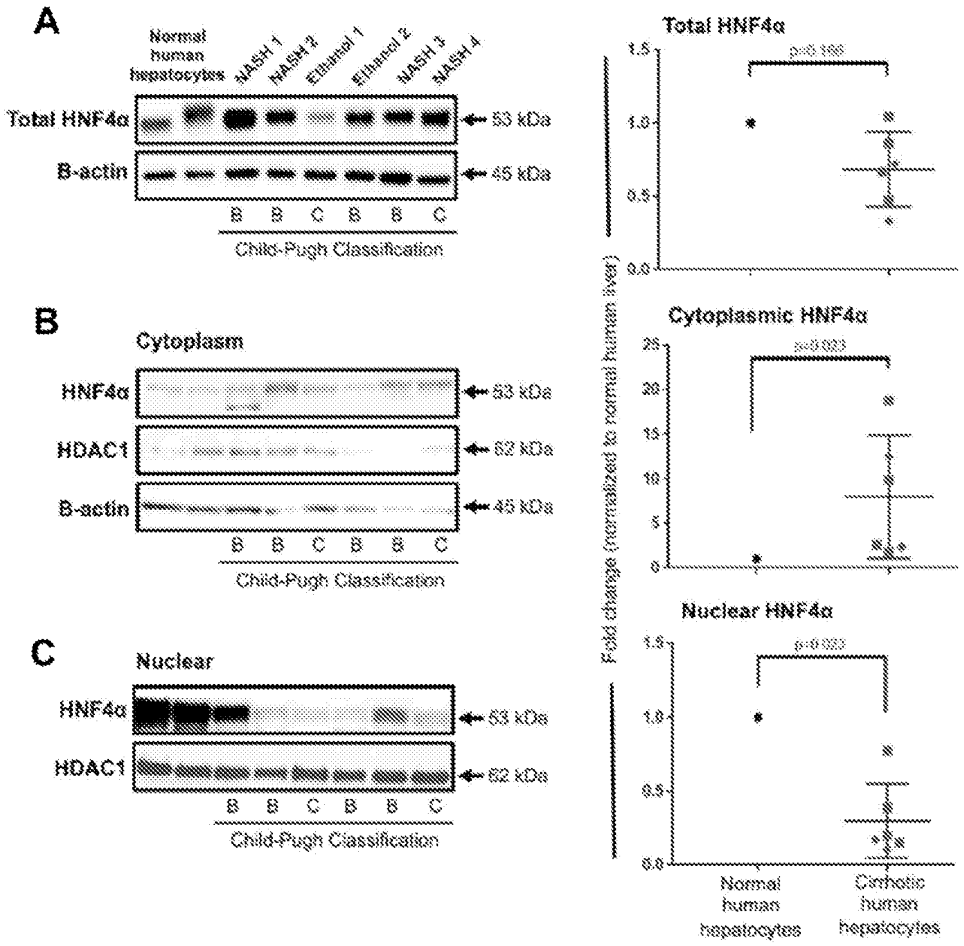


Figures 1A-1C

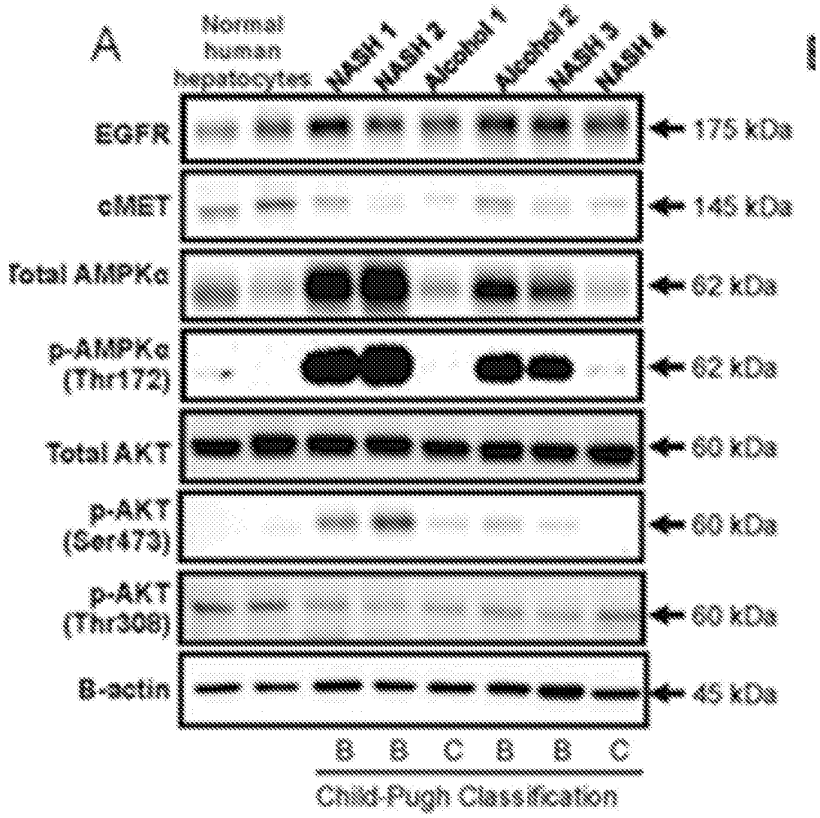

A
Normal human hepatocytes
NASH 1
NASH 2
Alcohol 1
Alcohol 2
NASH 3
NASH 4
EGFR
cMET
Total AMPKα
p-AMPKα (Thr172)
Total AKT
p-AKT (Ser473)
p-AKT (Thr308)
β-actin
175 kDa
145 kDa
62 kDa
62 kDa
60 kDa
60 kDa
60 kDa
45 kDa
B B C B B C
Child-Pugh Classification

Figure 2A

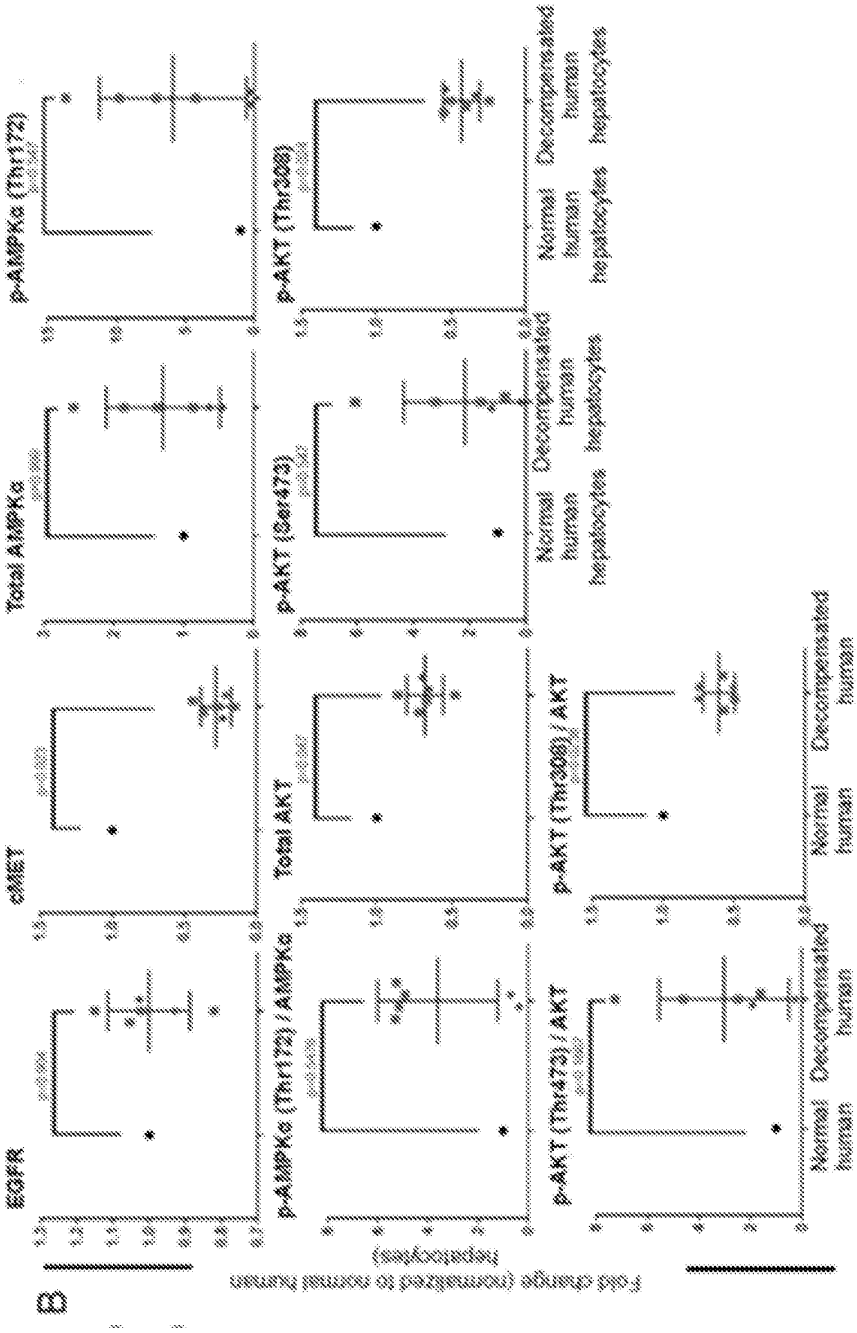

B
EGFR
cMET
p-AMPKα (Thr172) / AMPKα
Total AMPKα
p-AKT (Thr473) / AKT
Total AKT
p-AKT (Thr308) / AKT
p-AKT (Ser473)
p-AMPKα (Thr172)
p-AKT (Thr308)
Normal human hepatocytes
Decompensated human hepatocytes
Fold change (normalized to normal human hepatocytes)

