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C12Q 1/00 (2006.01), *C12Q 1/02* (2006.01)

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(54) Titre : METHODE DE TRAITEMENT ET DE PREVENTION DE LA DECALCIFICATION
(54) Title: METHOD OF TREATING AND PREVENTING BONE LOSS

(57) Abrégé/Abstract:
Methods of treating and preventing bone loss and/or enhancing bone formation are disclosed. The methods utilize 15-lipoxygenase inhibitors. These molecules can be delivered alone or in combination with agents which inhibit bone resorption or additional agents that regulate calcium resorption from bone or enhances bone accumulation. The invention additionally provides methods of diagnosing a predisposition to bone loss.

ABSTRACT

Methods of treating and preventing bone loss and/or enhancing bone formation are disclosed. The methods utilize 15-lipoxygenase inhibitors. These molecules can be delivered alone or in combination with agents which inhibit bone resorption or additional agents that regulate calcium resorption from bone or enhances bone accumulation. The invention additionally provides methods of diagnosing a predisposition to bone loss.

SEQUENCE LISTING

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The Government of the United States, Department of Veterans Affairs
Oregon Health & Sciences University

<120> Use of 15-Lipoxygenase Inhibitors for Treating and Preventing Bone Loss

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CLAIMS:

1. A method for identifying compounds that increase bone mineral density, the method comprising the steps of:

contacting a compound with 15-lipoxygenase; and,

determining whether the compound inhibits 15-lipoxygenase activity.

2. The method of claim 1, further comprising the step of testing the compound in a functional assay that demonstrates an effect of the compound on bone formation.

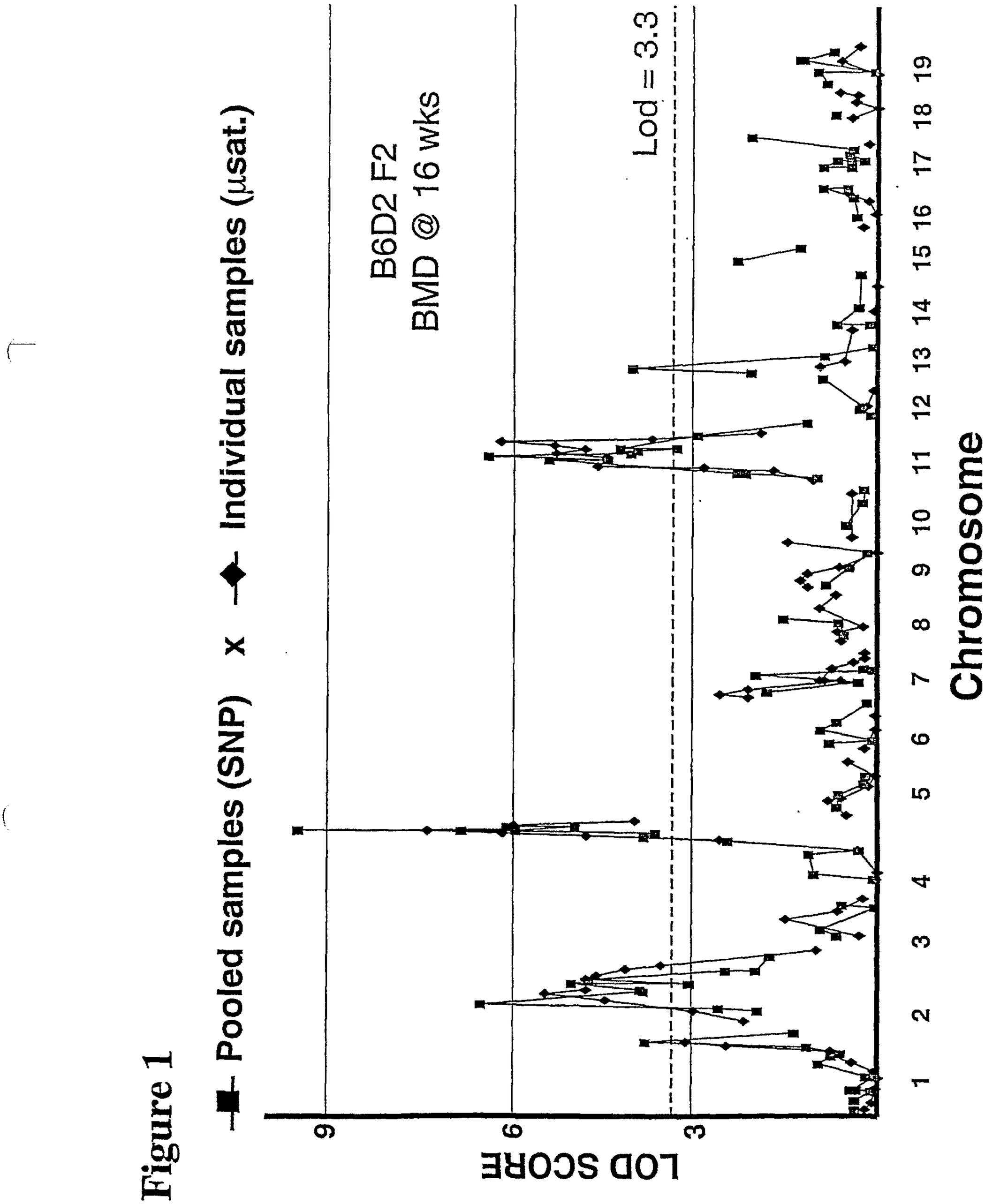
3. The method of claim 2, wherein the functional assay comprises contacting the compound with human mesenchymal stem cells and determining cellular differentiation into bone forming cells.

