2 2 APR 2002

G00002

163163

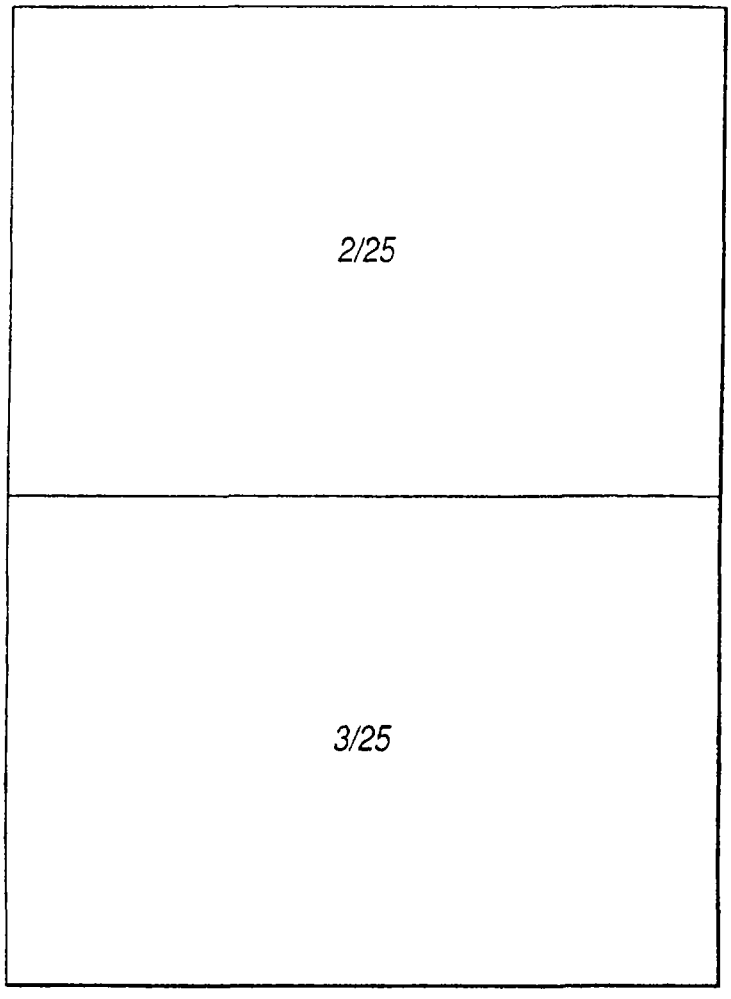


Fig.1A

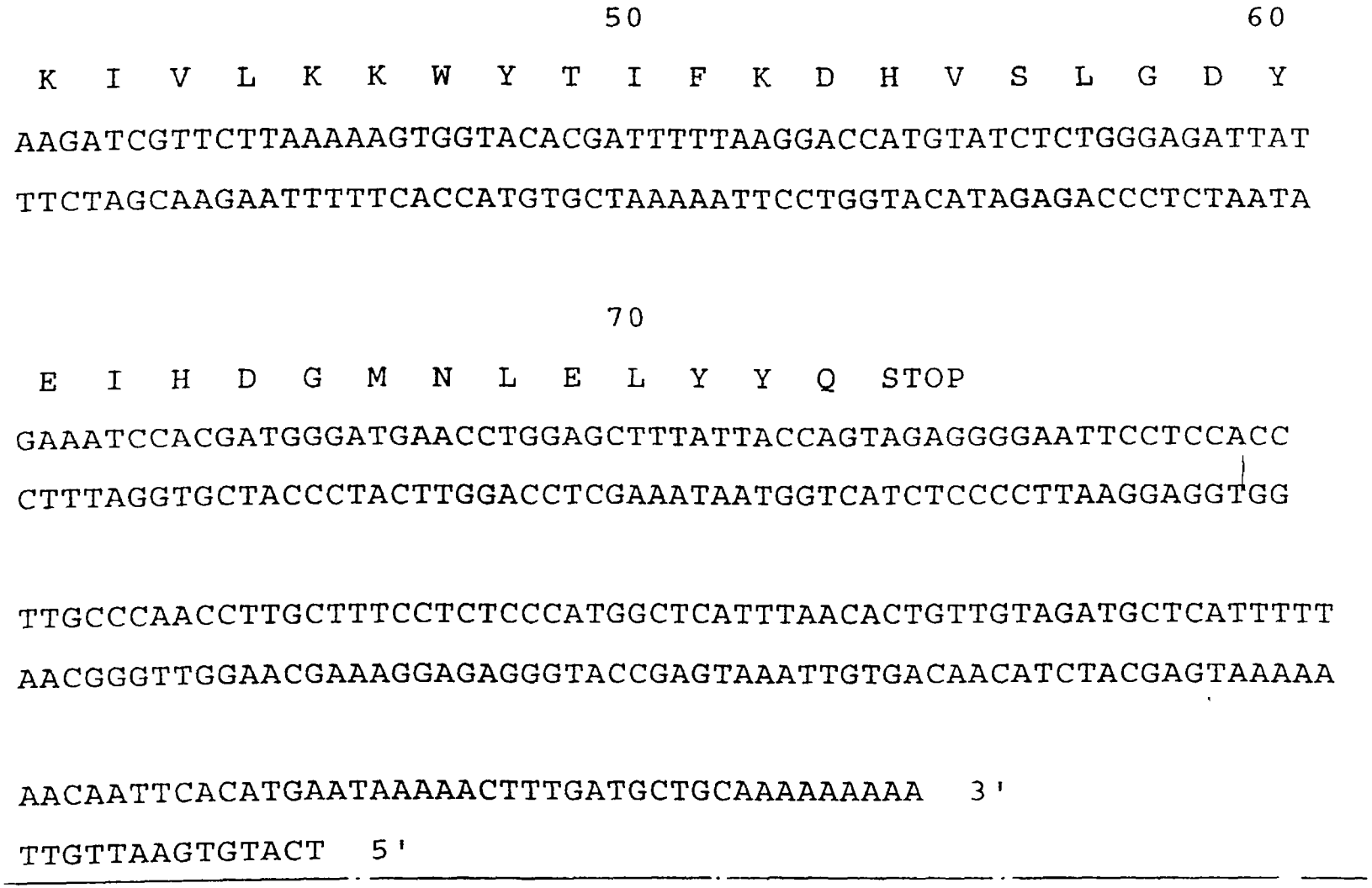


Fig.1A (i)

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```
                                    50                                  60
 K   I   V   L   K   K   W   Y   T   I   F   K   D   H   V   S   L   G   D   Y
AAGATCGTTCTTAAAAAGTGGTACACGATTTTTAAGGACCATGTATCTCTGGGAGATTAT
TTCTAGCAAGAATTTTTCACCATGTGCTAAAAATTCCTGGTACATAGAGACCCTCTAATA

                                    70
 E   I   H   D   G   M   N   L   E   L   Y   Y   Q  STOP
GAAATCCACGATGGGATGAACCTGGAGCTTTATTACCAGTAGAGGGGAATTCCTCCACC
CTTTAGGTGCTACCCTACTTGGACCTCGAAATAATGGTCATCTCCCCTTAAGGAGGTGG

TTGCCCAACCTTGCTTTCCTCTCCCATGGCTCATTTAACACTGTTGTAGATGCTCATTTTT
AACGGGTTGGAACGAAAGGAGAGGGTACCGAGTAAATTGTGACAACATCTACGAGTAAAAA

AACAATTCACATGAATAAAAACTTTGATGCTGCAAAAAAAAA  3'
TTGTTAAGTGTACT  5'
```

Fig.1A (ii)

```
ATG ATC GAG GTT GTT TGC AAC GAC CGT CTG GGG AAA AAG GTC CNC   45
Met Ile Glu Val Val Cys Asn Asp Arg Leu Gly Lys Lys Val Xaa
  1               5                  10                  15

GTT AAA TGC AAC ACG GAT GAT ACC ATC GGG GAC CTT AAG AAG CTG   90
Val Lys Cys Asn Thr Asp Asp Thr Ile Gly Asp Leu Lys Lys Leu
                 20                  25                  30

ATT GCA GCC TAA                                             102
Ile Ala Ala *
```

Fig.1B

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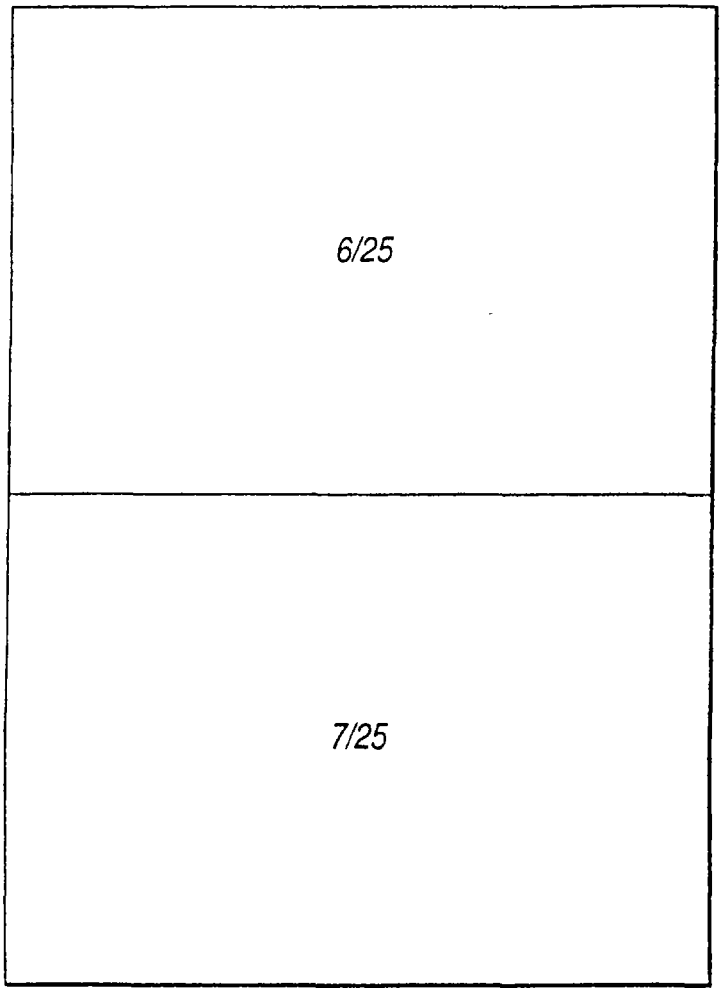


Fig.2A

AMINO ACID ALIGNMENTS

A.