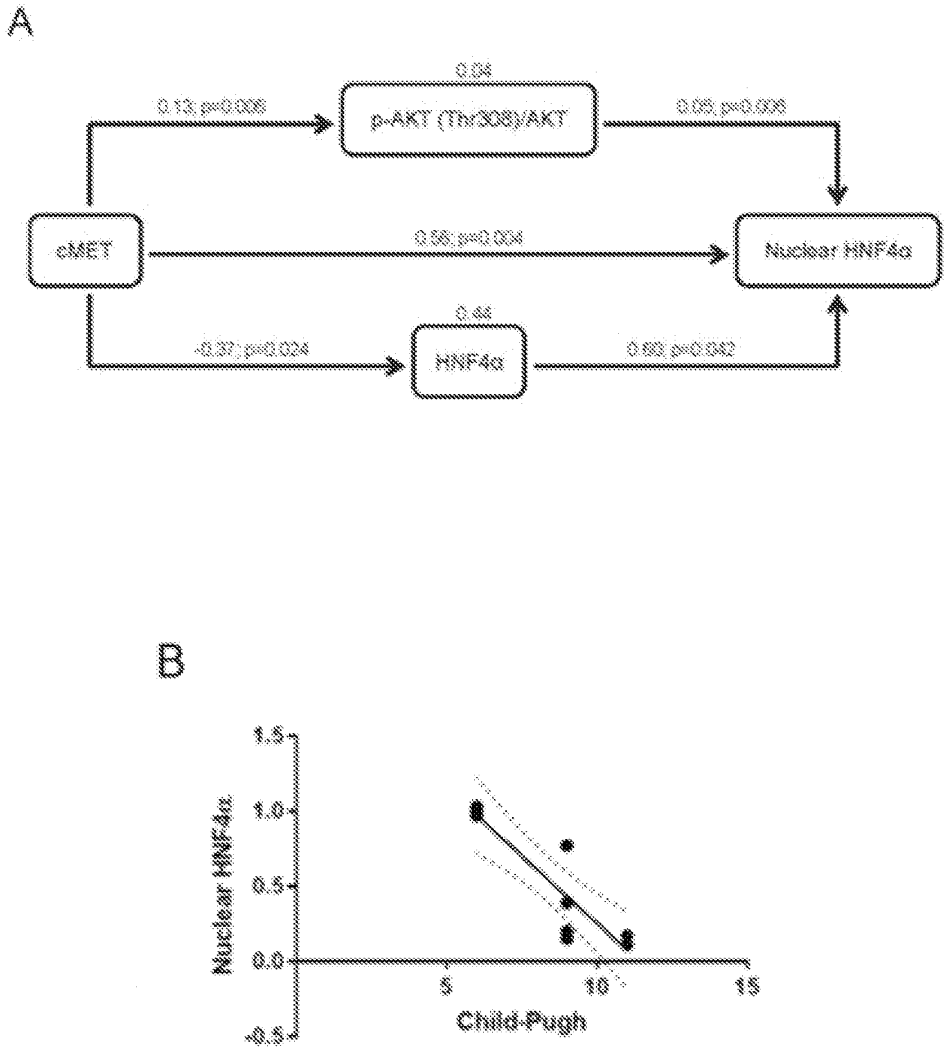
Figure 2B

C

TABLE 2. Spearman correlation to HNF4α.

Genes	HNF4α		Cytoplasmatic HNF4α		Nuclear HNF4α	
	r	p-values	r	p-values	r	p-values
HNF4α			-0.67	0.059	0.67	0.059
Cytoplasmatic HNF4α	-0.67	0.059			-0.62	0.086
Nuclear HNF4α	0.67	0.059	-0.62	0.086		
EGFR	0.43	0.250	-0.12	0.776	-0.27	0.493
cMET	**0.76**	**0.021**	**-0.80**	**0.014**	**0.71**	**0.037**
Total AMPKα	0.45	0.230	-0.18	0.644	0.25	0.521
p-AMPKα (Thr172)	0.25	0.521	0.22	0.581	0.22	0.744
p-AMPKα (Thr172)/AMPK	0.25	0.521	0.22	0.581	0.13	0.744
Total AKT	**0.88**	**0.003**	**-0.73**	**0.031**	0.65	0.067
p-AKT (Ser473)	0.35	0.359	-0.13	0.744	-0.20	0.613
p-AKT (Ser473)/AKT	0.02	0.982	0.18	0.194	-0.38	0.644
p-AKT (Thr308)	**0.73**	**0.031**	**-0.77**	**0.021**	**0.82**	**0.011**
p-AKT (Thr308)/AKT	0.62	0.086	**-0.72**	**0.037**	**0.73**	**0.031**

Figure 2C



Figures 3A and 3B

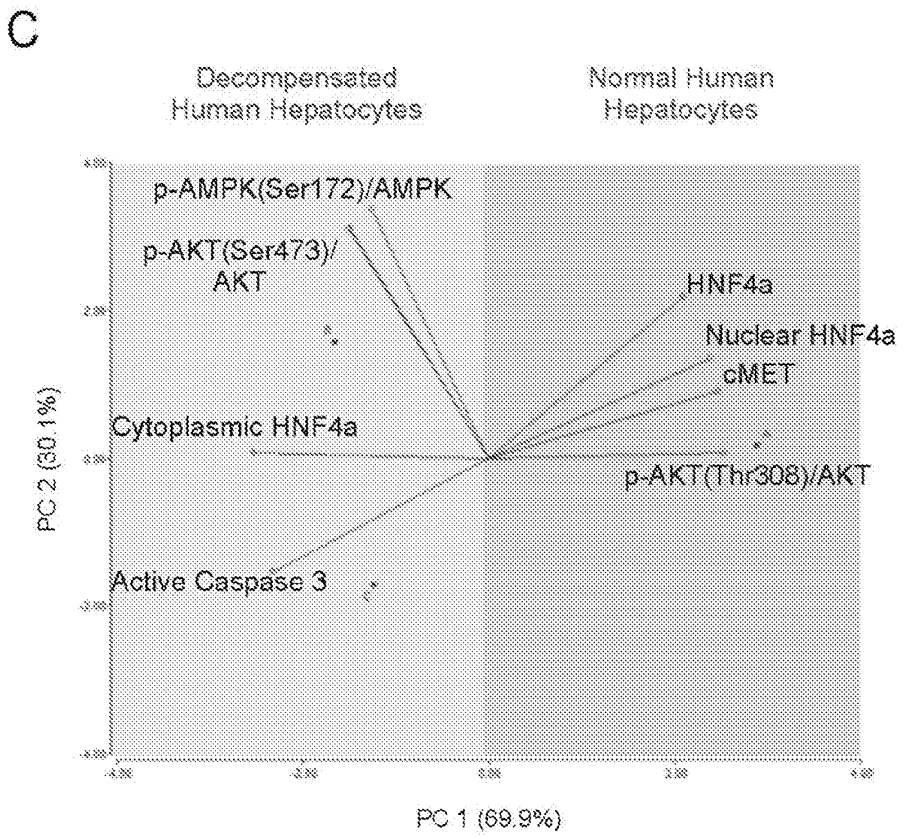

C
Decompensated Human Hepatocytes
Normal Human Hepatocytes
p-AMPK(Ser172)/AMPK
p-AKT(Ser473)/ AKT
HNF4a
Nuclear HNF4a
cMET
Cytoplasmic HNF4a
p-AKT(Thr308)/AKT
Active Caspase 3
PC 2 (30.1%)
PC 1 (69.9%)

Figure 3C

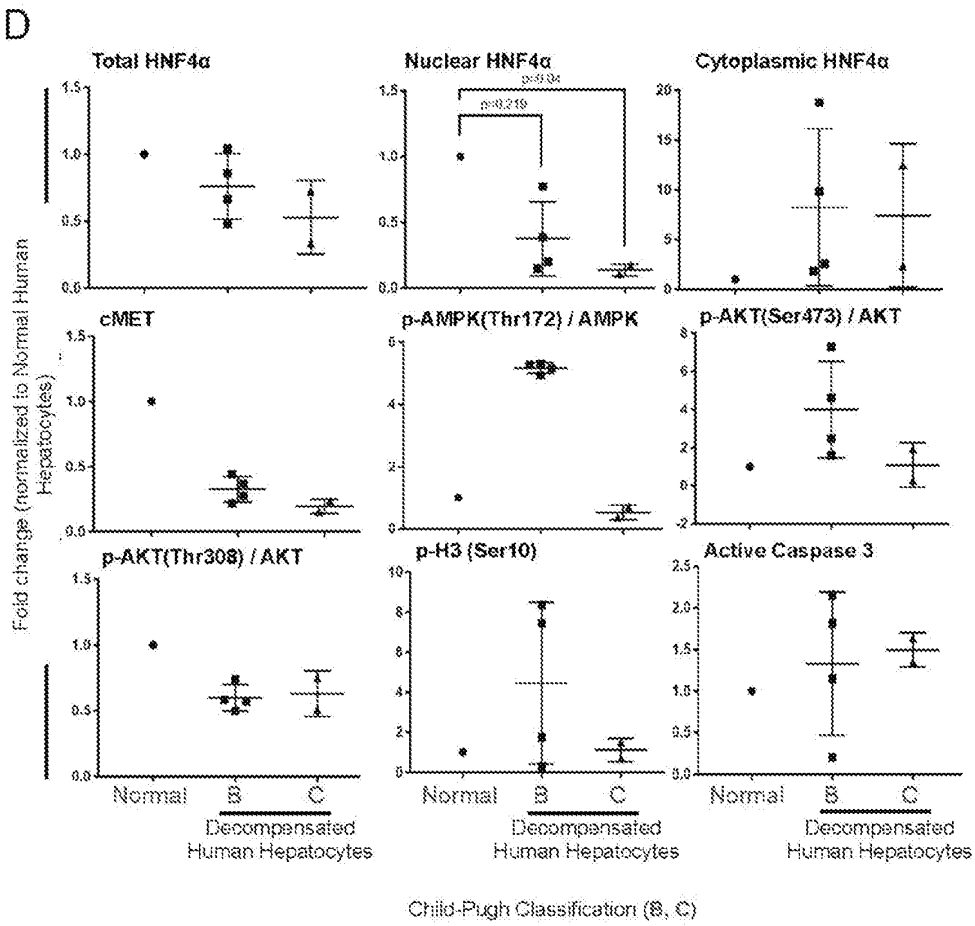
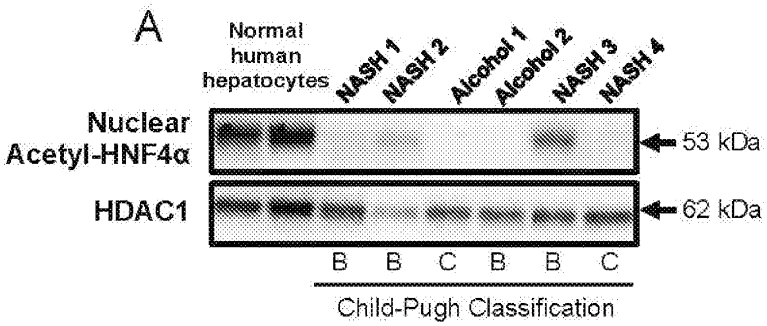
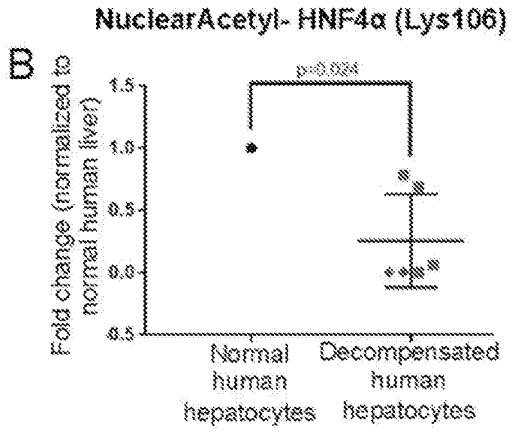
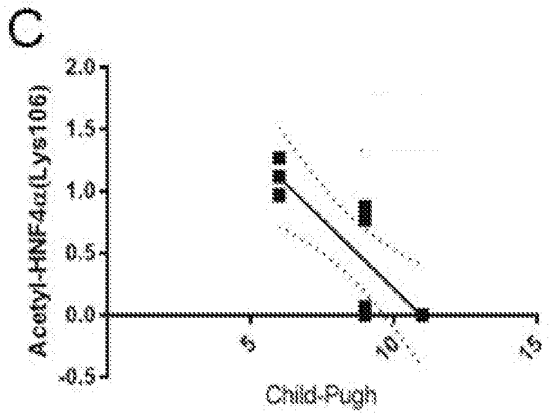

