

U-Shaped Dose Responses and Antitumor Activity

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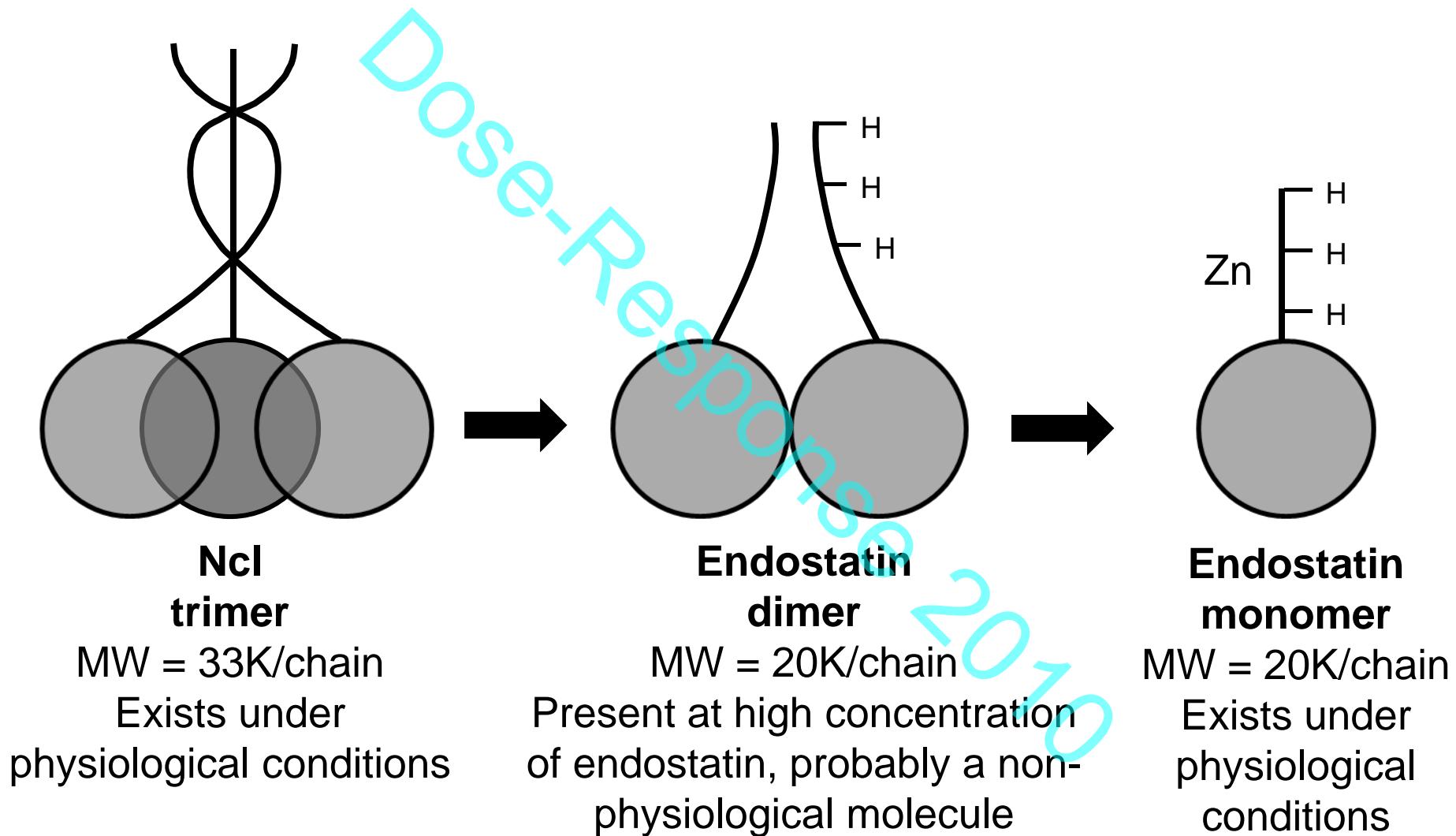
St. Elizabeth's Medical Center