```
                    10        20        30        40        50
                     *         *         *         *         *
Beacon      MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
Human       MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
Mouse       MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
C.elegans   MIEITVNDRLGKKVRIKCNPSDTIGDLKKLIAAQTGTRWEKIVLKKWYTI
F.hepatica        DRLGKKVRVKCNPTDKVGDLKKLIAAQTGTAPERIVLKKWYTI
Rice        MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
S.cerev     MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
```

Fig.2A (i)

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```
                    60          70
                     *           *
Beacon      FKDHVSLGDYEIHDGMNLELYYQ
Human       FKDHVSLGDYEIHDGMNLELYYQ
Mouse       FKDHVSLGDYEIHDGMNLELYYQ
C.elegans   YKDHITLMDYEIHEGFNFELYYQ
F.hepatica  YKDHVTLRDYEINDGMNLELYYQ
Rice        YKDHITLADYEIHDGMGLELYYN
S.cerev     LKDHICLEDYEVHDQTNLELYYL
```

Percentage homologies	
Human	73/73 = 100%
Mouse	73/73 = 100%
C.elegans	59/73 = 81%
F.hepatica	54/66 = 82%
Rice	58/73 = 79%
S.cerev	46/73 = 63%

Fig.2A (ii)

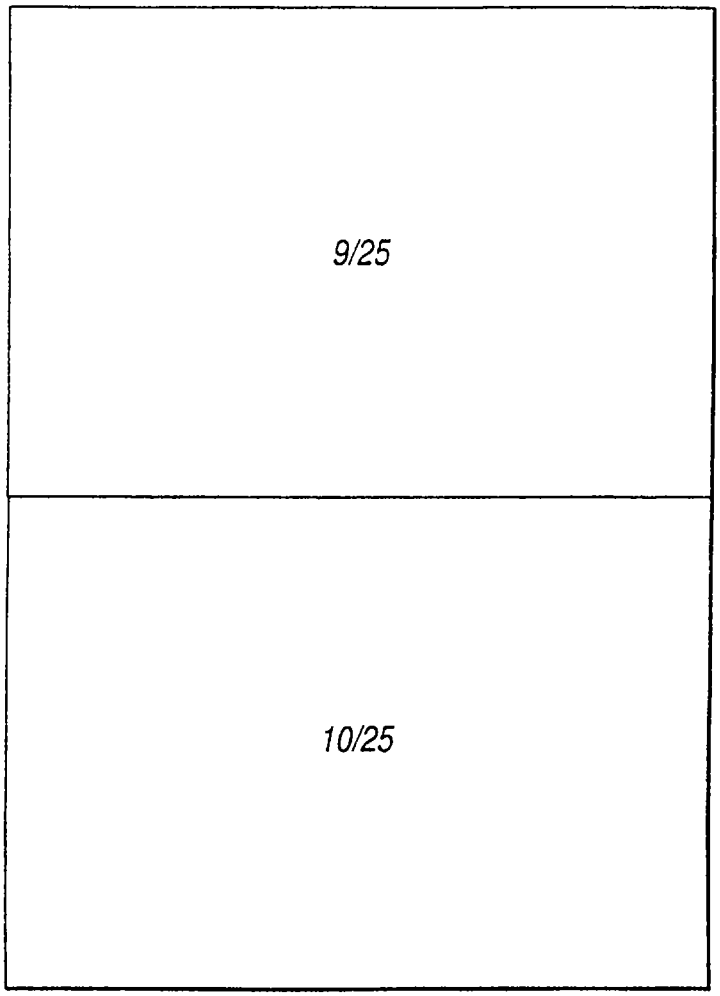


Fig.2B

B.

Human ubiquitin

```
                    10          20          30          40          50
                    *           *           *           *           *
Beacon      MIEVVCNDRLGKKVRVKCNTDDTIGDLKKLIAAQTGTRWNKIVLKKWYTI
             | |       || + ++    ||| ++|  |  + |   ++   |
Ugiquitin   MQIFVKT   LTGKTITLEVEPSDTIENVKAKIQDKEGIPPDQQRLIFAGKQ

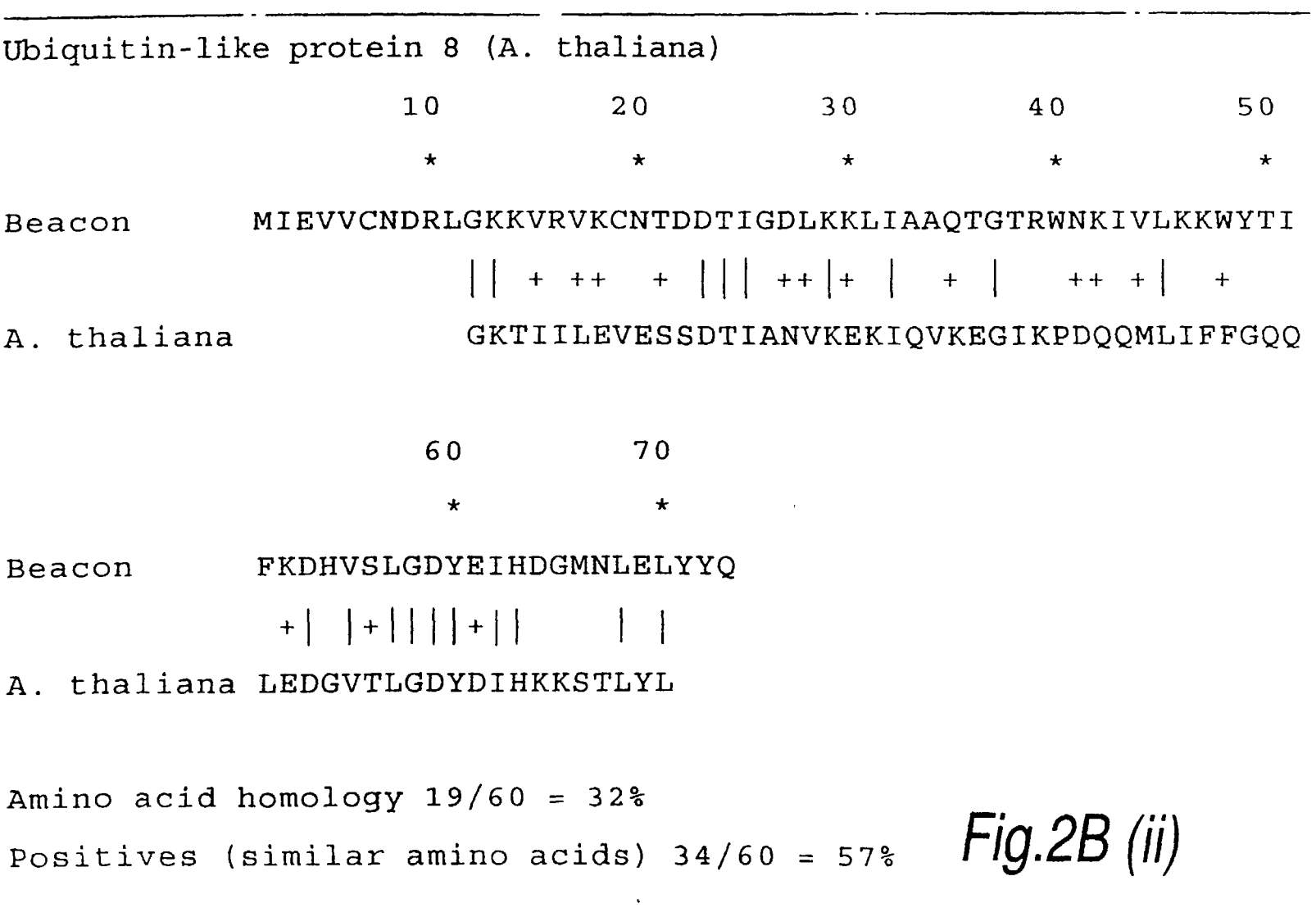
                    60          70
                    *           *
Beacon      FKDHVSLGDYEIHDGMNLELYYQ
             +|  +| ||+|      | |
Ubiquitin   LEDGRTLSDYNIQKESTLHLVLRLRGG
```

Amino acid homology 18/73 = 25%

Positives (similar amino acids) 29/73 = 40%

Fig.2B (i)

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Amino acid homology 19/60 = 32%

Positives (similar amino acids) 34/60 = 57%

Fig.2B (ii)

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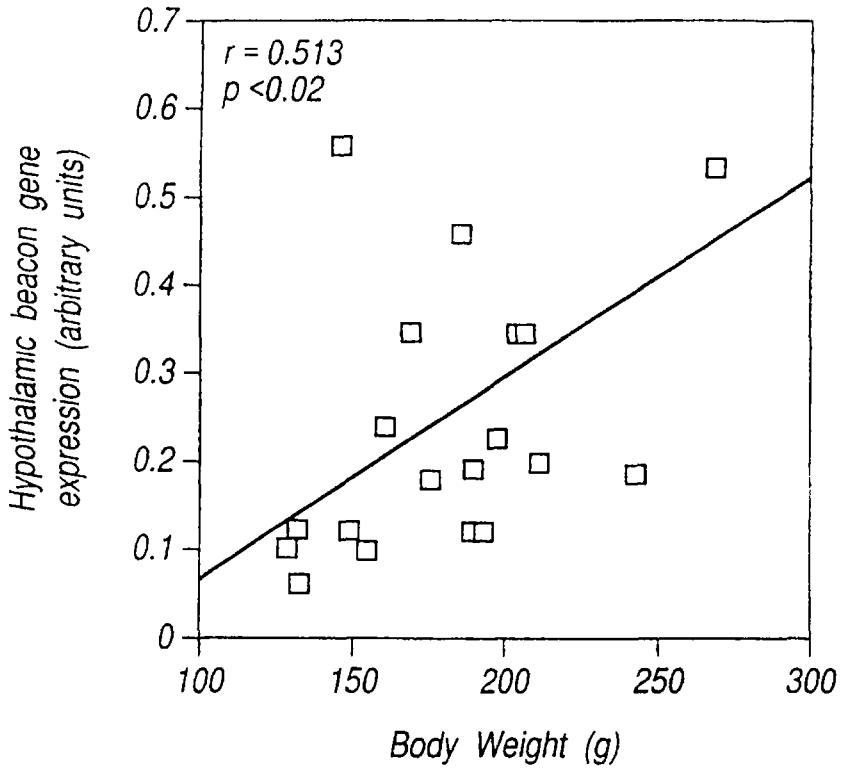

r = 0.513
p <0.02
Hypothalamic beacon gene expression (arbitrary units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
100
150
200
250
300
Body Weight (g)

