

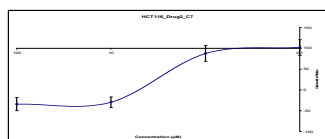
ANAVEX 7-1037, A NOVEL SMALL SYNTHETIC SIGMA LIGAND, INDUCES APOPTOSIS IN HUMAN HCT116 COLON CANCER CELLS *IN VITRO* AND SUPPRESSION OF HCT116 TUMOR GROWTH IN SCID MICE.

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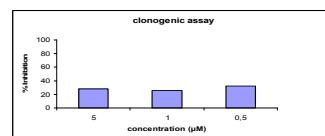
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- Sigma receptors are unique drug-binding proteins present in the central nervous system and in various peripheral tissues.
- It has been shown that sigma receptor subtypes are highly expressed in tumor cell lines from various tissues.
- Their high density in tumor and proliferating cells, makes sigma receptors potential target for diagnostic imaging as well as therapeutic agents.
- In the present study the compound Anavex 7-1037 (**C7**) was tested [chlorohydrate of 5-(Tricyclo[3,3,1,13,7]dec-1-yl)-dihydro-3-(dimethylamino-methyl)-5-phenylfuran-2(3H)-one].
- C7** is a low molecular weight, synthetic compound exhibiting high affinity for sigma-1 (nanomolar) and moderate (micromolar) affinity for sigma-2 and sodium channels.

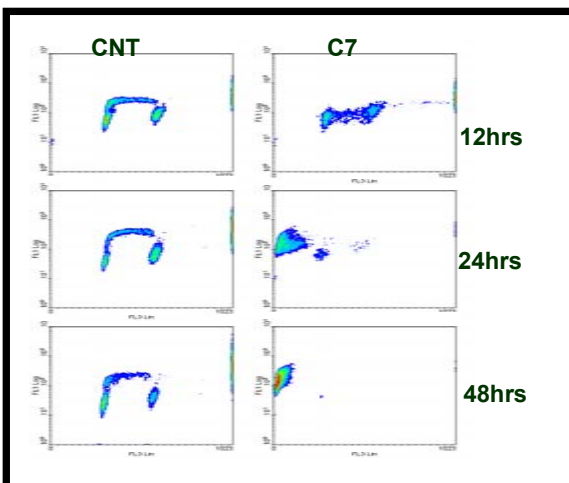
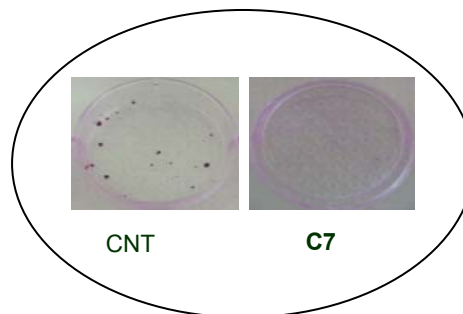
In vitro studies



SHORT TERM SRB ASSAY (2-days 5-dose) :
activity at low micromolar range.