Tufts Medical School

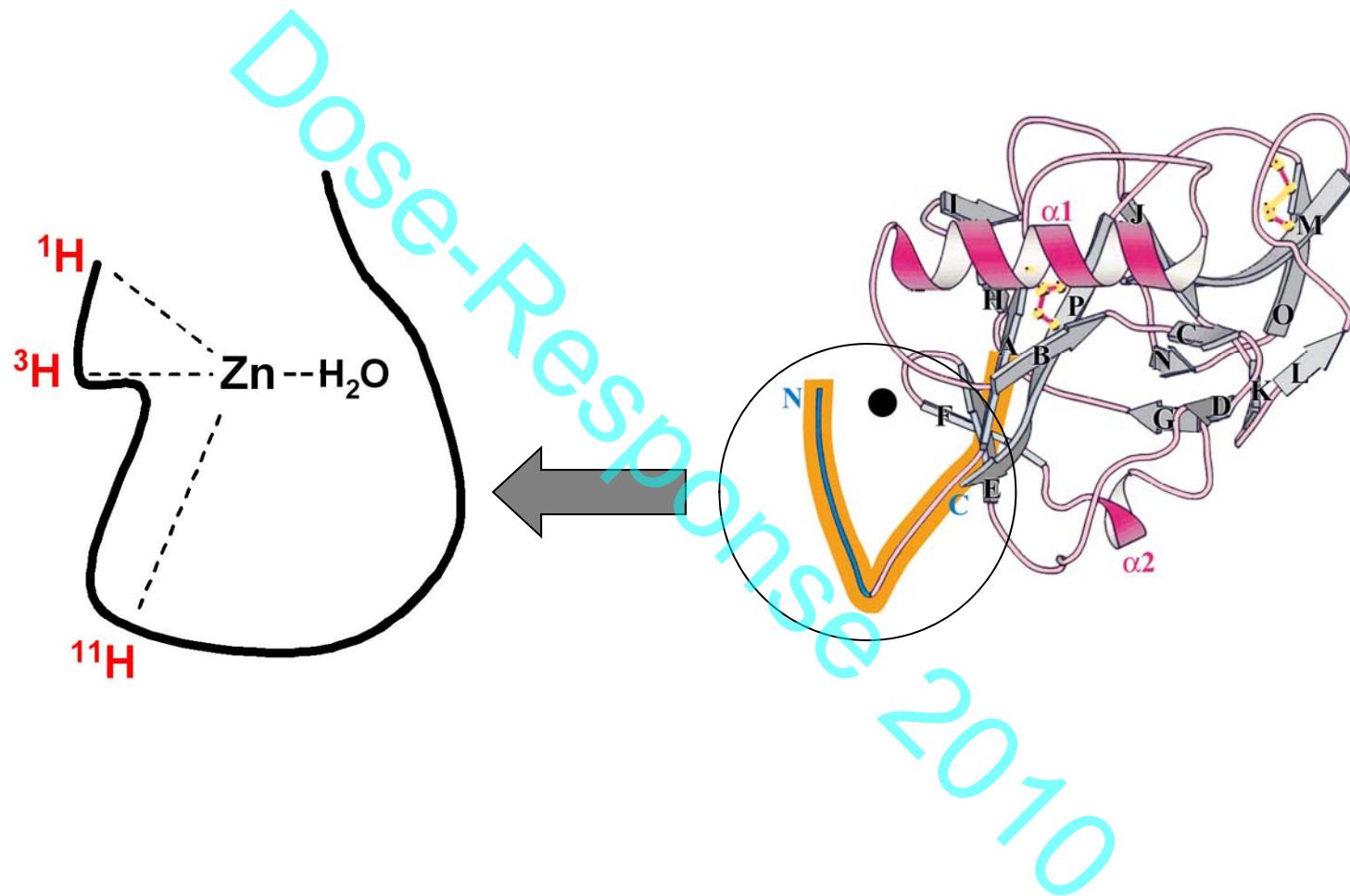
Boston, MA

Dose Response 2010