D
Total HNF4α
Nuclear HNF4α
Cytoplasmic HNF4α
cMET
p-AMPK(Thr172) / AMPK
p-AKT(Ser473) / AKT
p-AKT(Thr308) / AKT
p-H3 (Ser10)
Active Caspase 3
Fold change (normalized to Normal Human Hepatocytes)
Normal
B
C
Decompensated Human Hepatocytes
Child-Pugh Classification (B, C)

Figure 3D







Figures 4A-4C

PTM	Localization	Function	Reference
Phosphorylation	Y14	Reduced transactivation	22308320
	S78	Reduced transactivation	17389749
	S87	Decreases DNA binding	17389749
	S133	Decreases DNA binding	26302721
	S134	Decreases DNA binding	28196117
	S142	Transcriptional Inhibition	28196117
	S143	Transcriptional Inhibition	28196117
	S158	Stabilizes DNA binding and transactivation	16351573
	T166	Transcriptional Inhibition	21708125
	S167	Transcriptional Inhibition	17603092
	Y277	Decreases DNA binding	22308320
	Y279	Decreases DNA binding	22308320
	Y286	Transcriptional Inhibition	27709008
	T288	Transcriptional Inhibition	22308320
	S304	**Reduced binding and dimerization**	12740371
	S313	**Transcriptional Inhibition**	12740371
Acetylation	**K106**	**Stabilizes DNA Binding**	10882110
	K458	Transcriptional Inhibition	21708125
Sumoylation	K365	Protein Stability	22505616
	D367	Protein Stability	22505616
Ubiquitination	K234	Protein degradation	25700366
	K307	Protein degradation	25700366
	K309	Protein degradation	25700366

Figure 5

A

SUPPLEMENTARY TABLE 2. Spearman correlation to P-AKT (Thr308)/AKT.

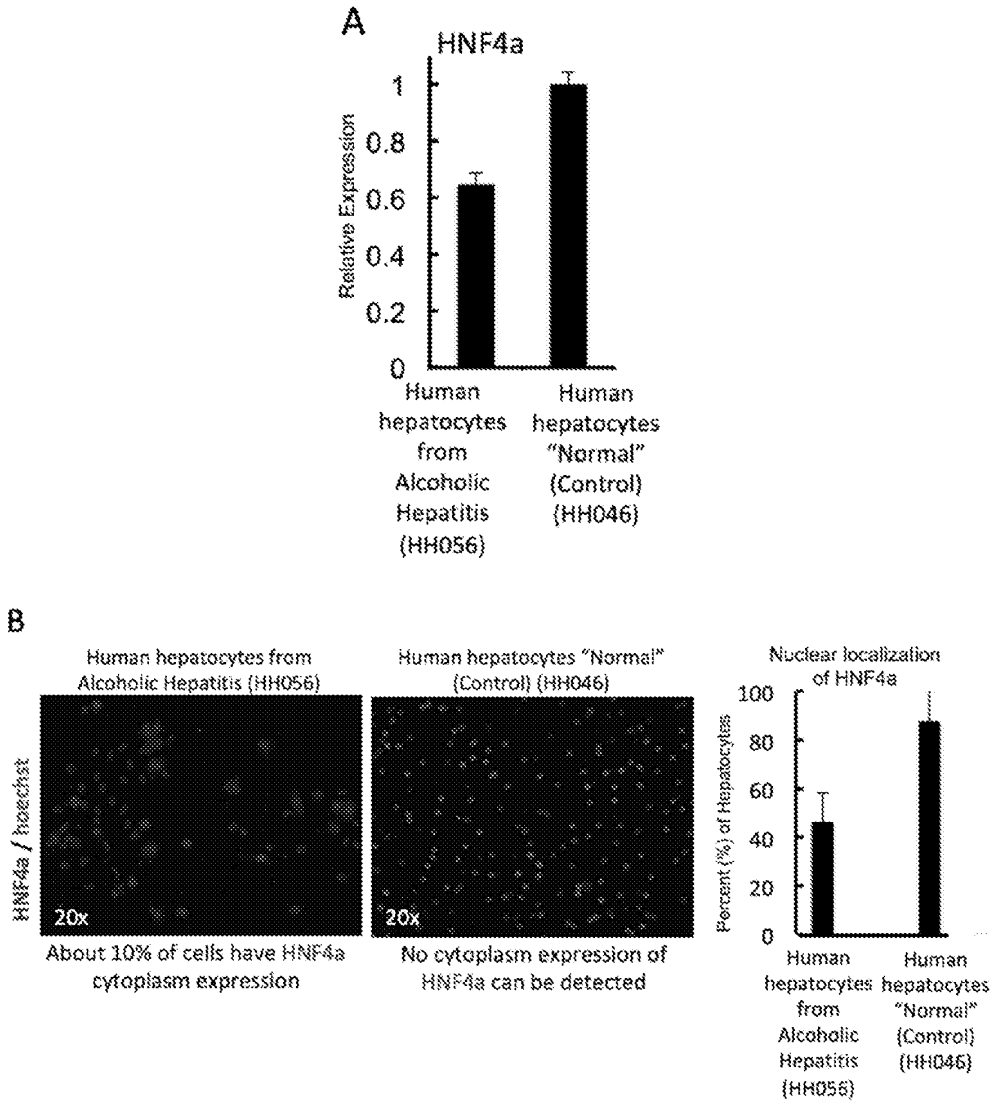
Genes	p-AKT (Thr308)/AKT	
	r	p-values
EGFR	0.02	0.982
cMET	**0.80**	**0.014**
Total AMPKα	0.08	0.843
p-AMPKα (Thr172)	-0.20	0.613
p-AMPKα (Thr172)/AMPK	-0.20	0.613
Total AKT	**0.71**	**0.037**
p-AKT (Ser473)	-0.32	0.410
p-AKT (Ser473)/AKT	-0.41	0.086

B

SUPPLEMENTARY TABLE 3. Spearman correlation to P-AKT (Ser473)/AKT.

Genes	p-AKT (Ser473)/AKT	
	r	p-values
EGFR	0.23	0.56
cMET	-0.36	0.35
Total AMPKα	**0.93**	**<0.0001**
p-AMPKα (Thr172)	**0.94**	**<0.0001**
p-AMPKα (Thr172)/AMPK	**0.71**	**0.032**
Total AKT	-0.04	0.919
p-AKT (Thr308)	-0.32	0.394
p-AKT (Thr308)/AKT	-0.41	0.268

Figures 6A-6B



Figures 7A-7B

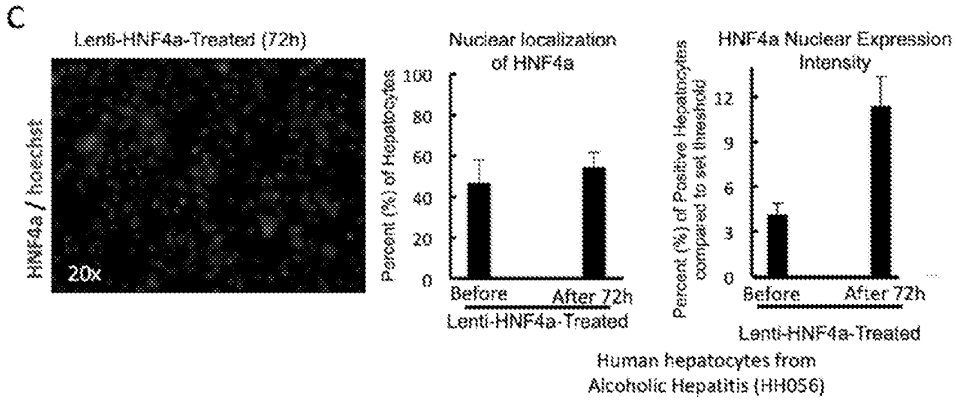

C
Lenti-HNF4a-Treated (72h)
HNF4a / hoechst
20x
Nuclear localization of HNF4a
Percent (%) of Hepatocytes
100
80
60
40
20
0
Before
After 72h
Lenti-HNF4a-Treated
HNF4a Nuclear Expression Intensity
Percent (%) of Positive Hepatocytes compared to set threshold
12
9
6
3
0
Before
After 72h
Lenti-HNF4a-Treated
Human hepatocytes from Alcoholic Hepatitis (HH056)