4. The method of claim 2, wherein the functional assay comprises administering the compound to a non-human animal and measuring an index of bone formation.

5. The method of claim 4, wherein the index measured is bone mineral density.

6. The method of claim 4, wherein the index is a biomechanical parameter of bone.

7. The method of claim 3, wherein determining cellular differentiation comprises performing an alkaline phosphatase assay, a calcium assay, a total DNA preparation assay, or combinations thereof.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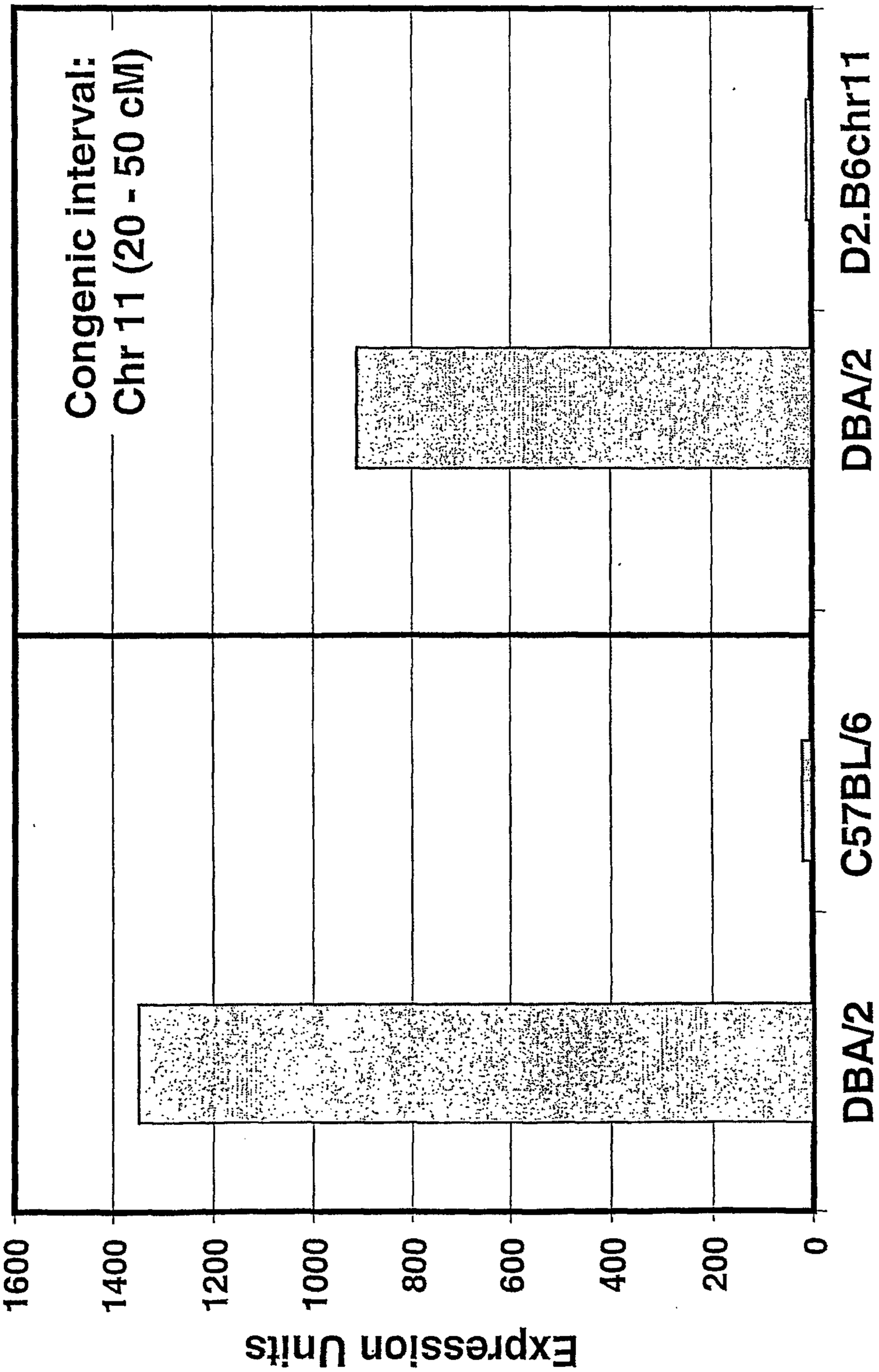
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Figure 2