Oligomerization of endostatin

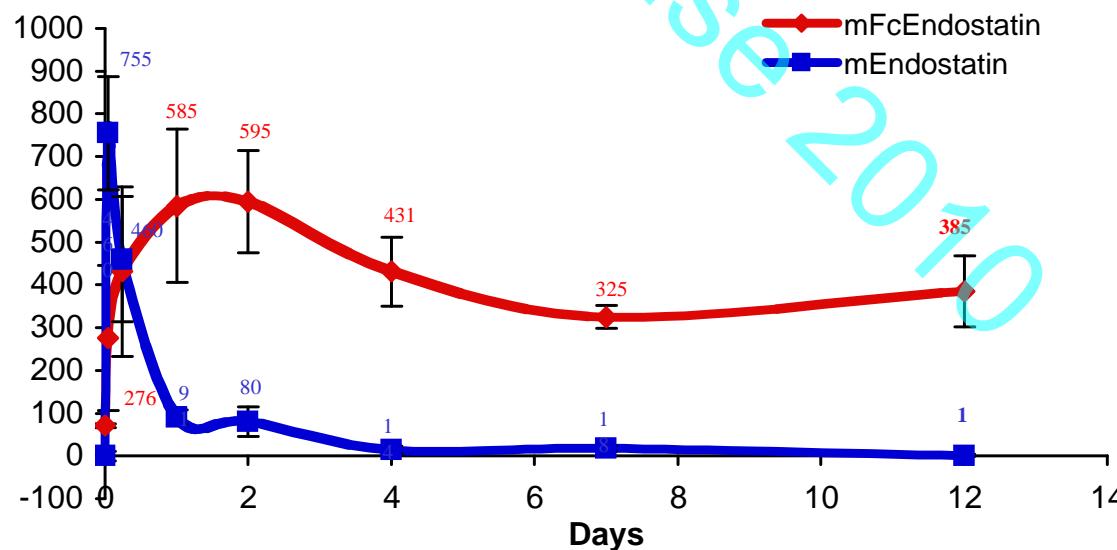
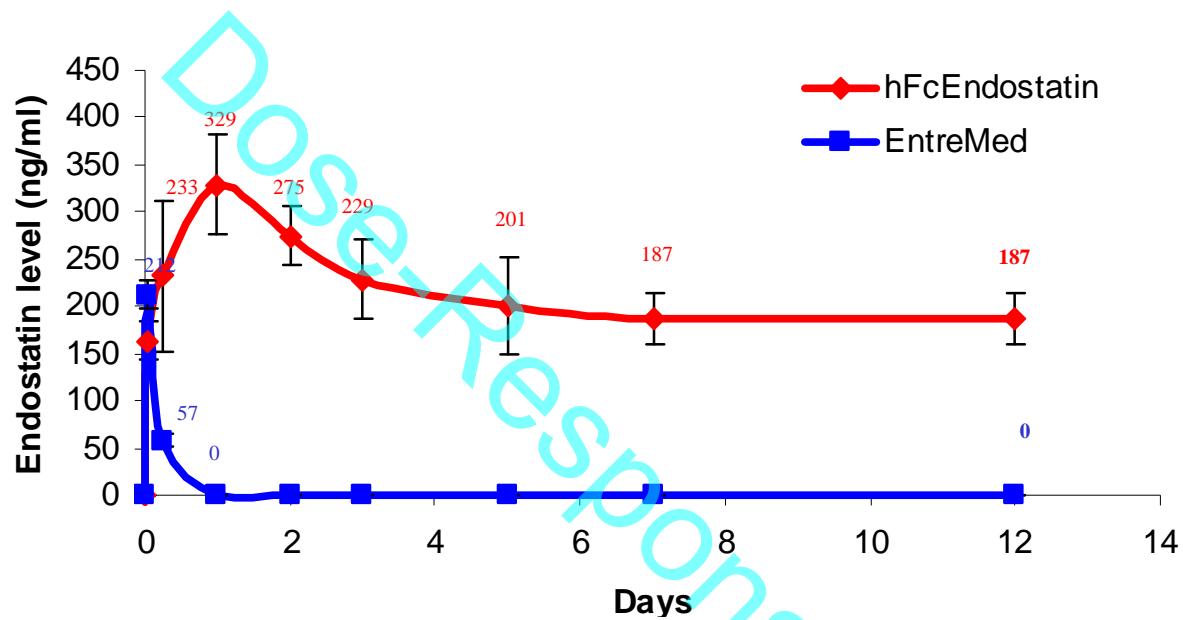