Figure 7C

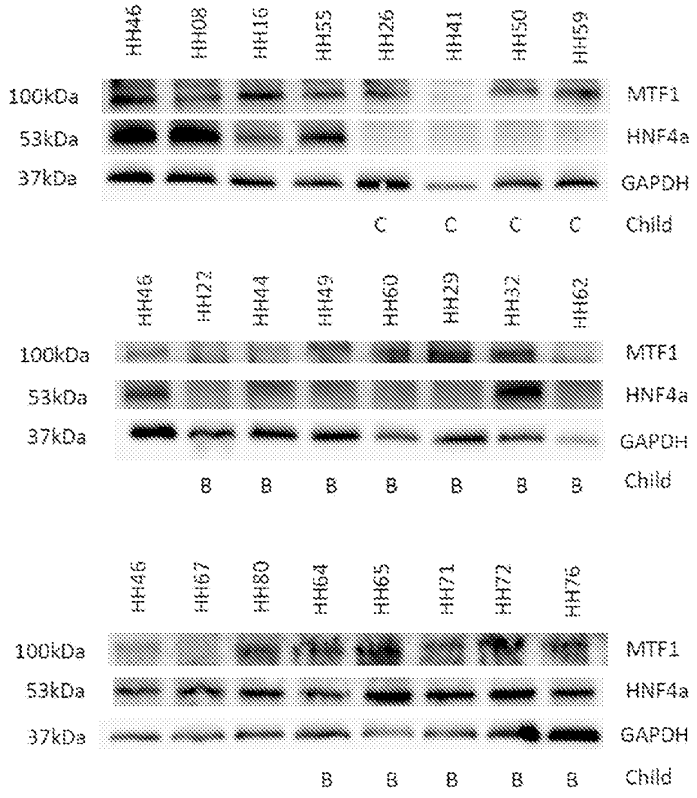
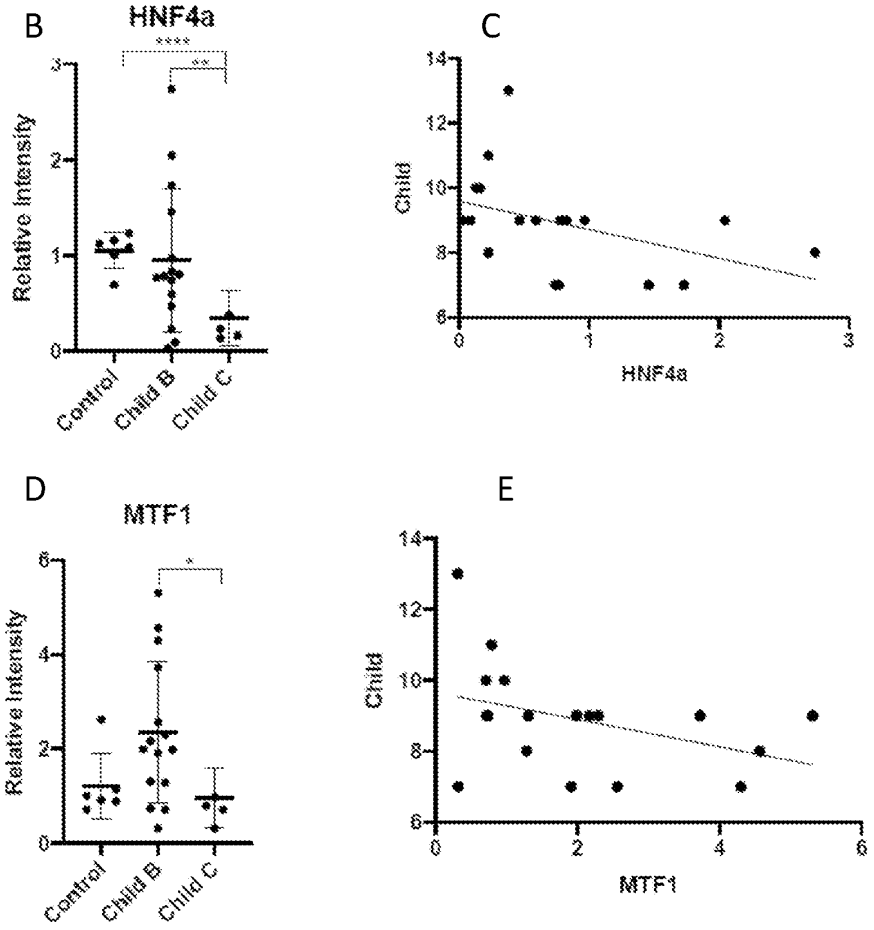

HH46
HH08
HH16
HH55
HH26
HH41
HH50
HH59
100kDa
53kDa
37kDa
MTF1
HNF4a
GAPDH
C C C C
Child
HH46
HH22
HH44
HH49
HH60
HH29
HH32
HH62
100kDa
53kDa
37kDa
MTF1
HNF4a
GAPDH
B B B B B B B
Child
HH46
HH67
HH80
HH64
HH65
HH71
HH72
HH76
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53kDa
37kDa
MTF1
HNF4a
GAPDH
B B B B B
Child

Figure 8A



Figures 8B-8E

F

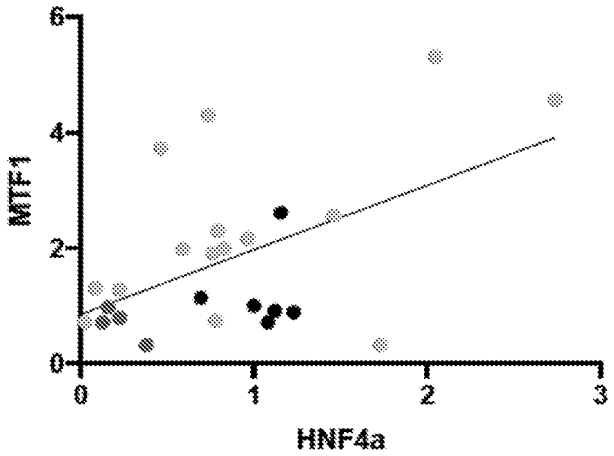


Figure 8F

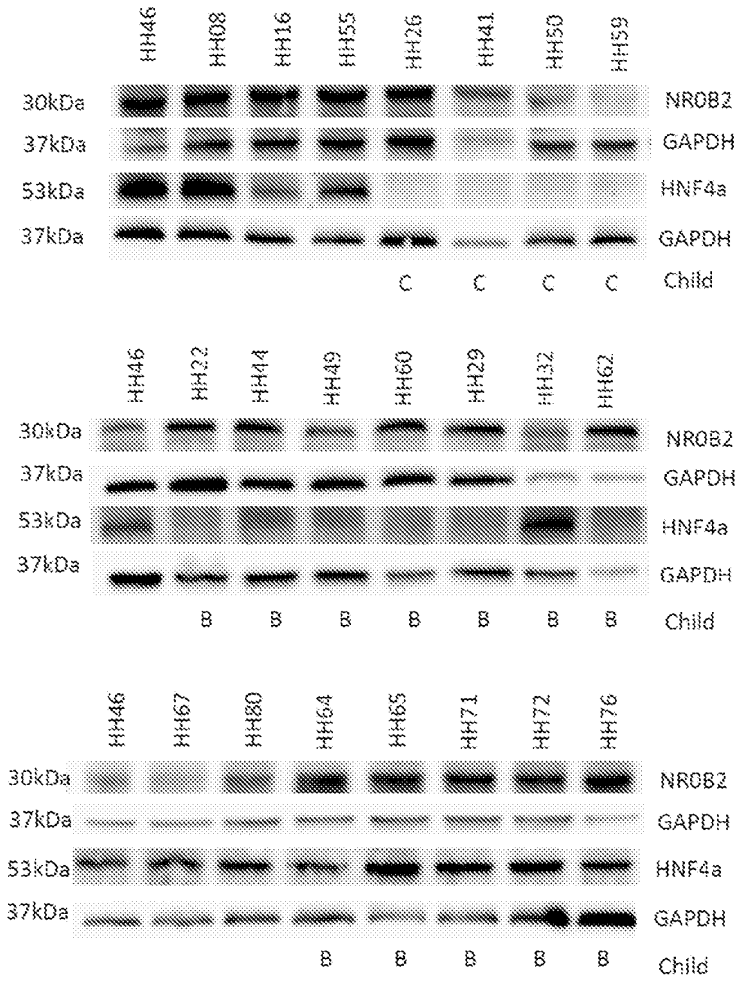
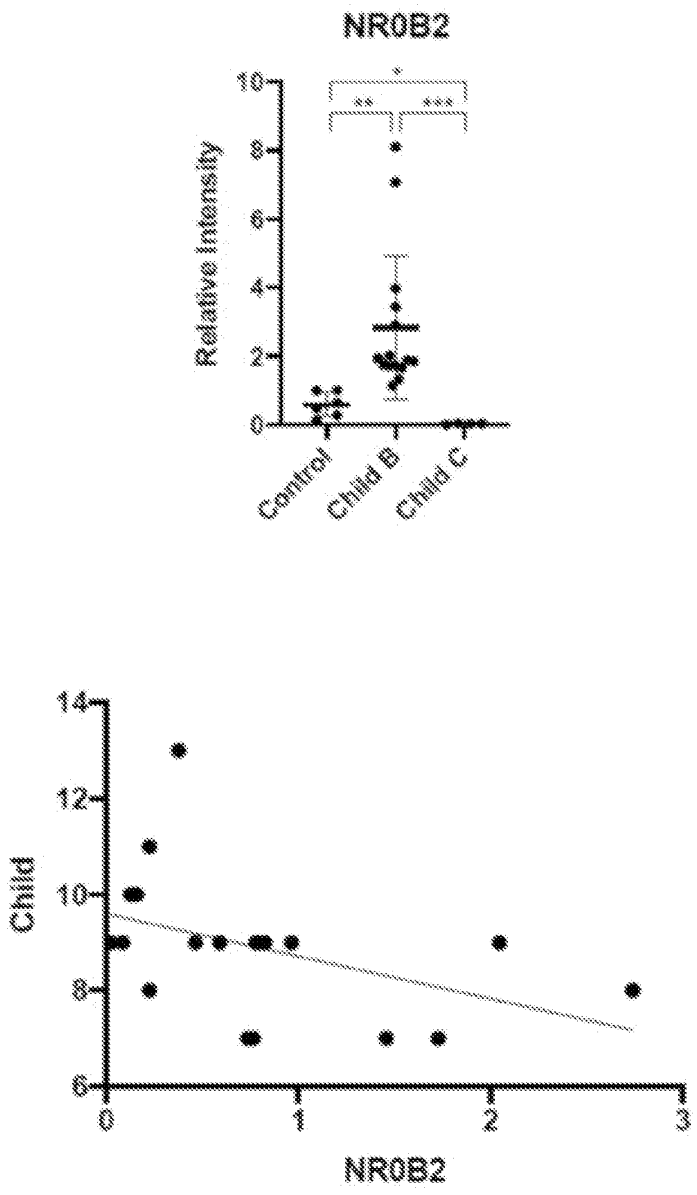