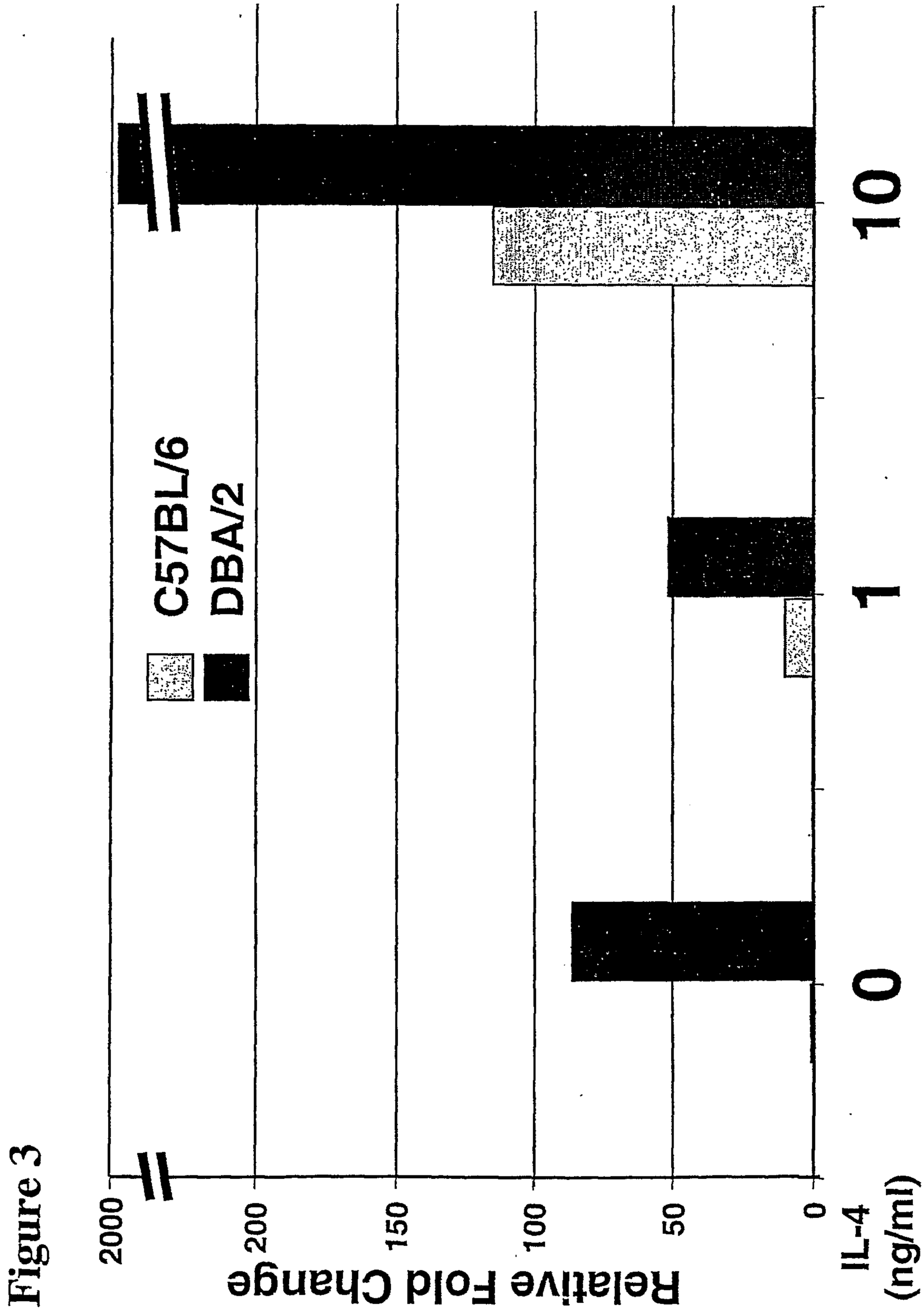
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