Fig.3A

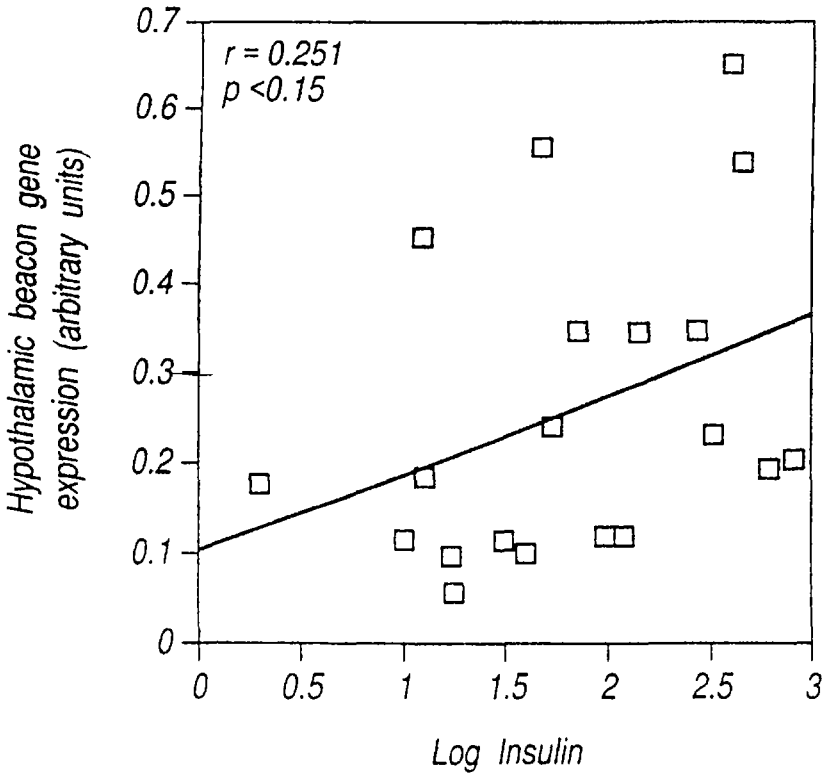

r = 0.251
p <0.15
Hypothalamic beacon gene expression (arbitrary units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
3
Log Insulin

Fig.3B

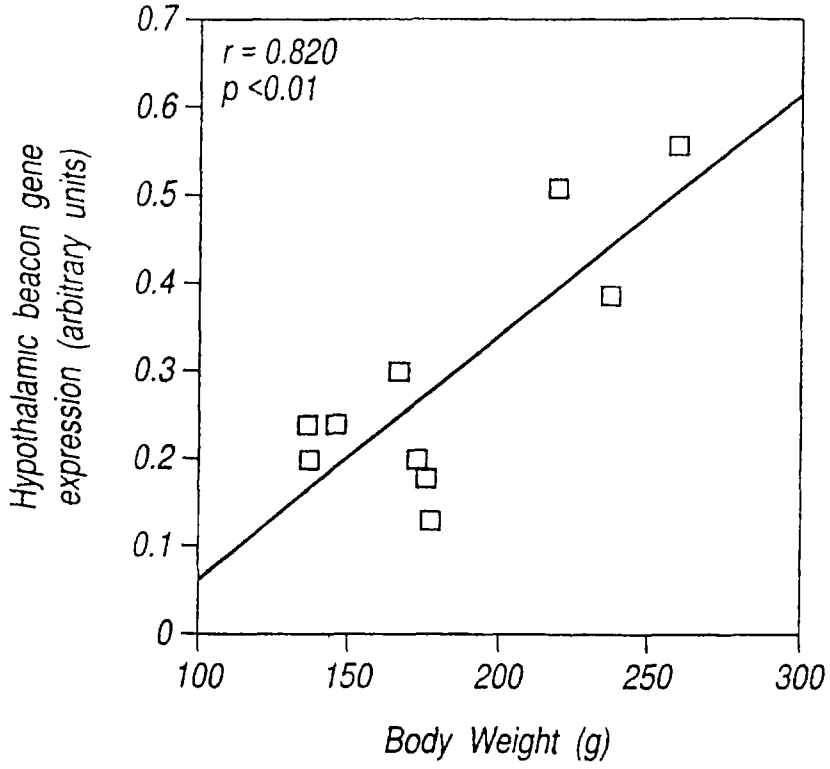

r = 0.820
p <0.01
Hypothalamic beacon gene expression (arbitrary units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
100
150
200
250
300
Body Weight (g)

Fig.4A

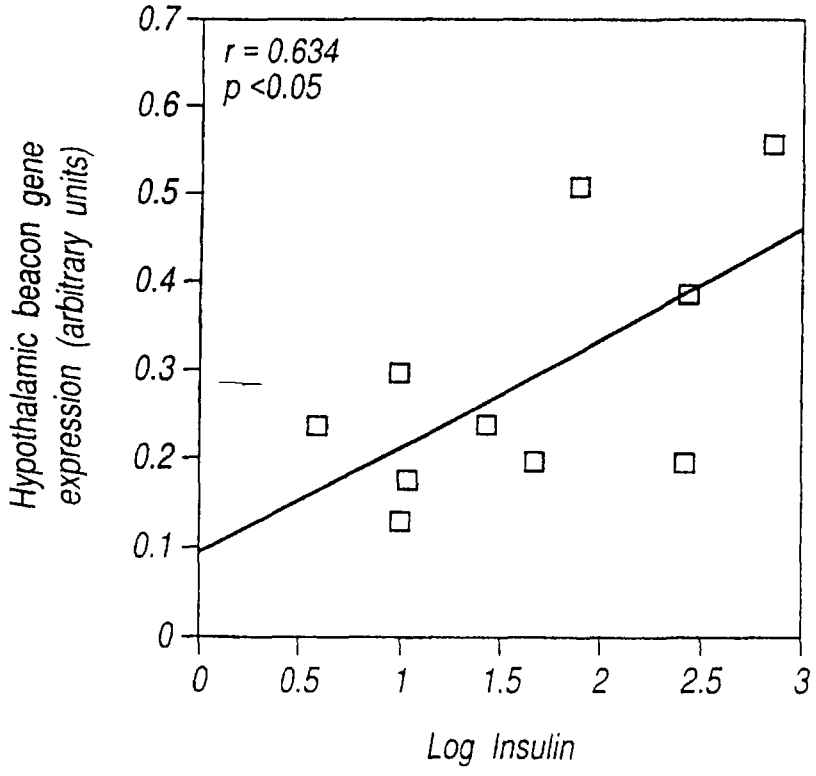

r = 0.634
p <0.05
Hypothalamic beacon gene expression (arbitrary units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
3
Log Insulin

Fig.4B

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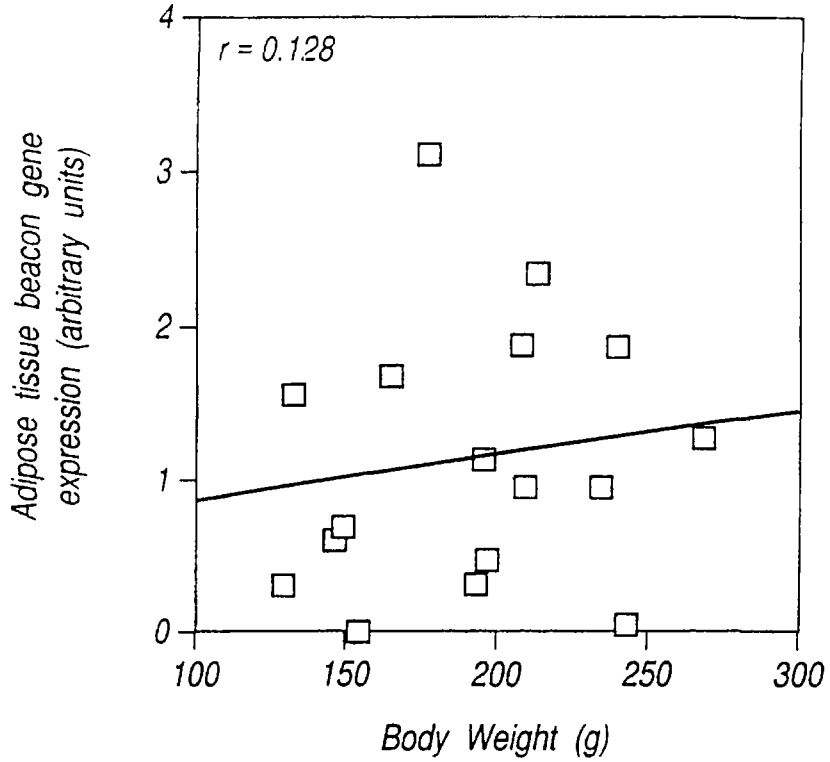


Fig.5A

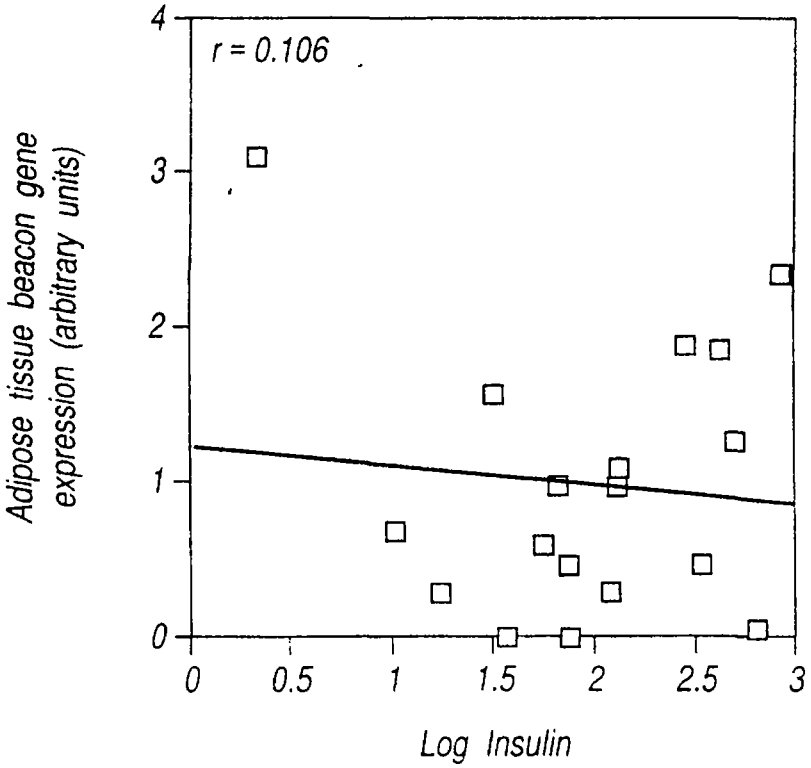


Fig.5B

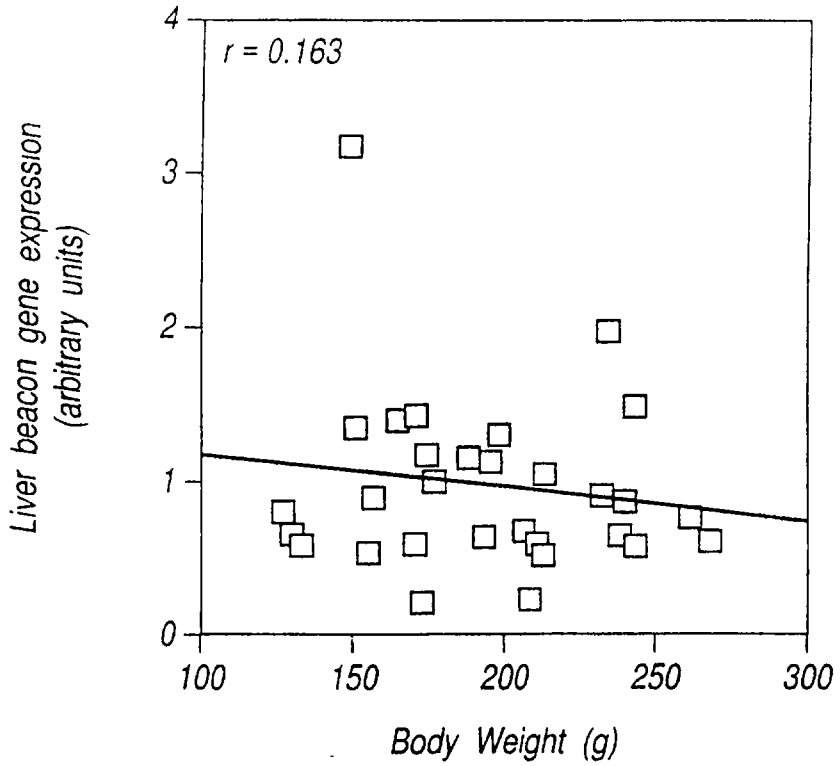

r = 0.163
Liver beacon gene expression (arbitrary units)
0
1
2
3
4
100
150
200
250
300
Body Weight (g)