Crystal structure of endostatin

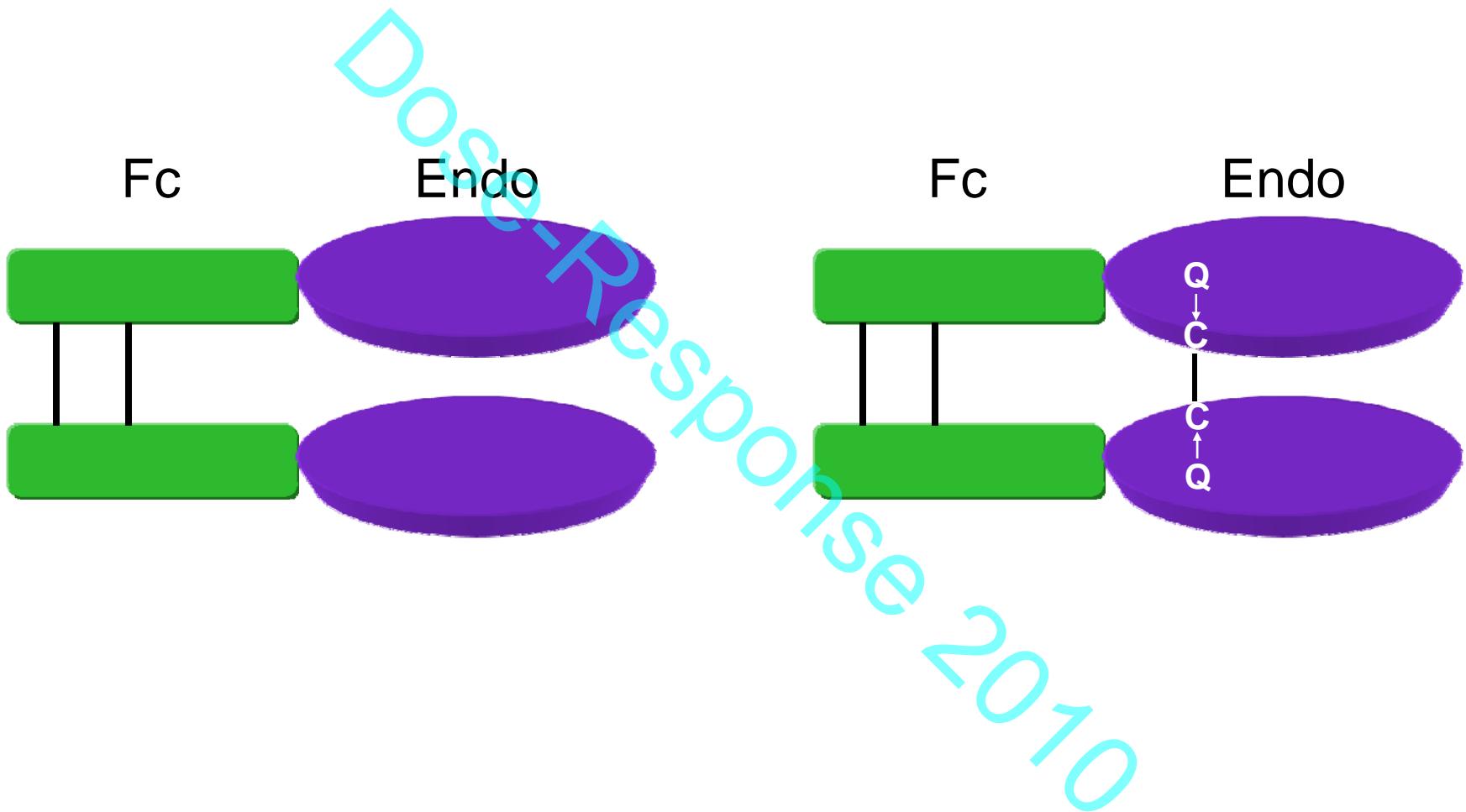


Tjin et al., (J. Folkman and K. Javaherian) Cancer Research, 65: 3656, 2005

Pharmacokinetic analysis of hFcES and hES in C57B mice (100 µg/mouse)