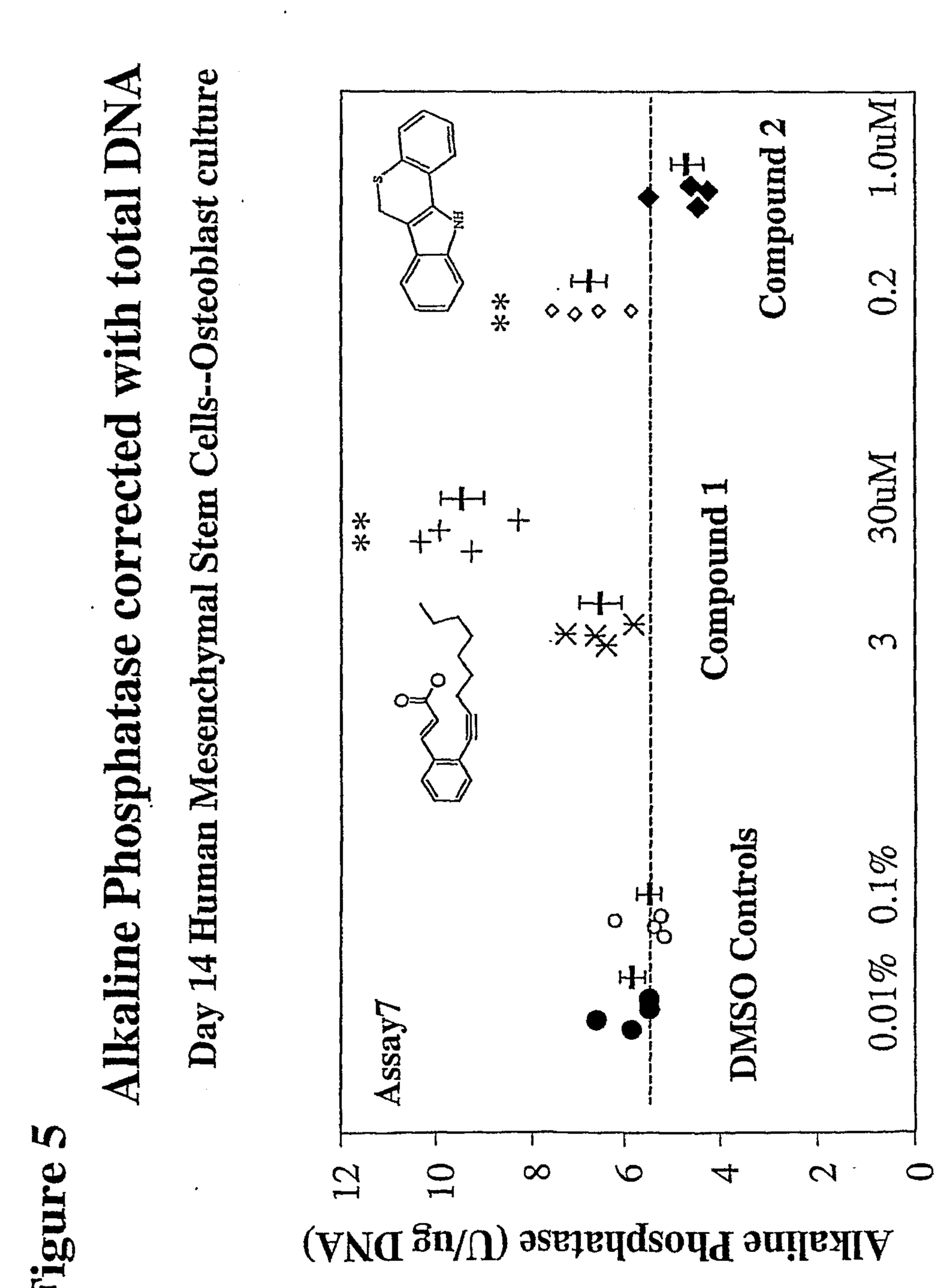
Figure 3