Fig.5C

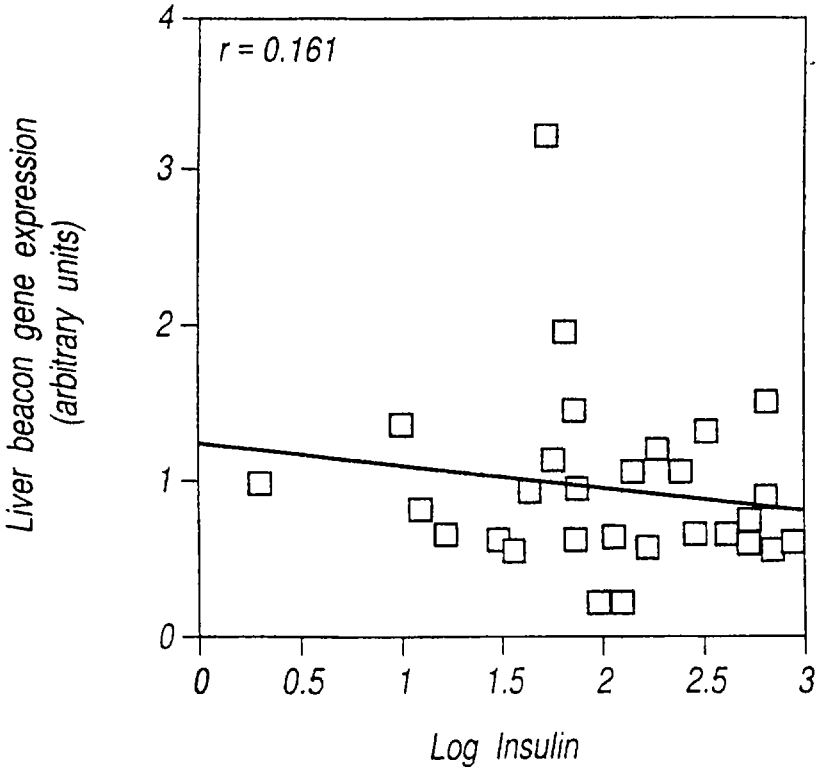

r = 0.161
Liver beacon gene expression (arbitrary units)
0
1
2
3
4
0
0.5
1
1.5
2
2.5
3
Log Insulin

Fig.5D

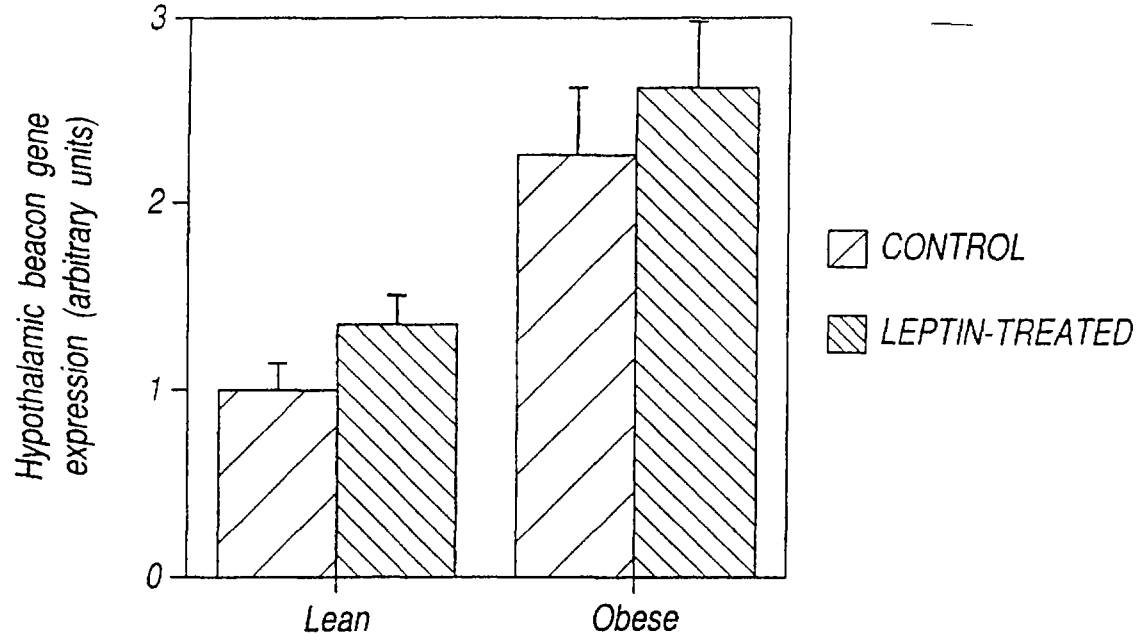

Hypothalamic beacon gene expression (arbitrary units)
3
2
1
0
Lean
Obese
CONTROL
LEPTIN-TREATED

Fig.6

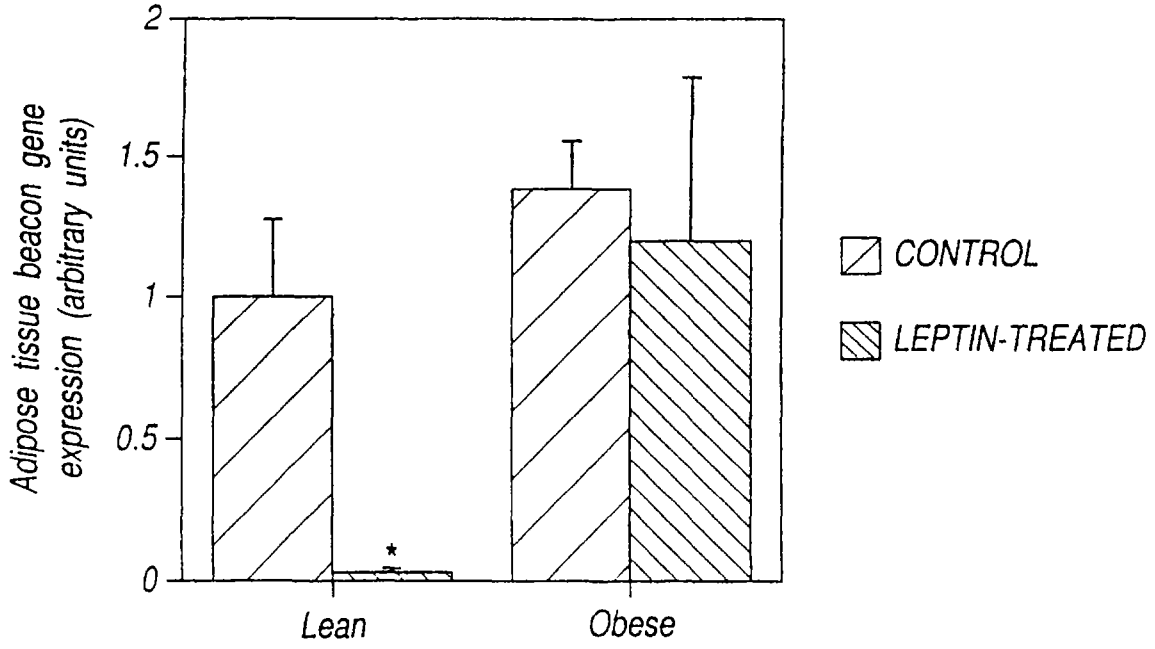

Adipose tissue beacon gene expression (arbitrary units)
2
1.5
1
0.5
0
*
Lean
Obese
CONTROL
LEPTIN-TREATED

Fig.7

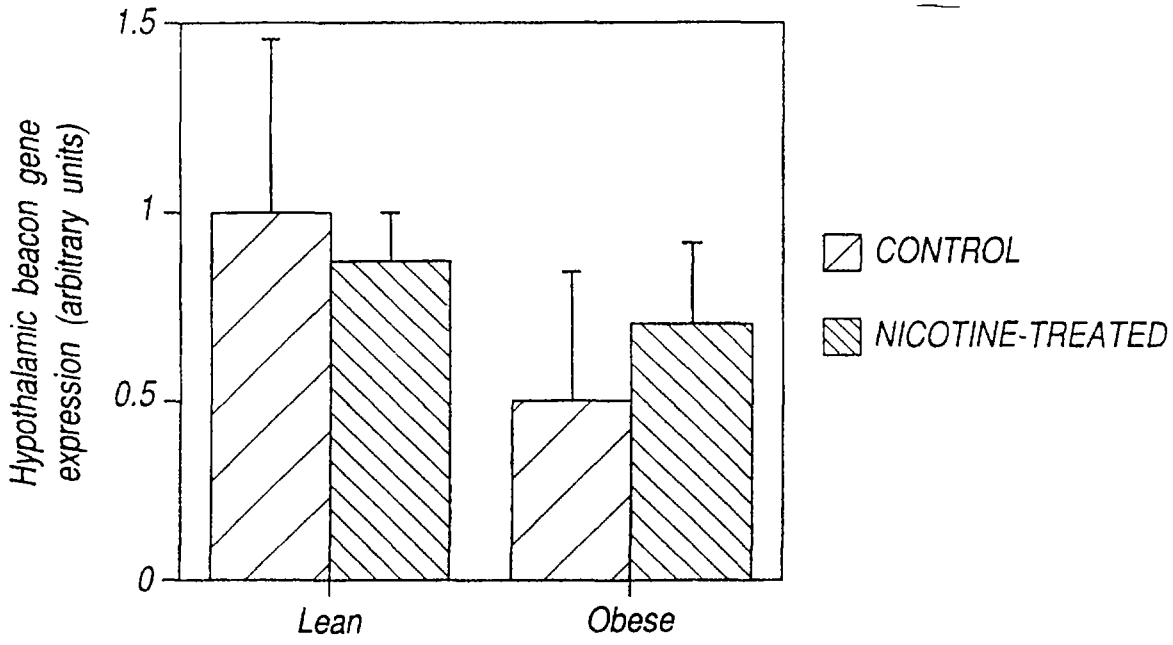

1.5
1
0.5
0
Hypothalamic beacon gene expression (arbitrary units)
Lean
Obese
CONTROL
NICOTINE-TREATED