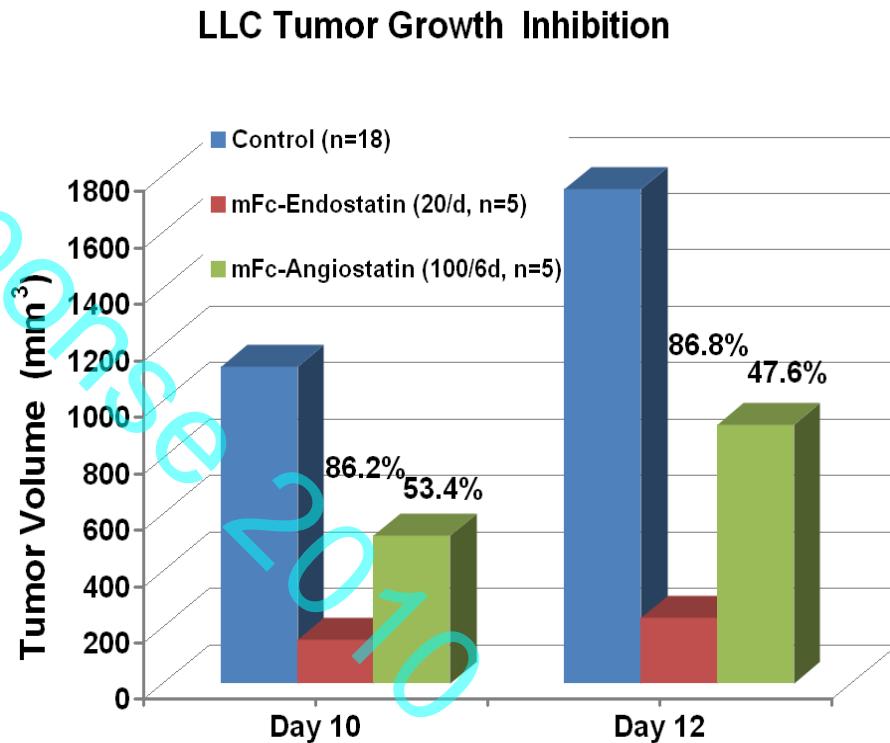
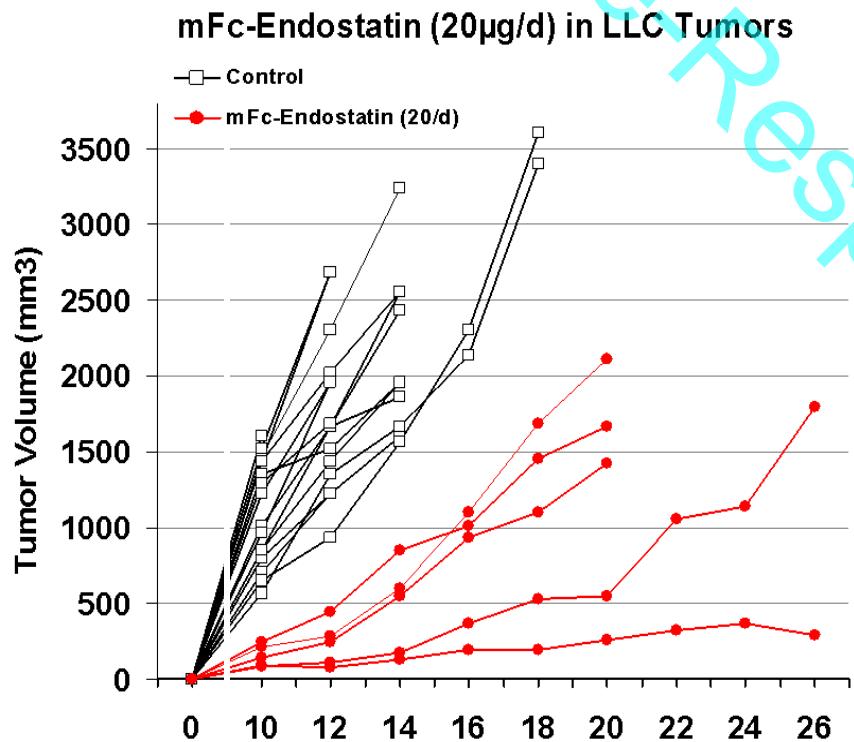