Figure 4



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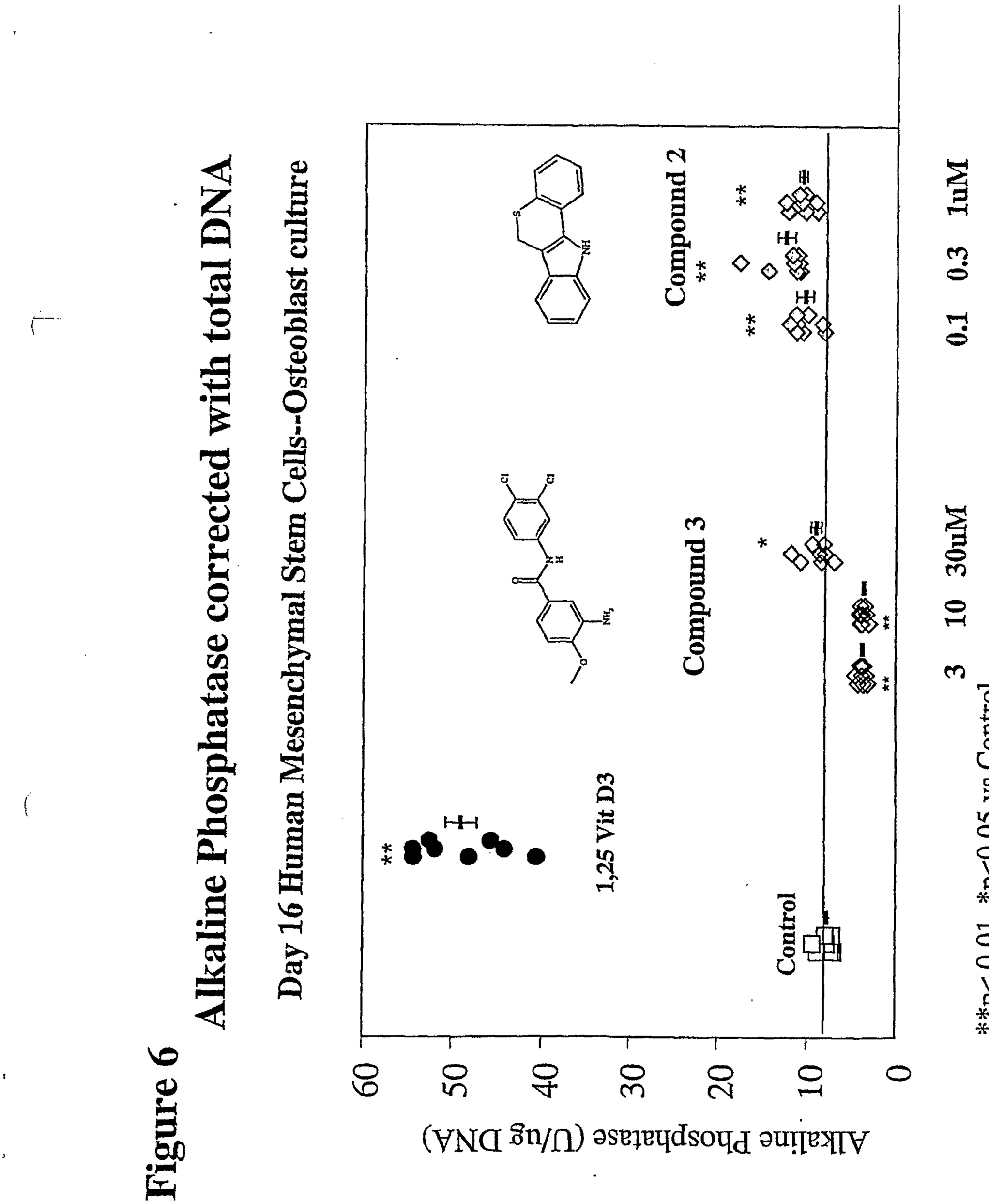
**p<,0.01, *p<0.05 vs Control.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Day 16 Human Mesenchymal Stem Cells--Osteoblast culture
Alkaline Phosphatase (U/ug DNA)
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50
40
30
20
10
0
Control
1,25 Vit D3
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Compound 3
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*
0.1 0.3 1uM
3 10 30uM
**p<,0.01, *p<0.05 vs Control.