HH46
HH08
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37kDa
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37kDa
NR0B2
GAPDH
HNF4a
GAPDH
C C C C
Child
HH46
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HH62
30kDa
37kDa
53kDa
37kDa
NR0B2
GAPDH
HNF4a
GAPDH
B B B B B B B
Child
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HH67
HH80
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HH72
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GAPDH
HNF4a
GAPDH
B B B B B
Child

Figure 9A



Figures 9B and 9C

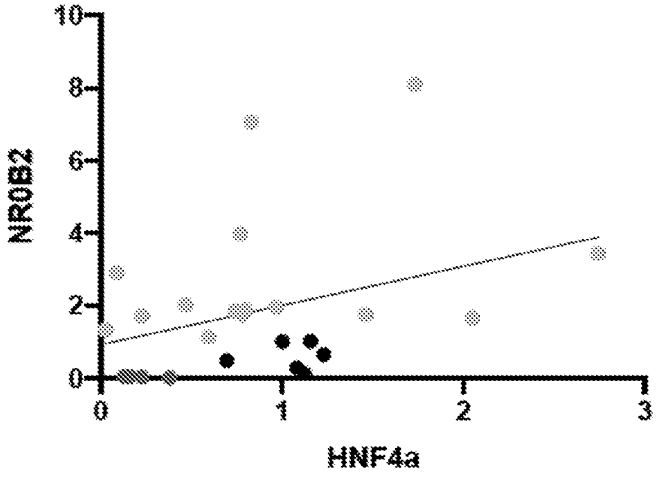


Figure 9D

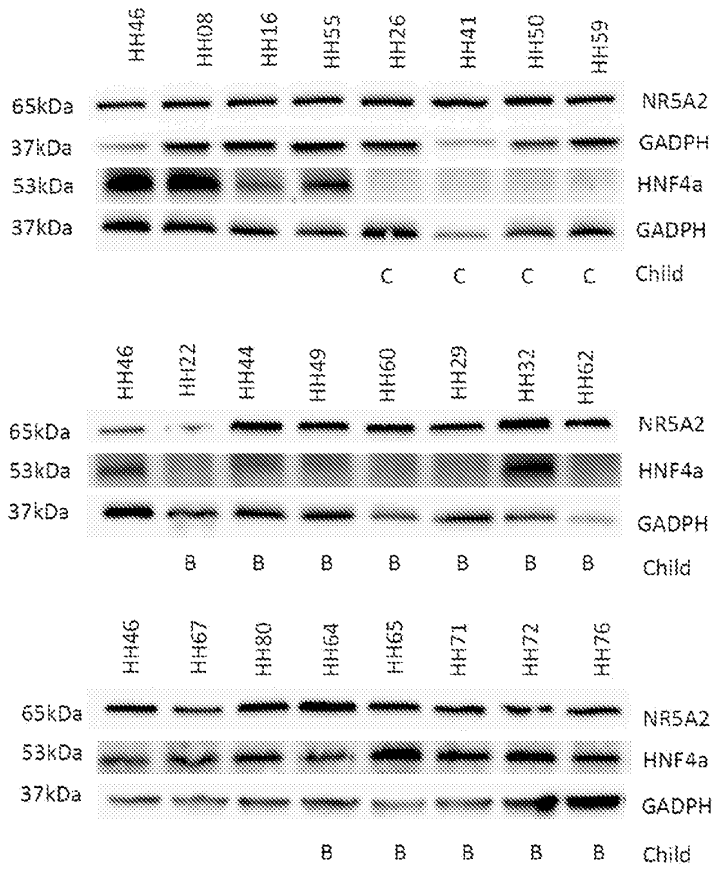
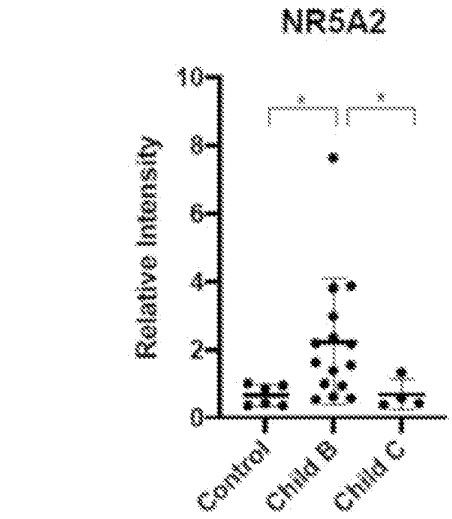
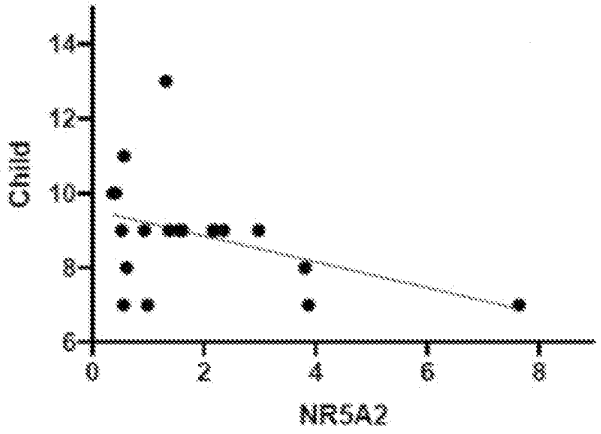

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HH50
HH59
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37kDa
53kDa
37kDa
NR5A2
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HNF4a
GADPH
C C C C
Child
HH46
HH22
HH44
HH49
HH60
HH29
HH32
HH62
65kDa
53kDa
37kDa
NR5A2
HNF4a
GADPH
B B B B B B B
Child
HH46
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HH80
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HH65
HH71
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HH76
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37kDa
NR5A2
HNF4a
GADPH
B B B B B
Child