Fig.8A

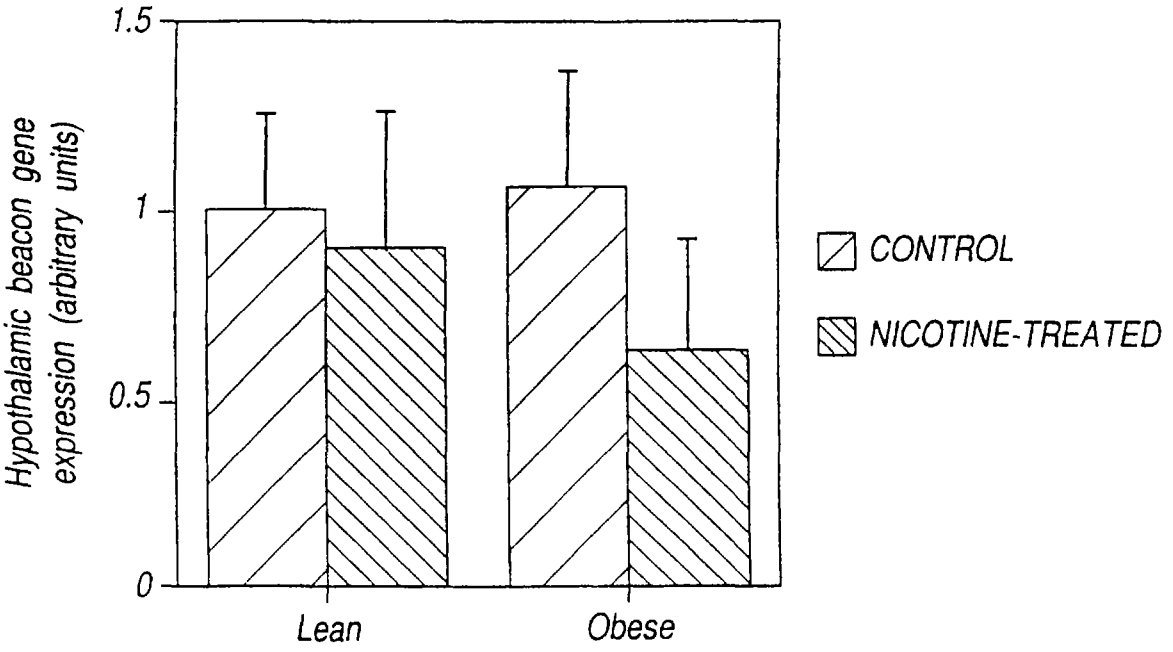

1.5
1
0.5
0
Hypothalamic beacon gene expression (arbitrary units)
Lean
Obese
CONTROL
NICOTINE-TREATED

Fig.8B

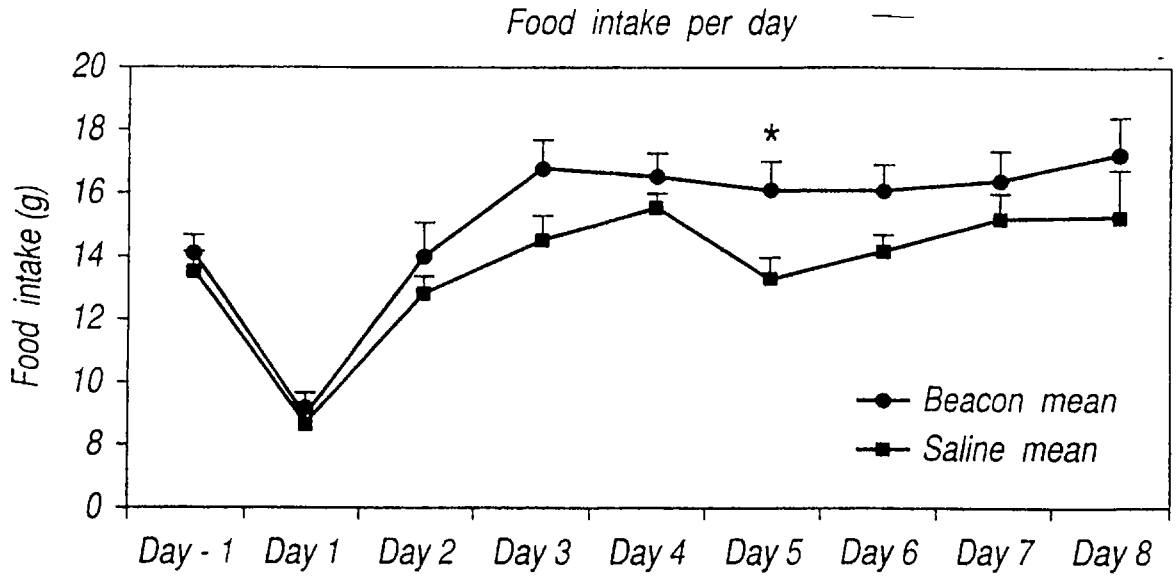
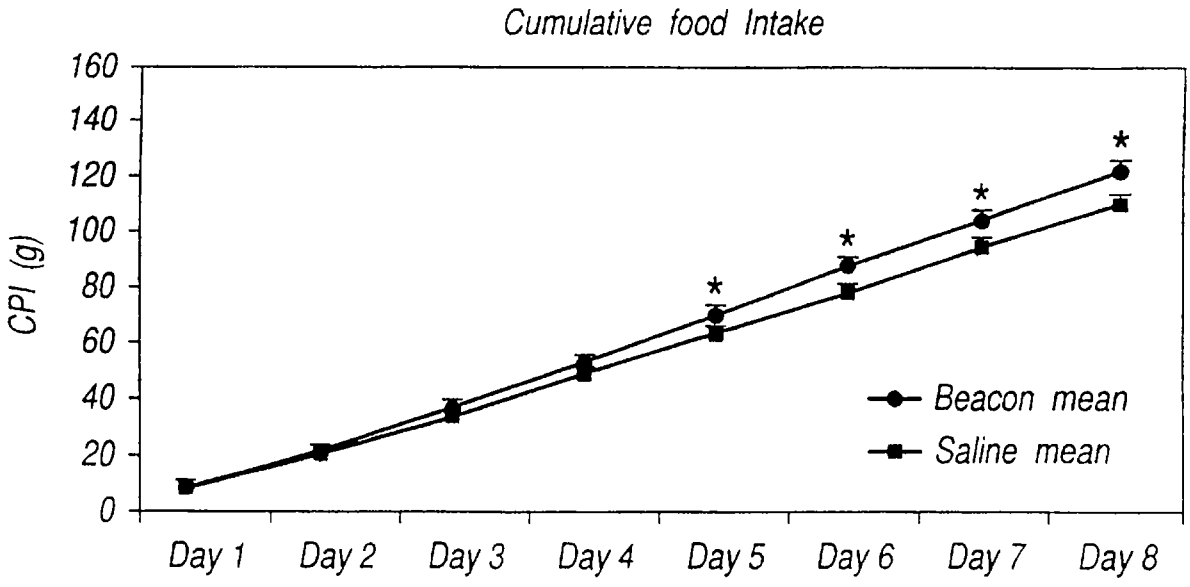


Fig.9A



* = significant. $p<0.05$

Fig.9B

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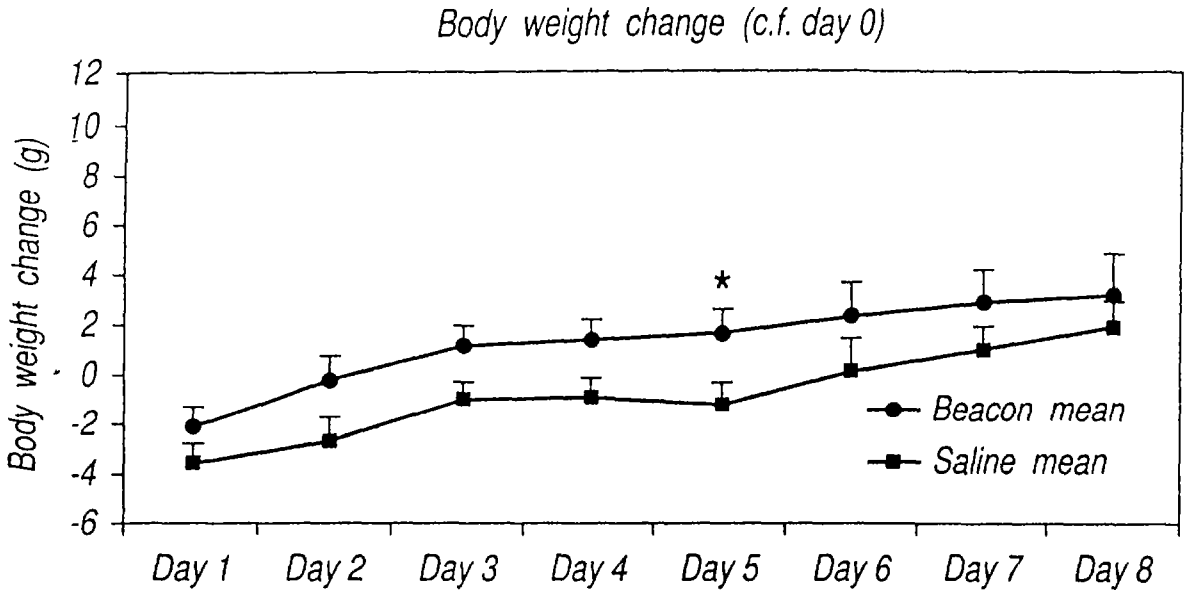