Figure 6

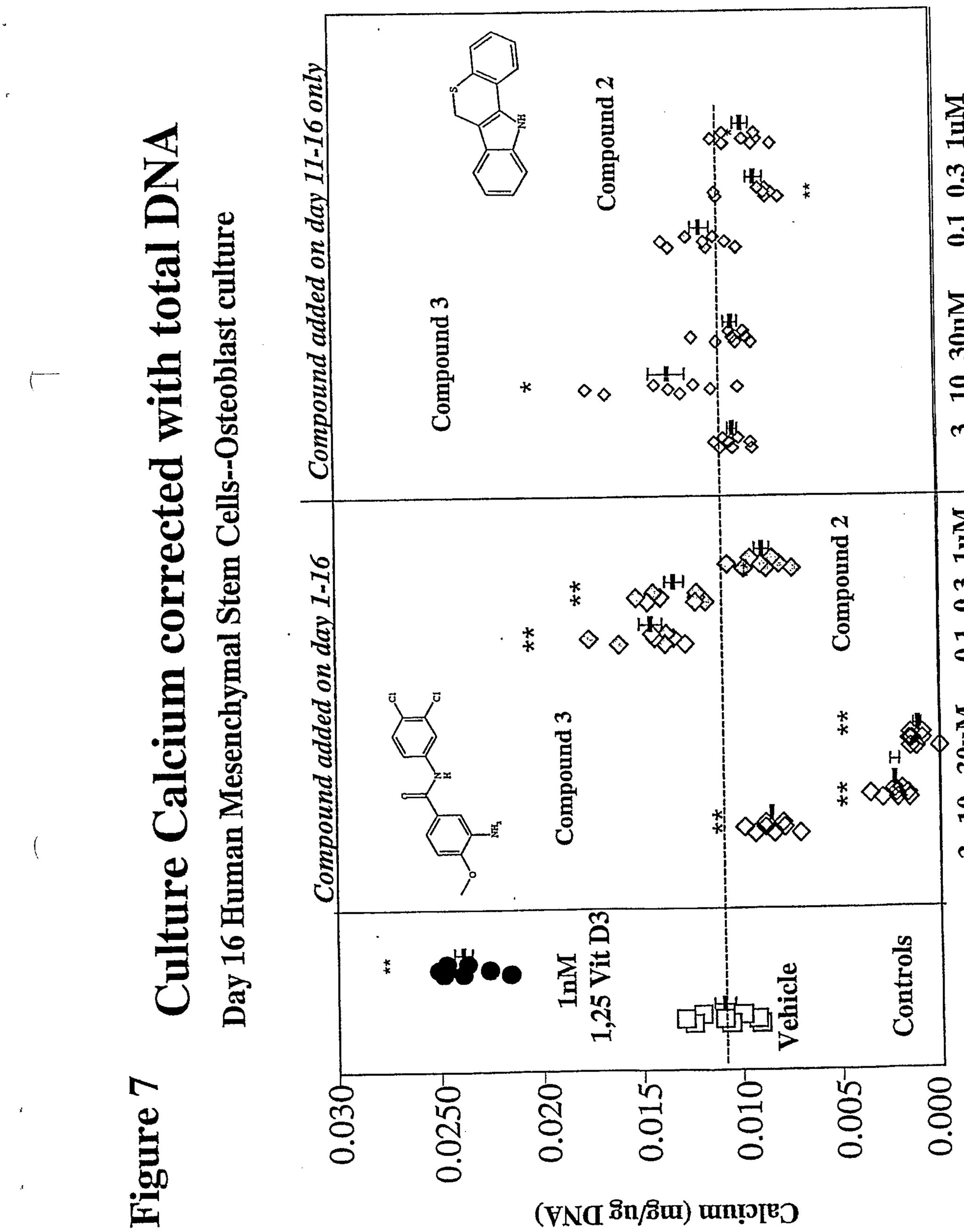
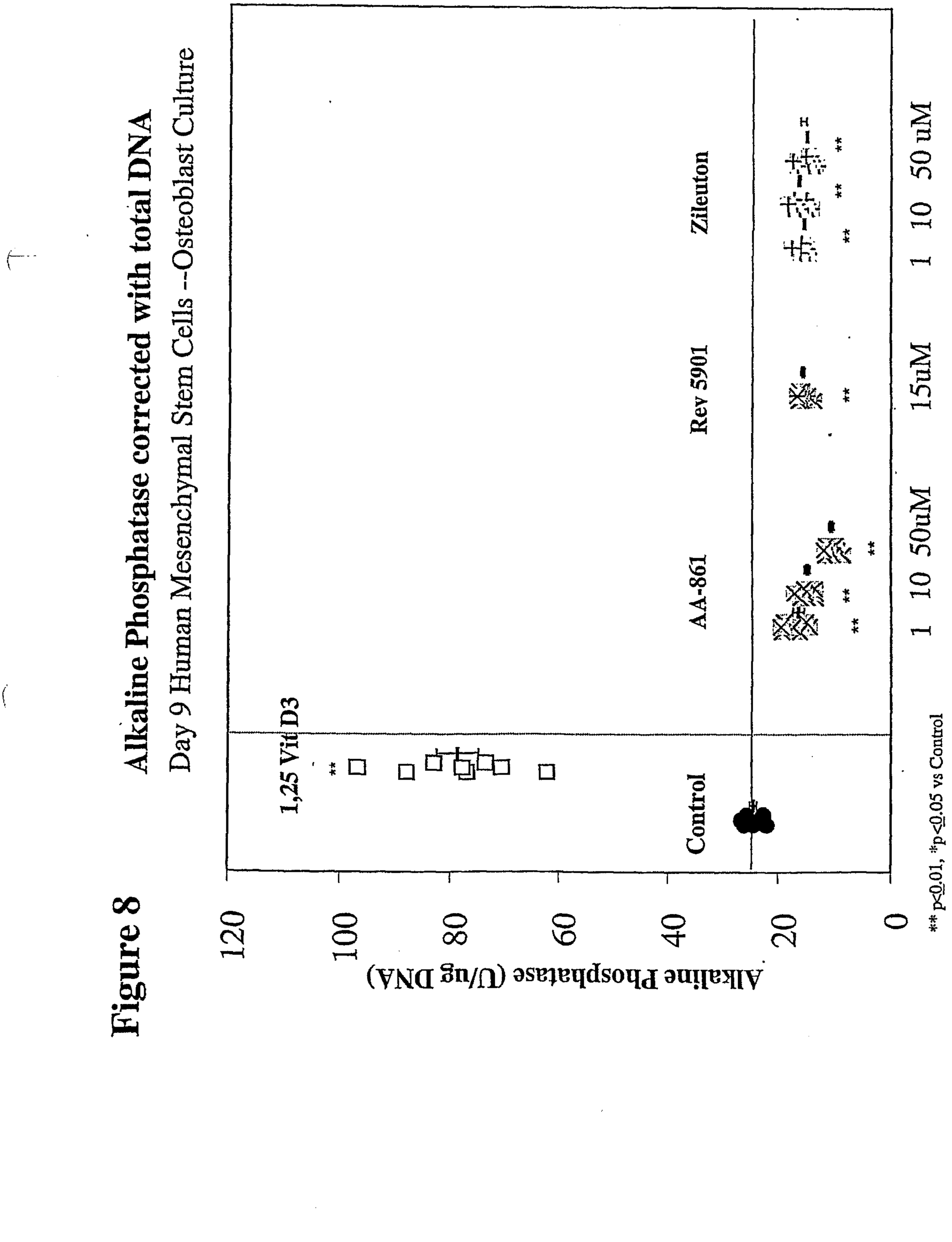


Figure 7

**p<,0.01, *p<0.05 vs Control.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1 10 50uM
** p≤0.01, * p≤0.05 vs Control
Alkaline Phosphatase (U/ug DNA)
120
100
80
60
40
20
0