Figure 10A





Figures 10B-10C

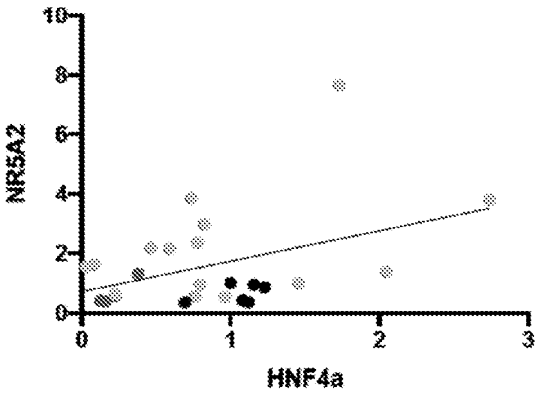


Figure 10D

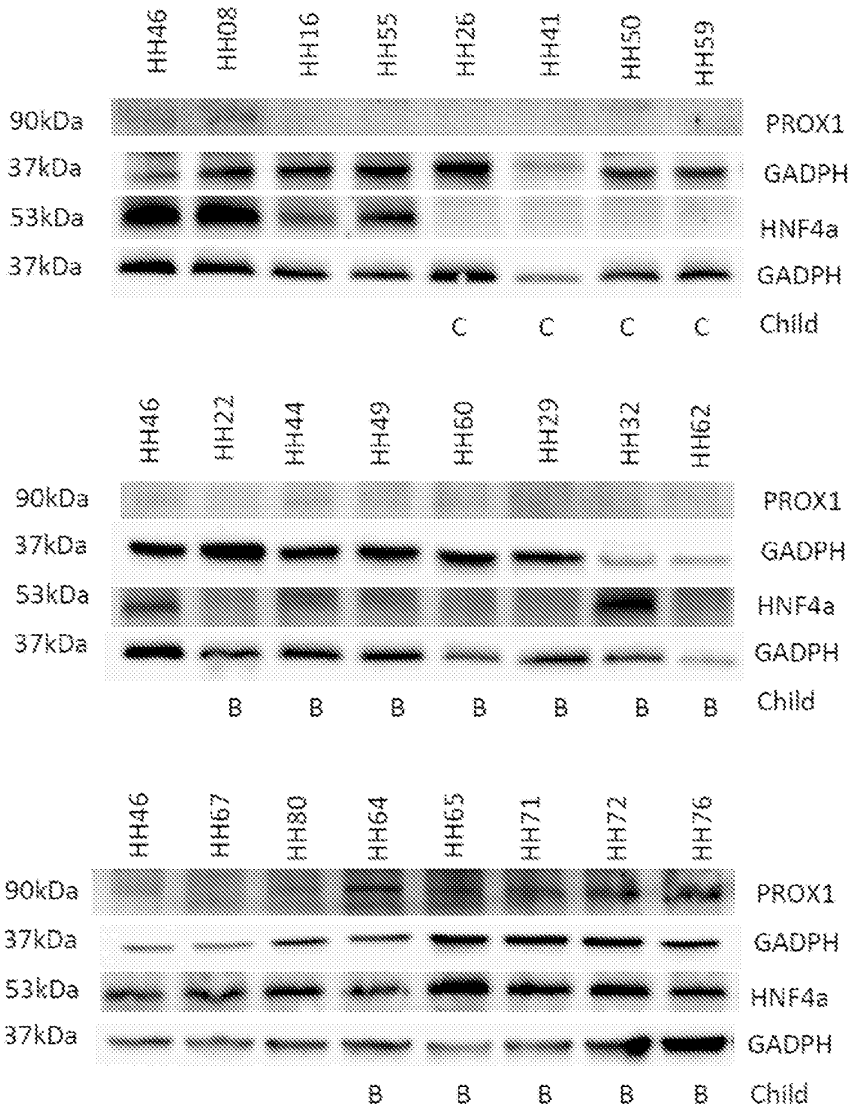
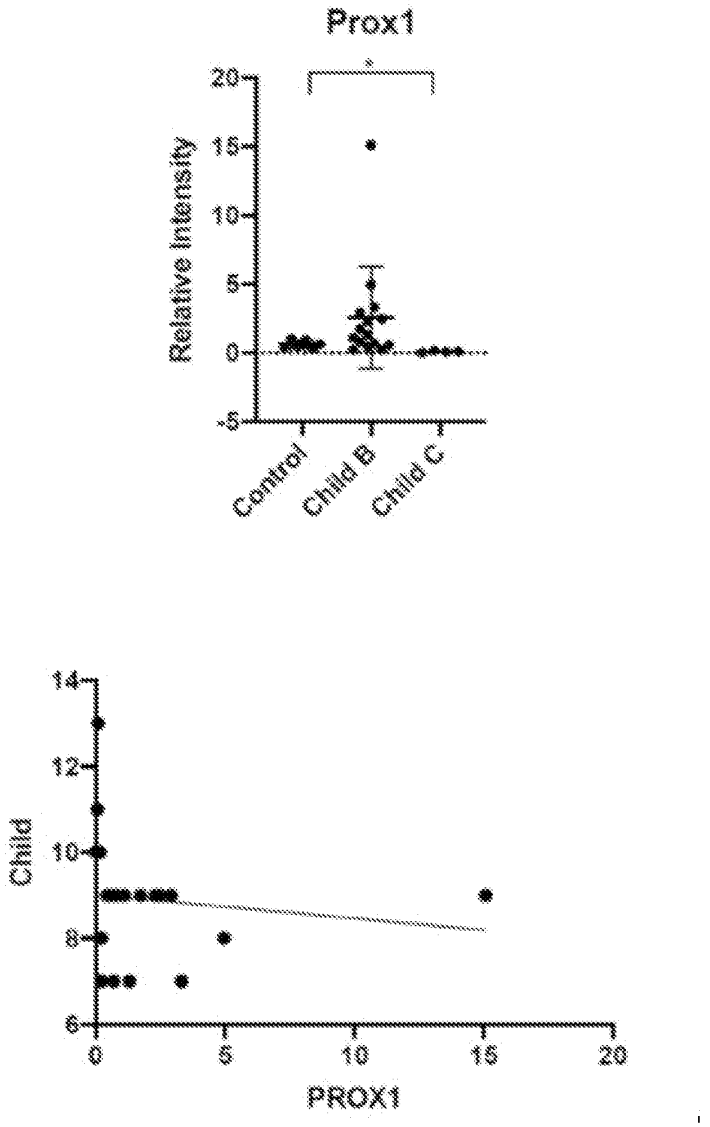

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PROX1
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GADPH
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HNF4a
37kDa
GADPH
C C C C
Child
HH46
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HH44
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HH60
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HH32
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90kDa
PROX1
37kDa
GADPH
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37kDa
GADPH
B B B B B B B
Child
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HH65
HH71
HH72
HH76
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HNF4a
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GADPH
B B B B B
Child

Figure 11A



Figures 11B and 11C

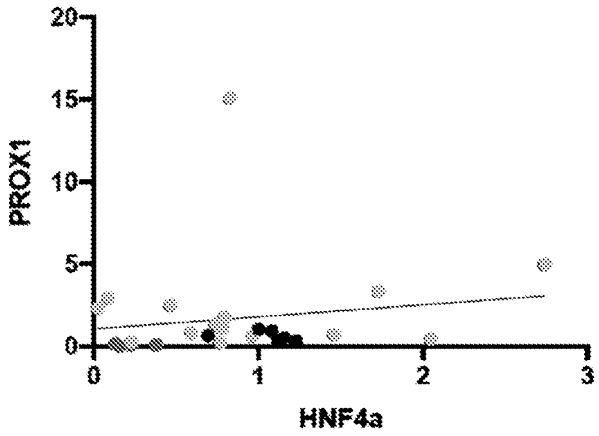


Figure 11D

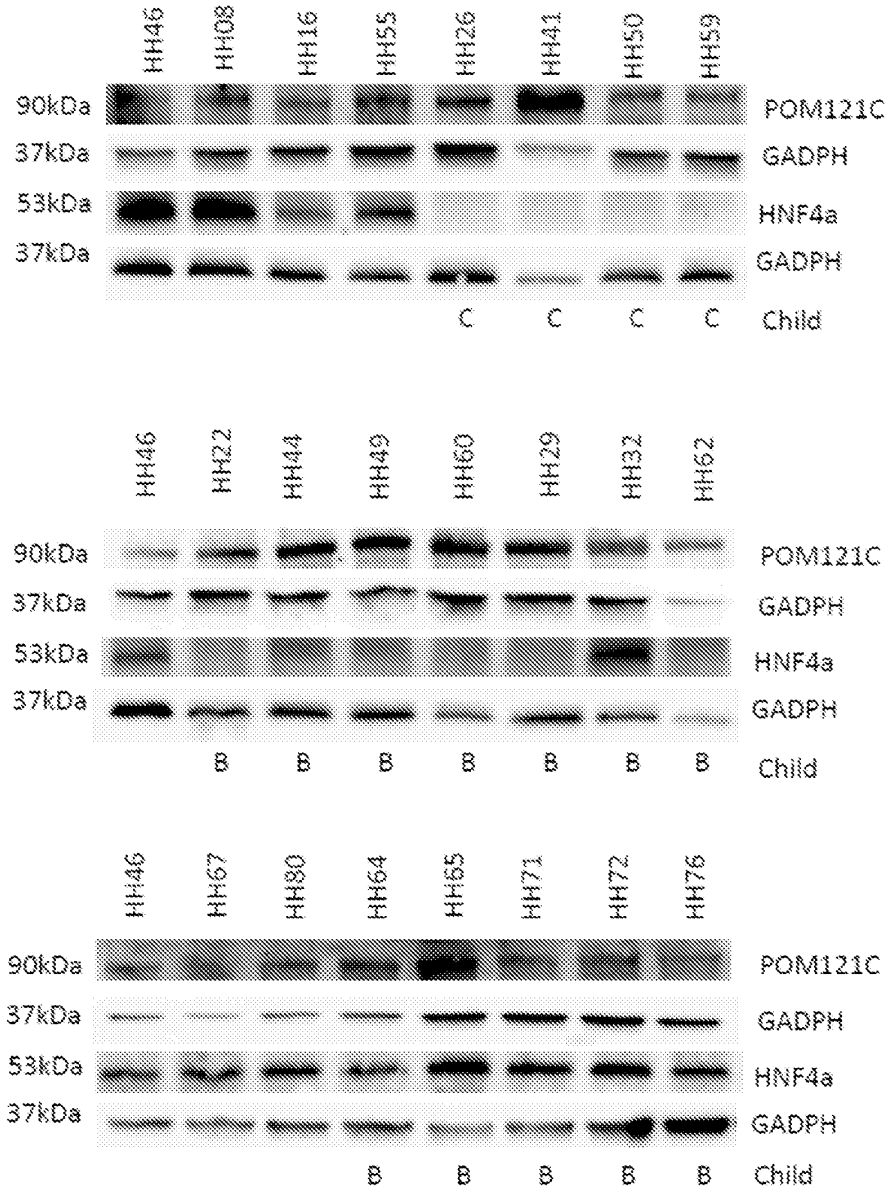
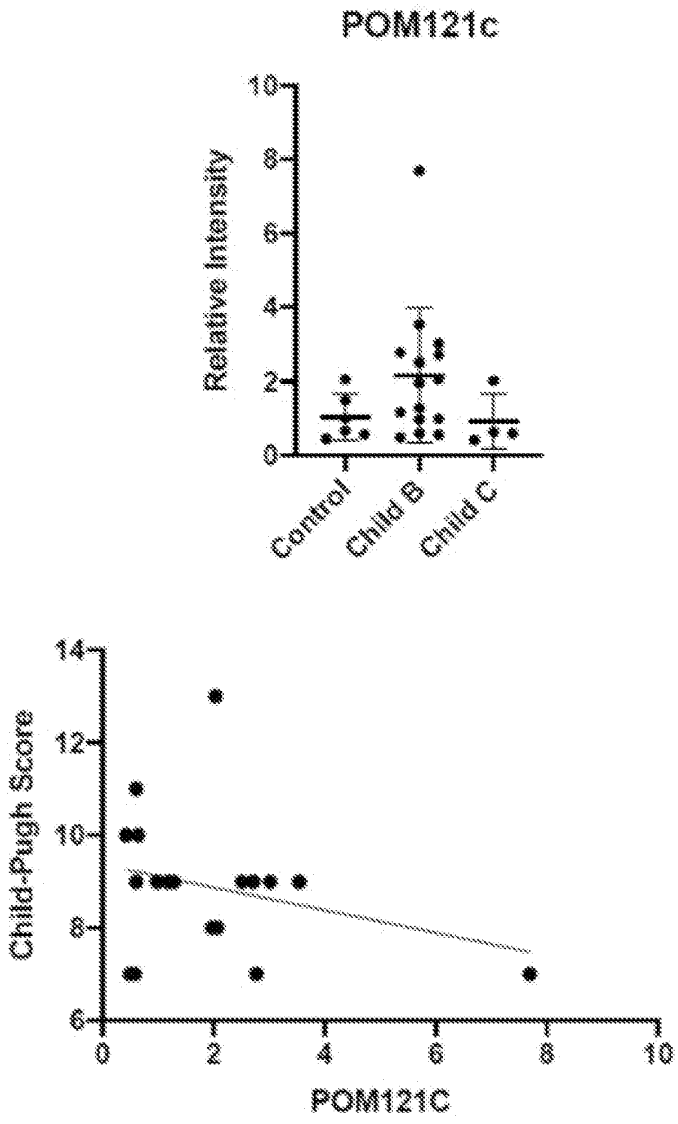