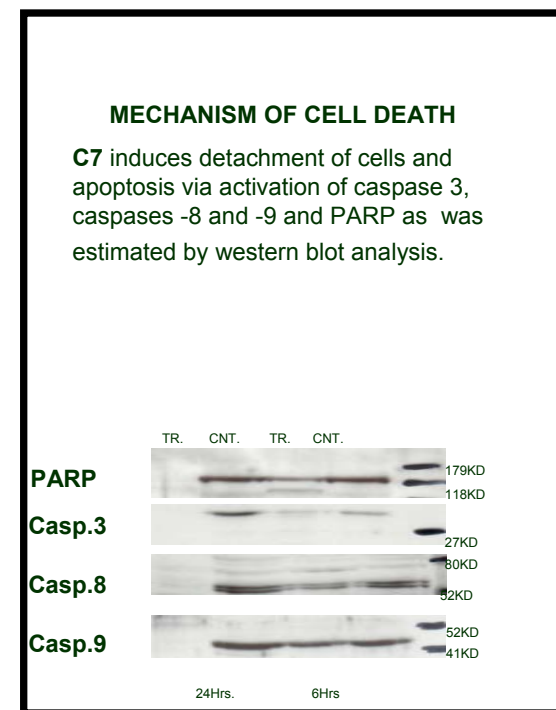


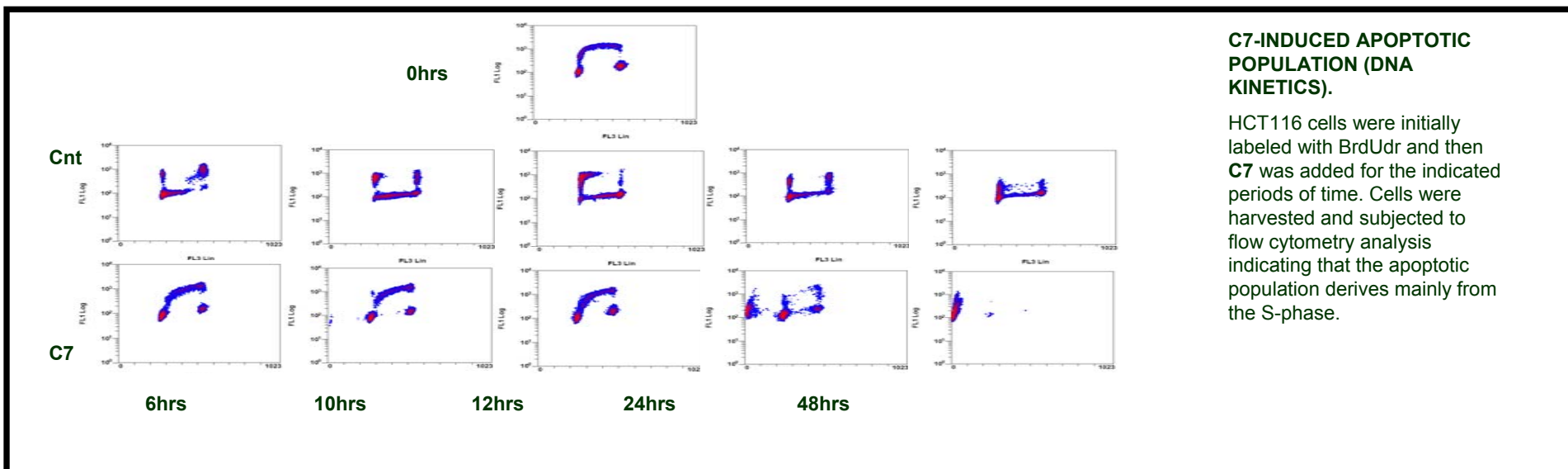
LONG TERM CLONOGENIC ASSAY (14-days 3-dose):
activity below 1μM.



C7-EFFECT ON CELL CYCLE

HCT116 cells were treated with **C7** for the indicated time periods. Cells were labeled with BrdUrdU, harvested and subjected to flow cytometry analysis, demonstrating arrest of the cell cycle.



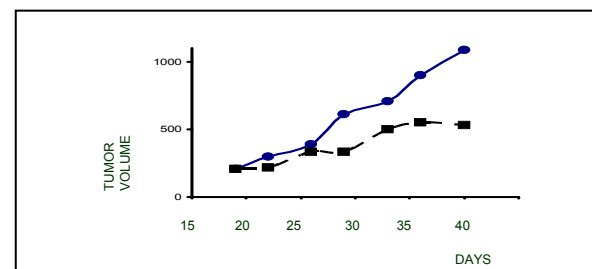


In vivo studies

C7-TREATMENT OF HCT116-XENOGRAFTED SCID MICE

C7 was administered i.p. following the Q4D3 schedule repeated for two weeks.

Average tumor size (in mm³) was calculated for untreated mice (●) and treated (100mg/kg, ■).



Conclusions

ANAVEX 7-1037 (C7)

- exhibits significant GI50 potency
- induces arrest and apoptosis affecting initially those cells that are in the S-phase of the cycle
- can significantly delay the growth of HCT116 xenografts
- This and other patented original sigma ligands are currently tested in vivo on different xenografts (prostate, breast, melanoma etc).