Figure 8

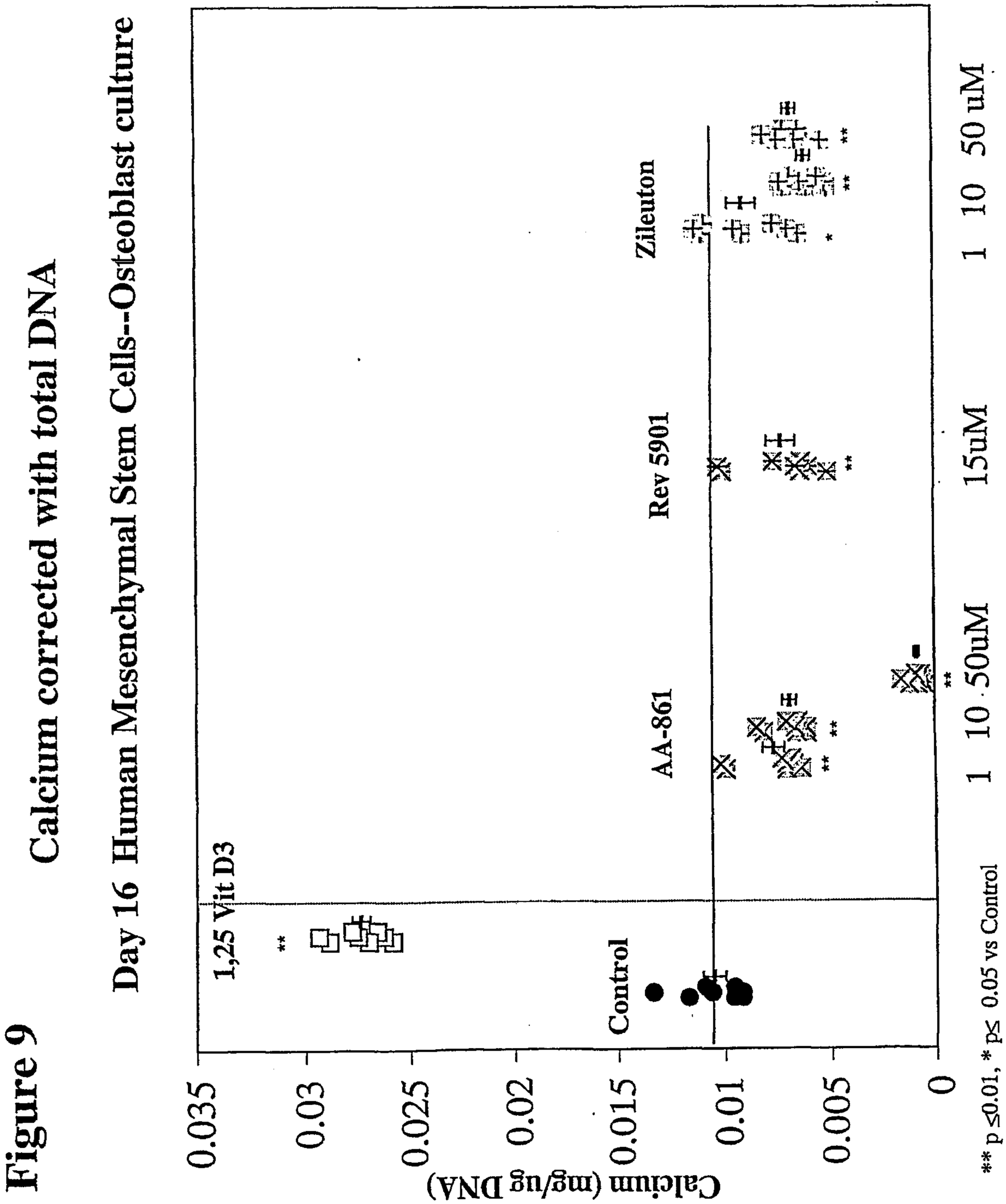
Calcium corrected with total DNA
Day 16 Human Mesenchymal Stem Cells--Osteoblast culture
1,25 Vit D3
AA-861
Zileuton
Rev 5901
Control
Calcium (mg/ug DNA)
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
1 10 50uM
15uM
** p ≤0.01, * p≤ 0.05 vs Control

Figure 9