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POM121C
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HNF4a
37kDa
GADPH
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POM121C
37kDa
GADPH
53kDa
HNF4a
37kDa
GADPH
B B B B B B B
Child
HH46
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HH65
HH71
HH72
HH76
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HNF4a
37kDa
GADPH
B B B B B
Child

Figure 12A



Figures 12B and 12C

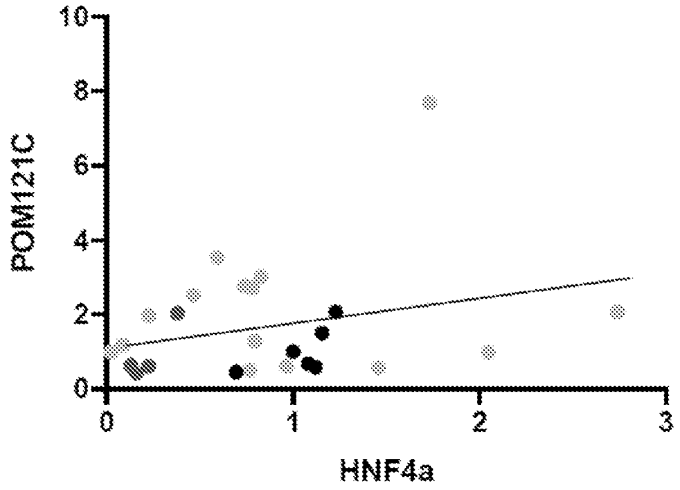


Figure 12D

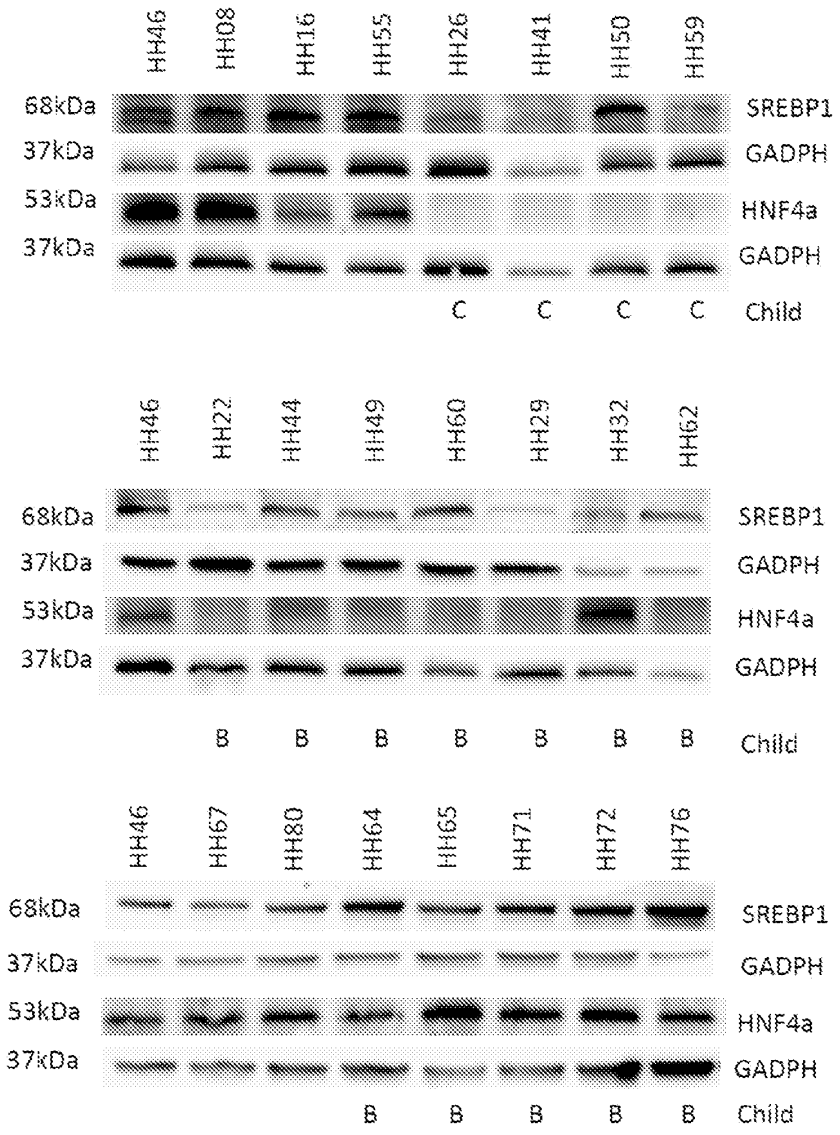
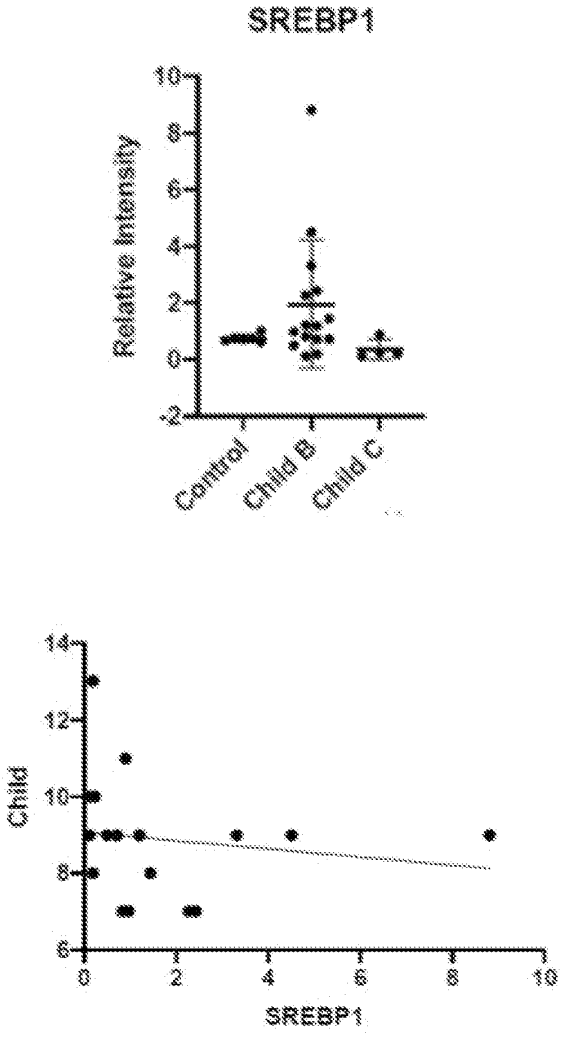

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SREBP1
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GADPH
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HNF4a
37kDa
GADPH
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68kDa
SREBP1
37kDa
GADPH
53kDa
HNF4a
37kDa
GADPH
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HH72
HH76
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37kDa
GADPH
B B B B B
Child