Fig.9C

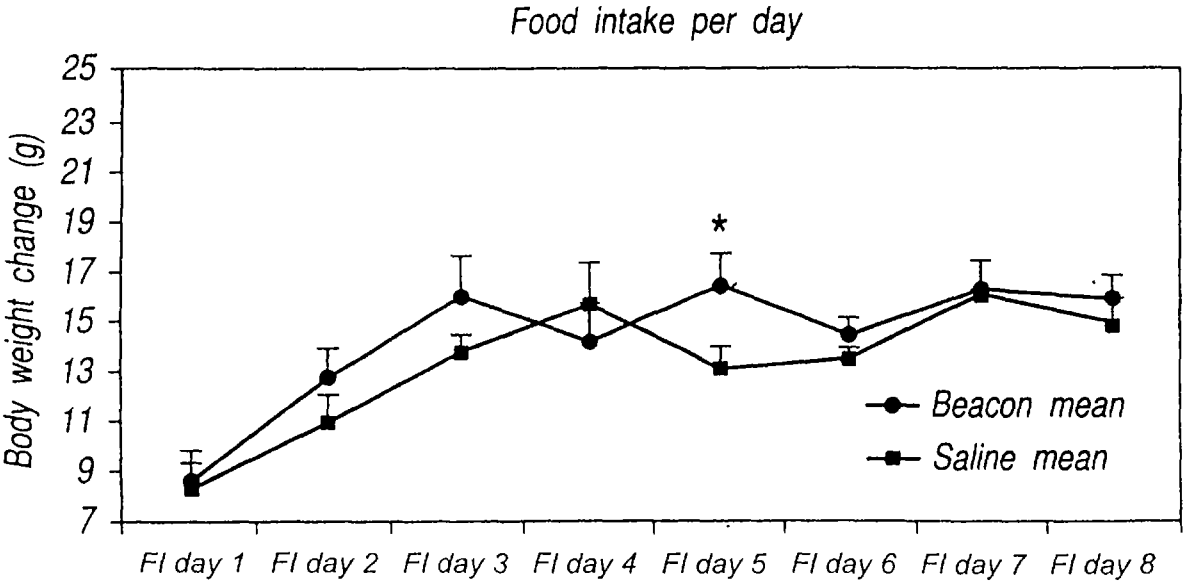


Fig.10A

* = significant, $p<0.05$

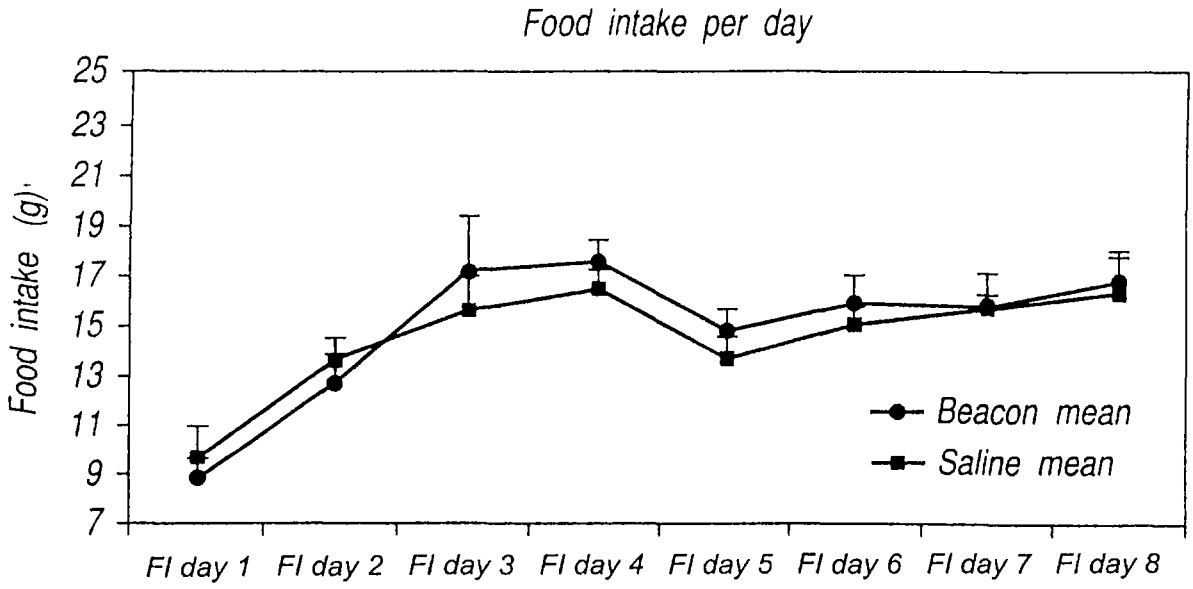


Fig.10B

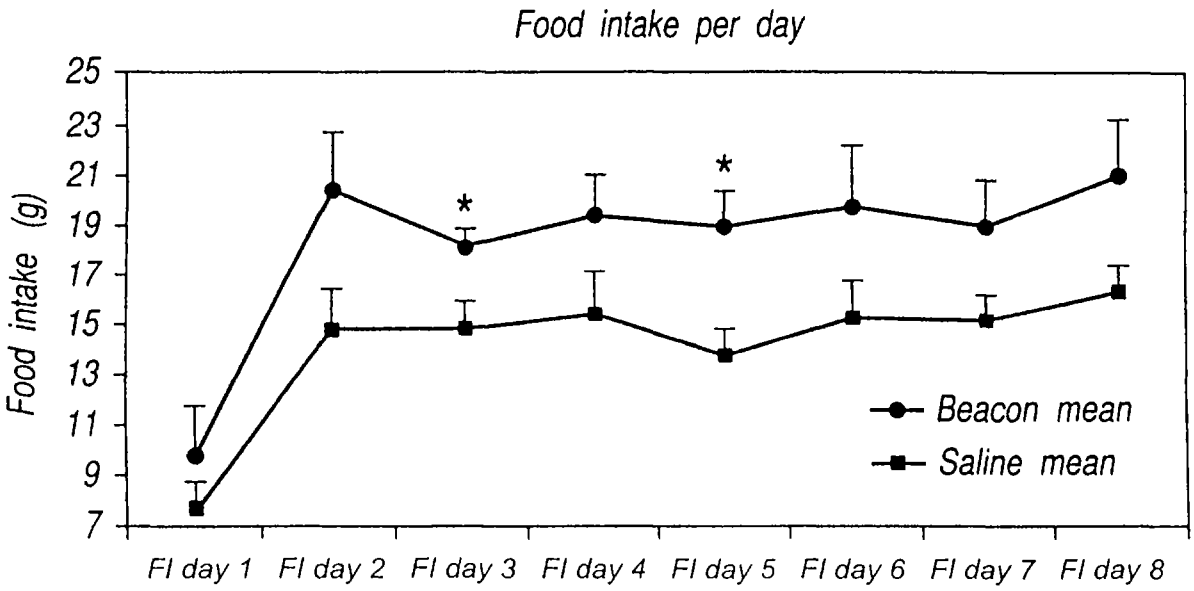


Fig.10C

* = significant, $p<0.05$

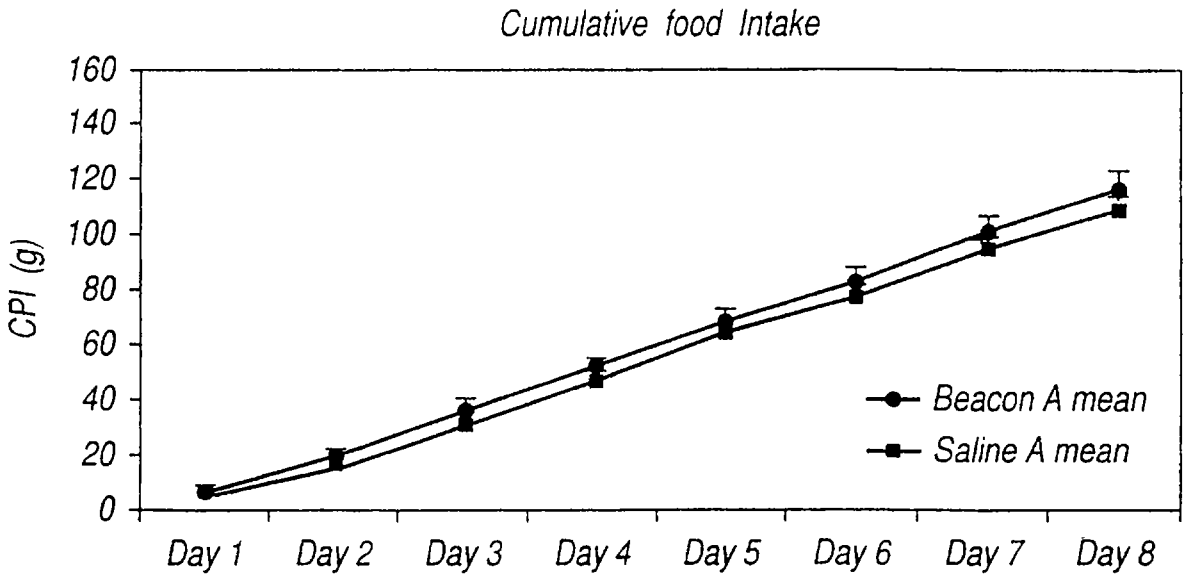
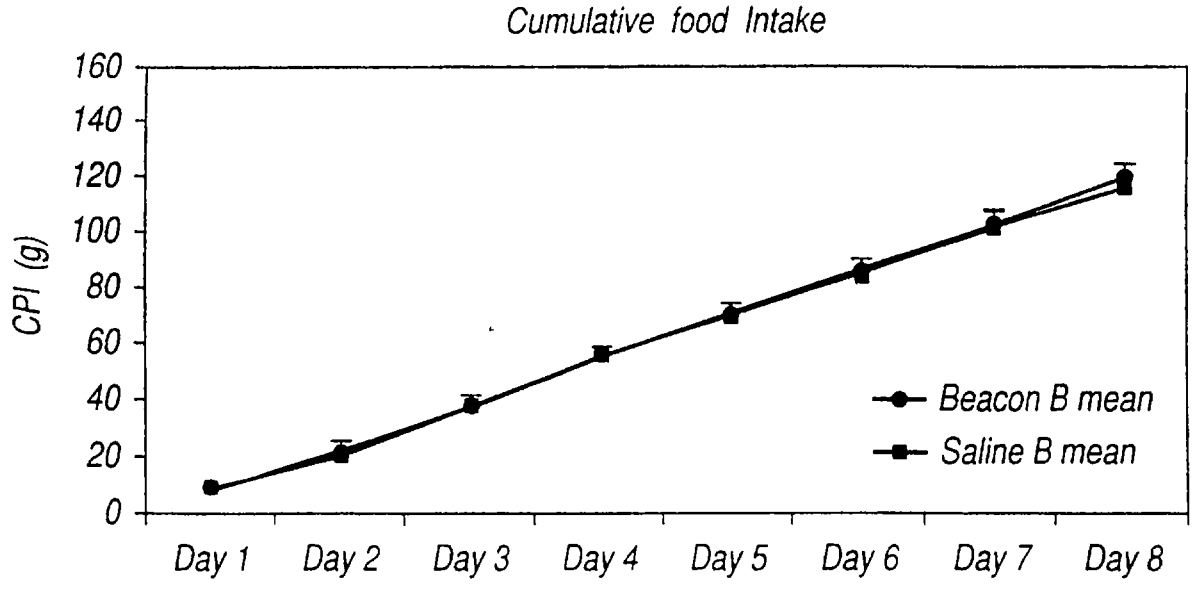


Fig.11A



* = significant. $p<0.05$

Fig.11B

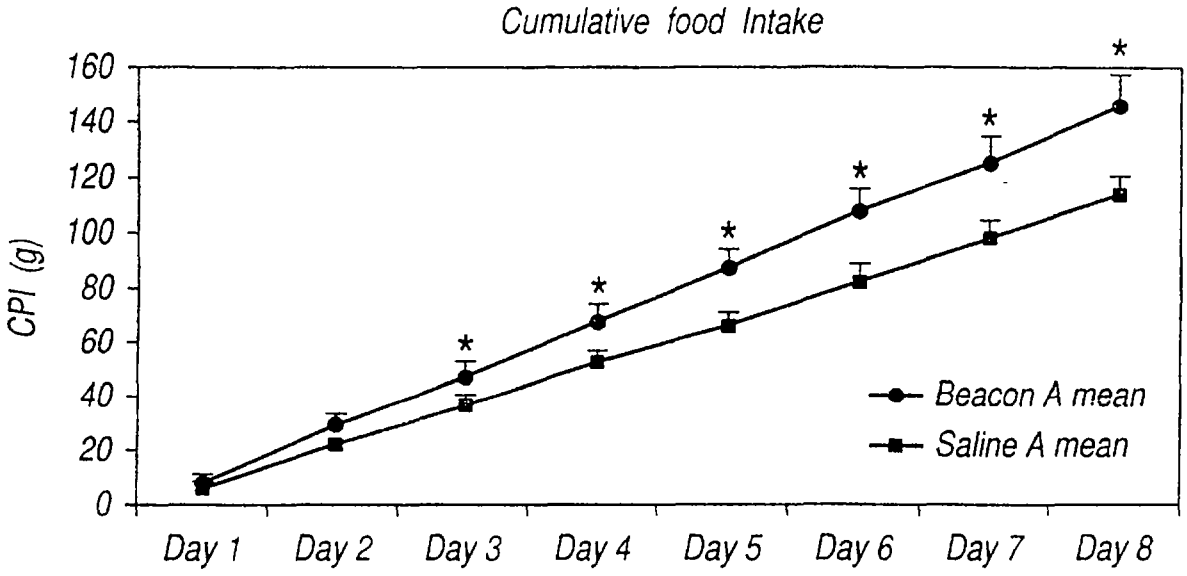

Cumulative food Intake
CPI (g)
160
140
120
100
80
60
40
20
0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Beacon A mean
Saline A mean
*