Figure 13A



Figures 13B and 13C

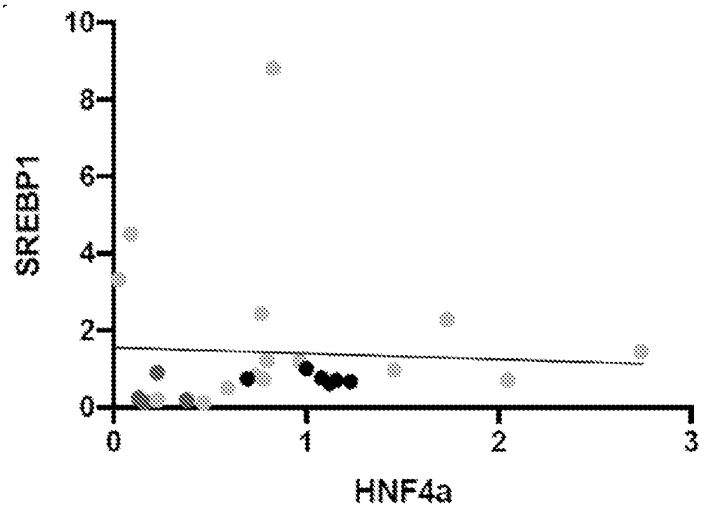


Figure 13D

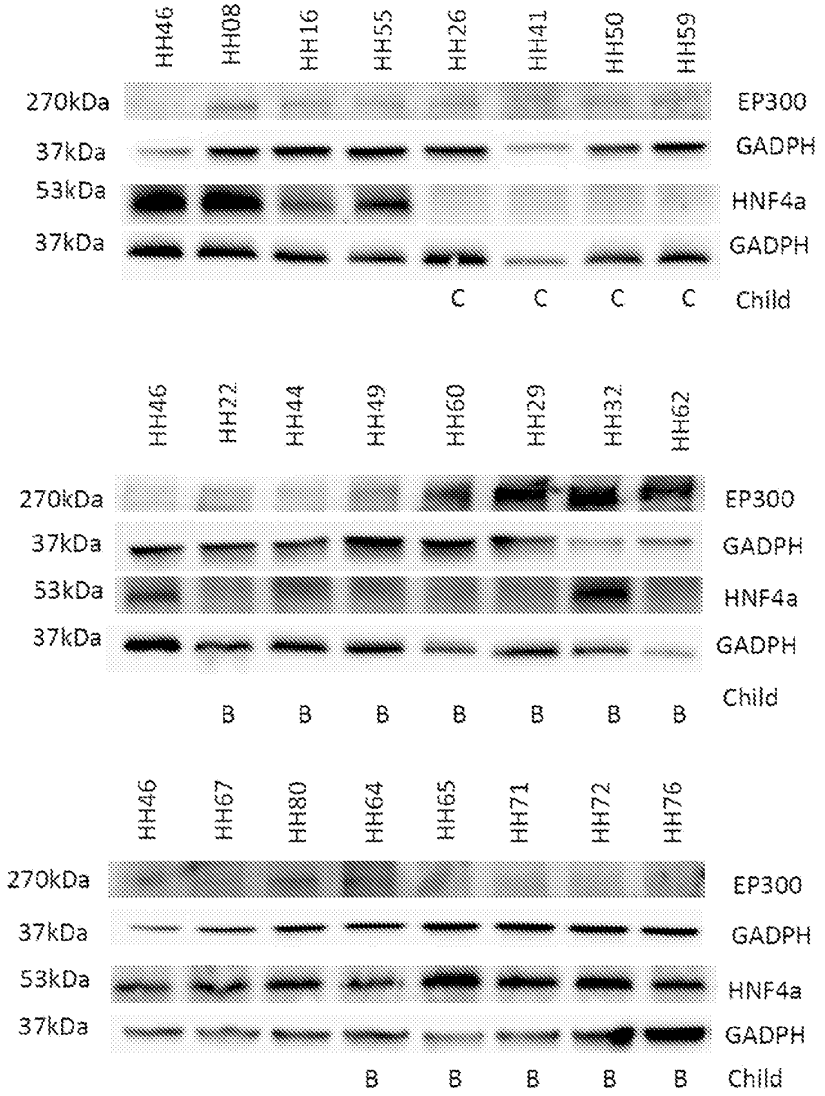
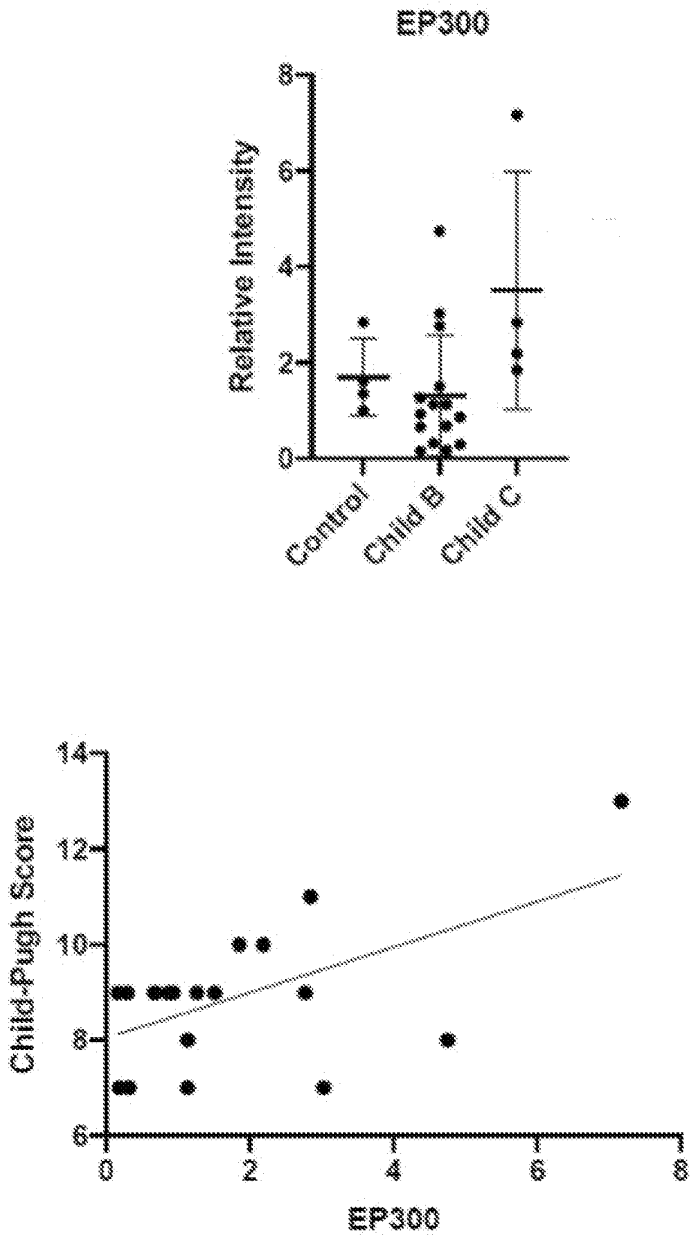

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HH26
HH41
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HH59
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EP300
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GADPH
53kDa
HNF4a
37kDa
GADPH
C C C C
Child
HH46
HH22
HH44
HH49
HH60
HH29
HH32
HH62
270kDa
EP300
37kDa
GADPH
53kDa
HNF4a
37kDa
GADPH
Child
B B B B B B B
HH46
HH67
HH80
HH64
HH65
HH71
HH72
HH76
270kDa
EP300
37kDa
GADPH
53kDa
HNF4a
37kDa
GADPH
B B B B B
Child

Figure 14A



Figures 14B and 14C

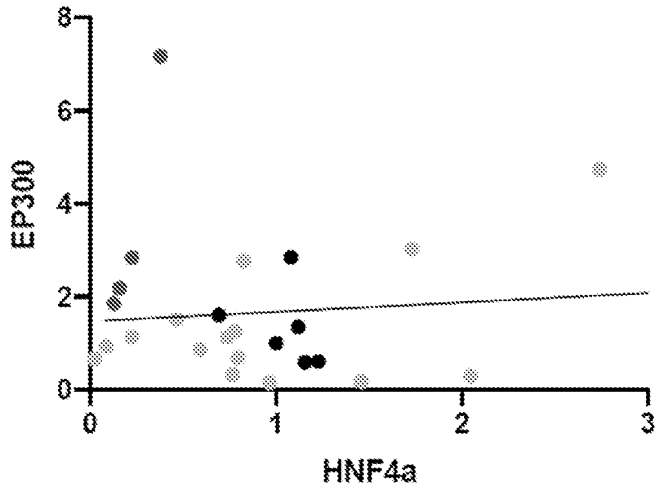
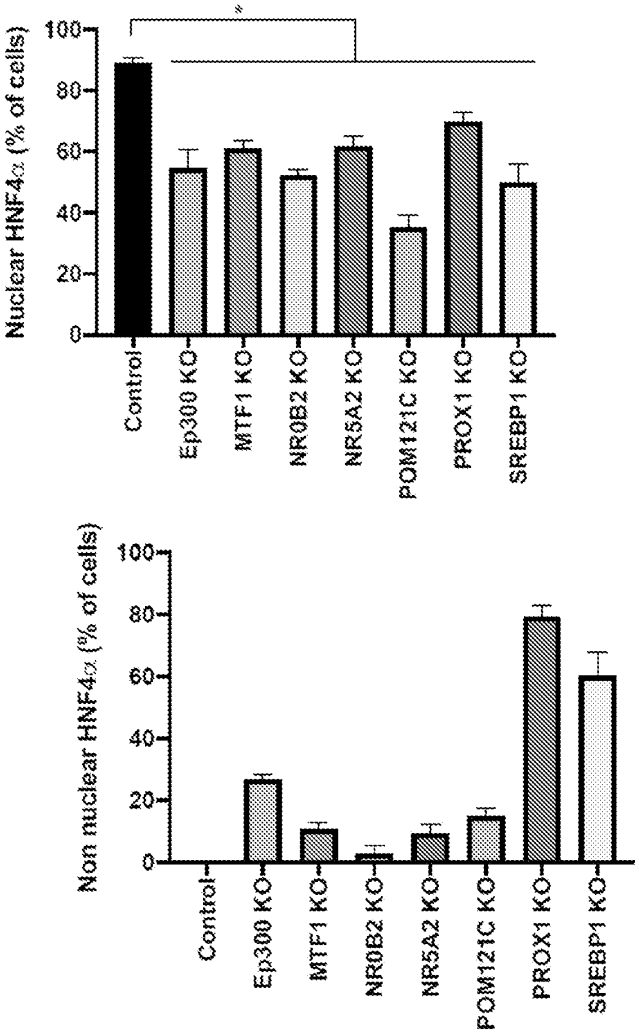


Figure 14D



Figures 15A and 15B

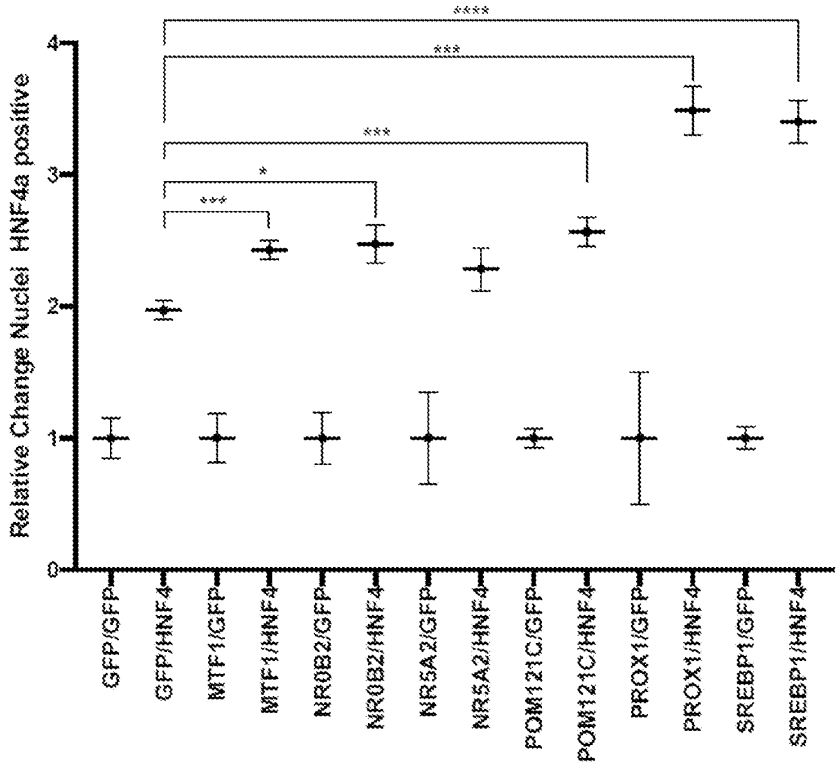

Relative Change Nuclei HNF4a positive
0
1
2
3
4
****
***
***
*
***
GFP/GFP
GFP/HNF4
MTF1/GFP
MTF1/HNF4
NR0B2/GFP
NR0B2/HNF4
NR5A2/GFP
NR5A2/HNF4
POM121C/GFP
POM121C/HNF4
PROX1/GFP
PROX1/HNF4
SREBP1/GFP
SREBP1/HNF4

Figure 16