Fig.11C

Beacon v. Body Weight and % Fat in Group A animals

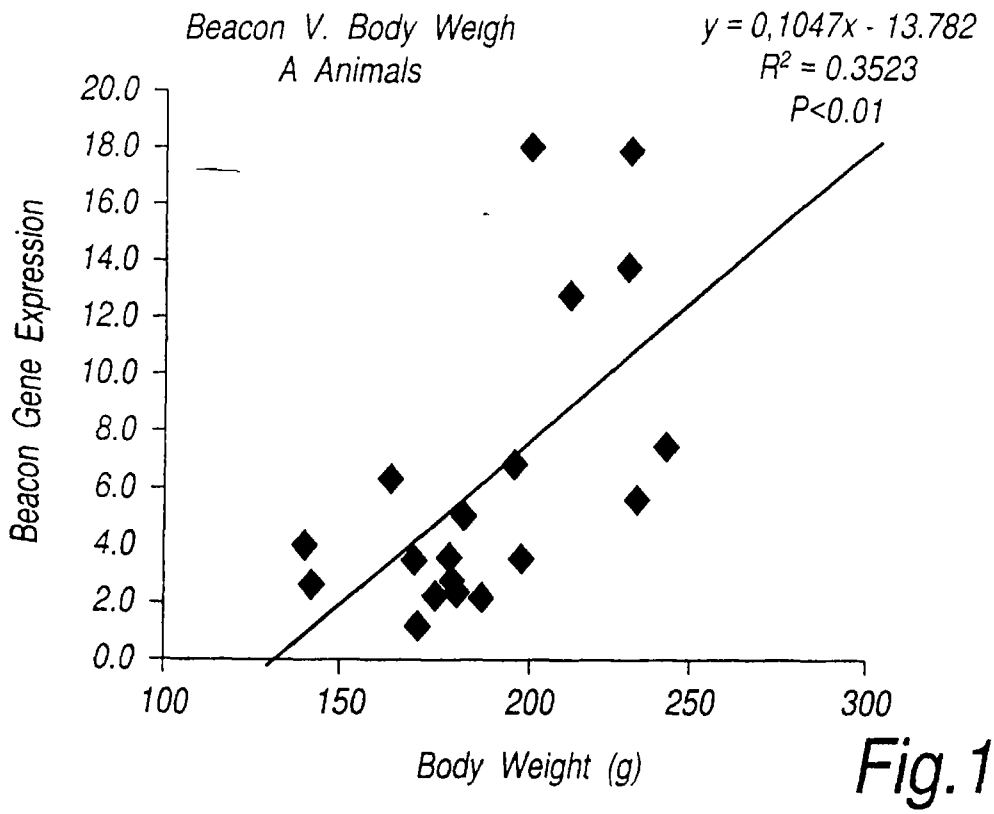


Fig.12A

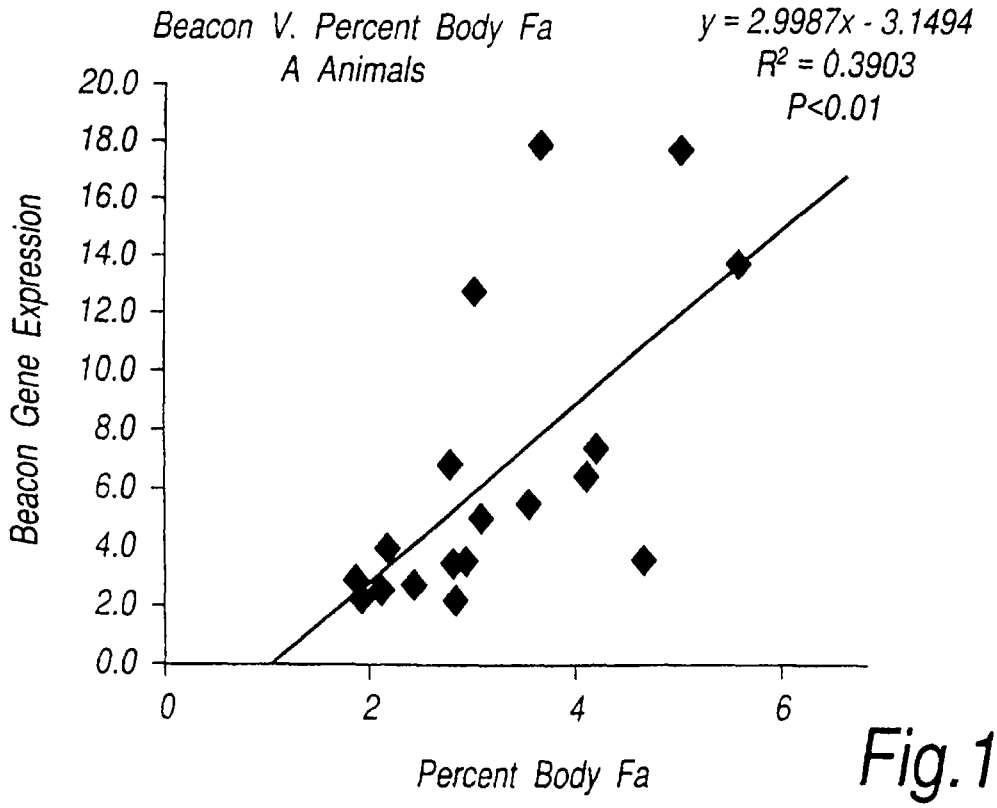


Fig.12B

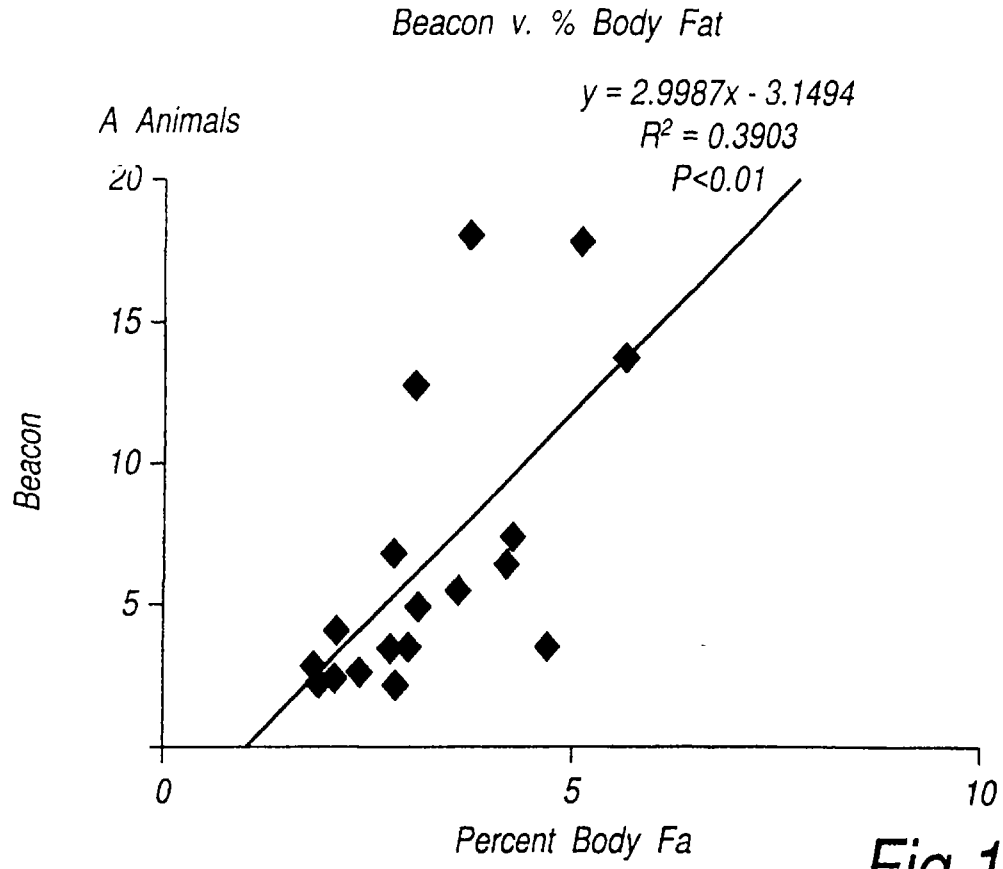


Fig.13A

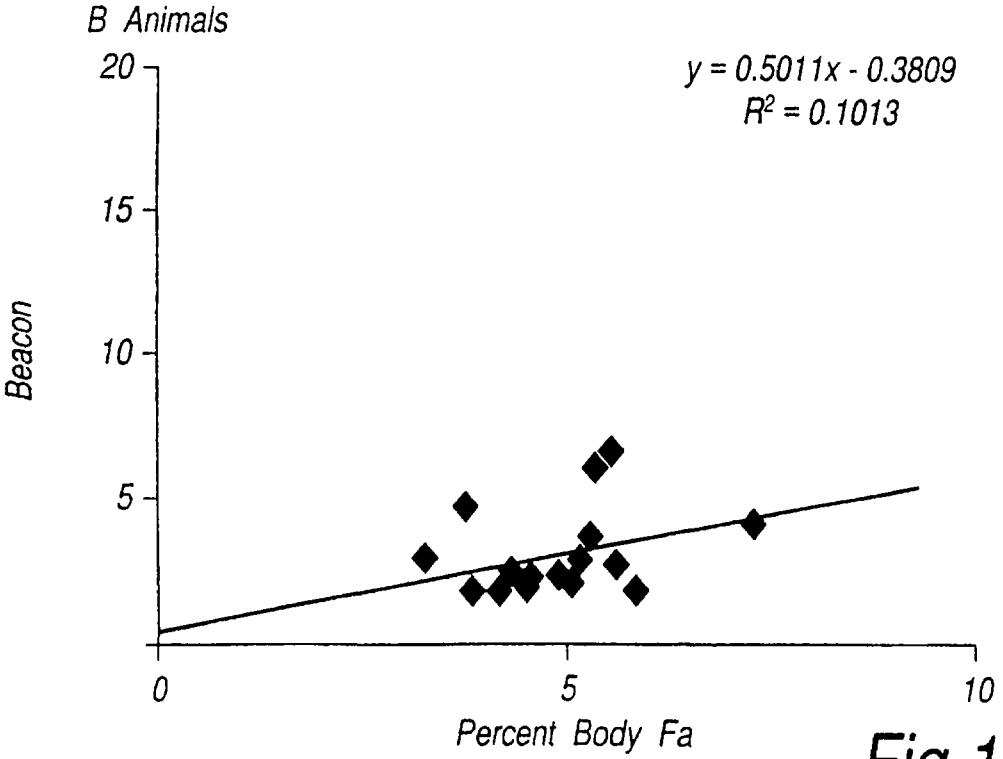


Fig.13B

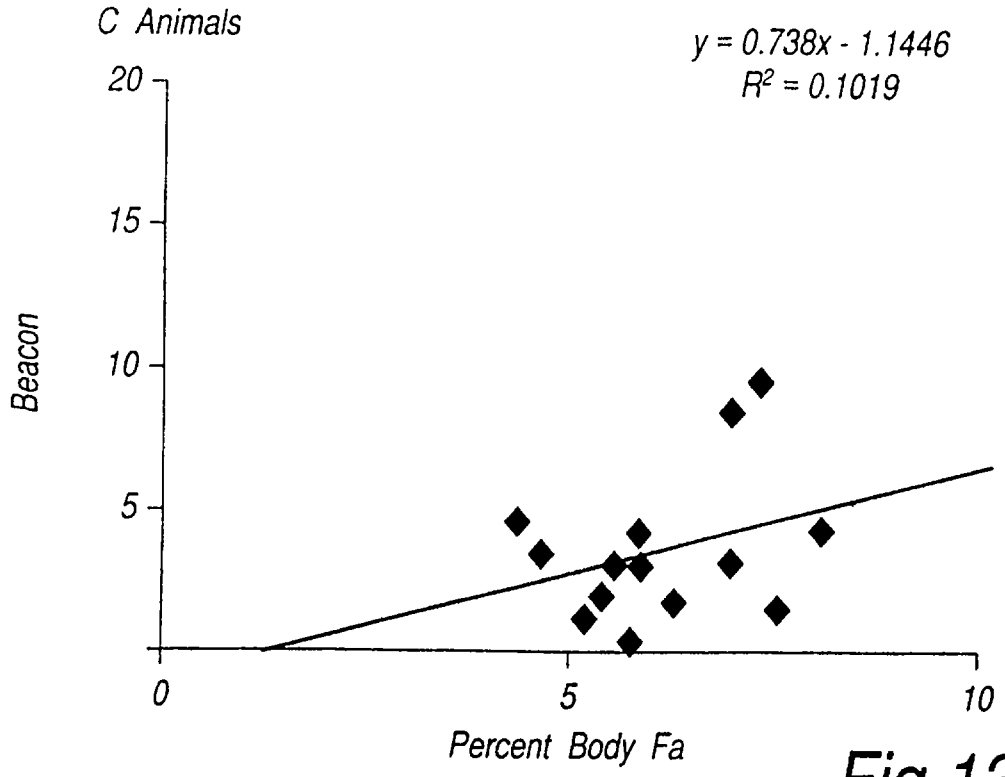


Fig.13C

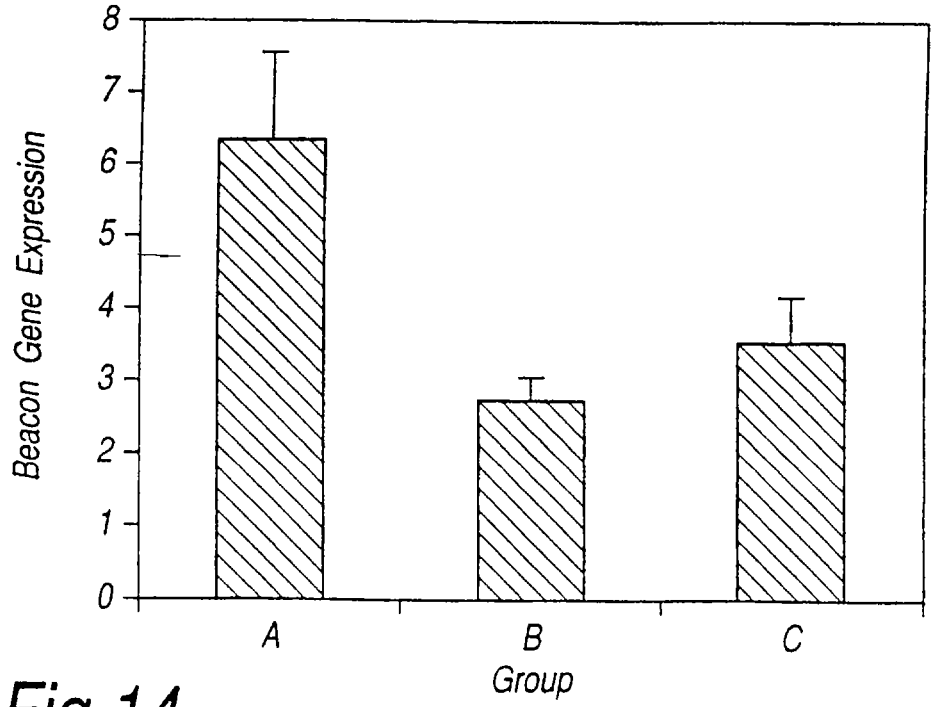


Fig.14

P<0.01 between Group A and B

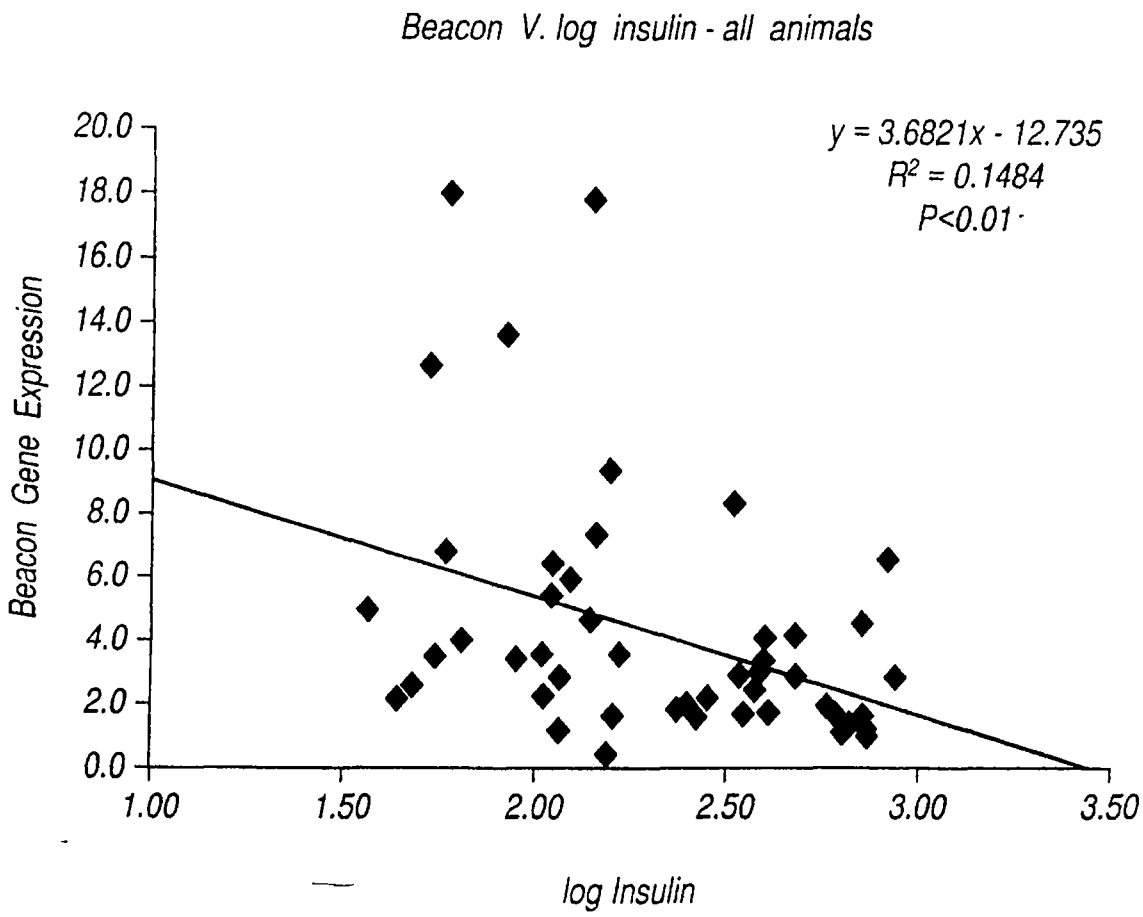

Beacon V. log insulin - all animals
y = 3.6821x - 12.735
R2 = 0.1484
P<0.01
Beacon Gene Expression
20.0
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
1.00
1.50
2.00
2.50
3.00
3.50
log Insulin

Fig.15