Fc-Endostatin and endostatin dimer

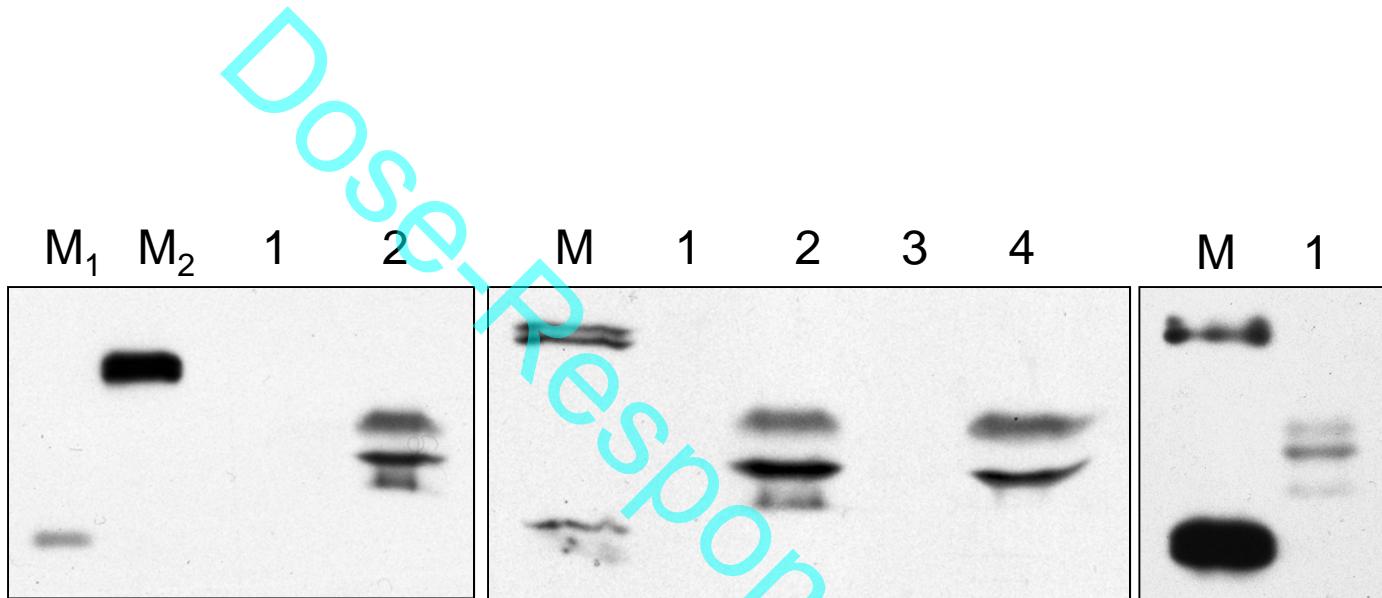


3. Results: LLC tumor growth

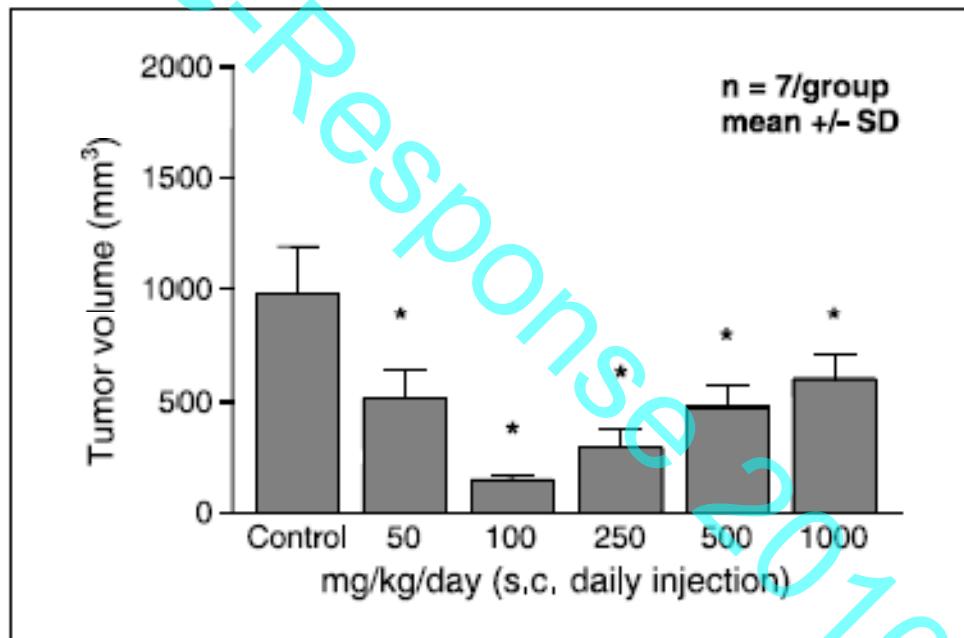
Tumor growth kinetic in P1 LLC: Endostatin & Angiostatin treatment



Size of NC1-Endostatin in human serum



Dose-Response 2010



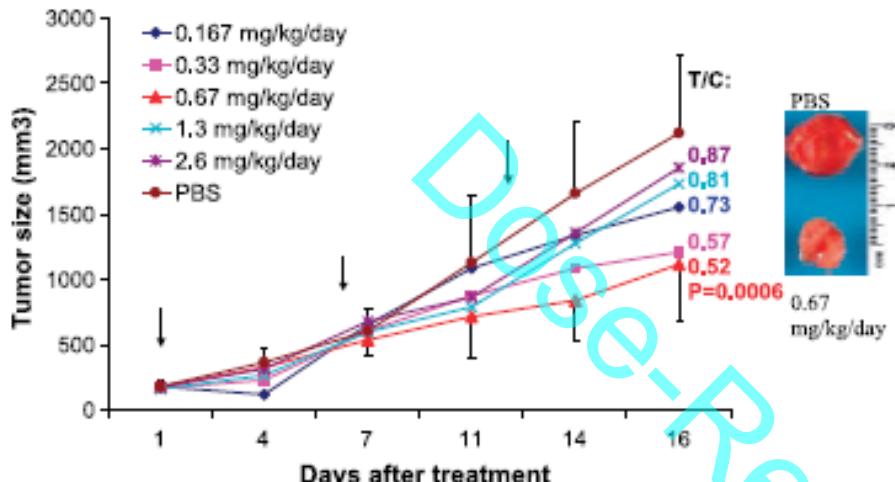
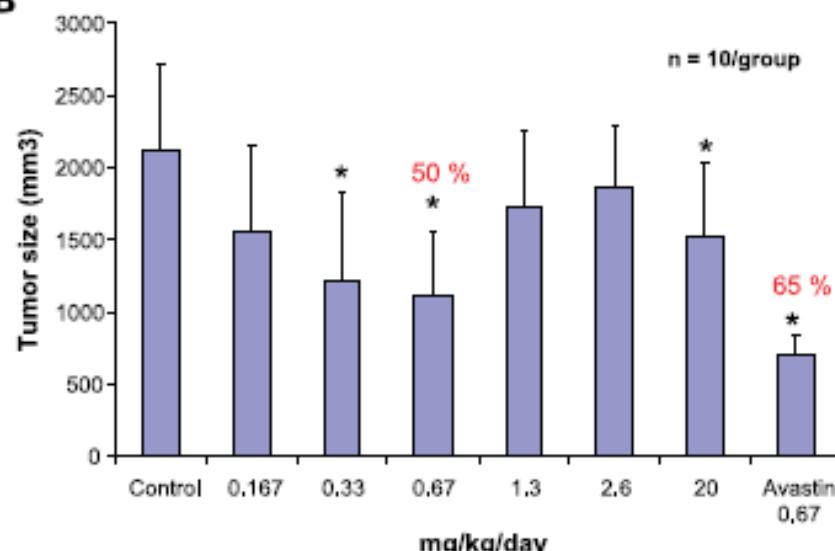
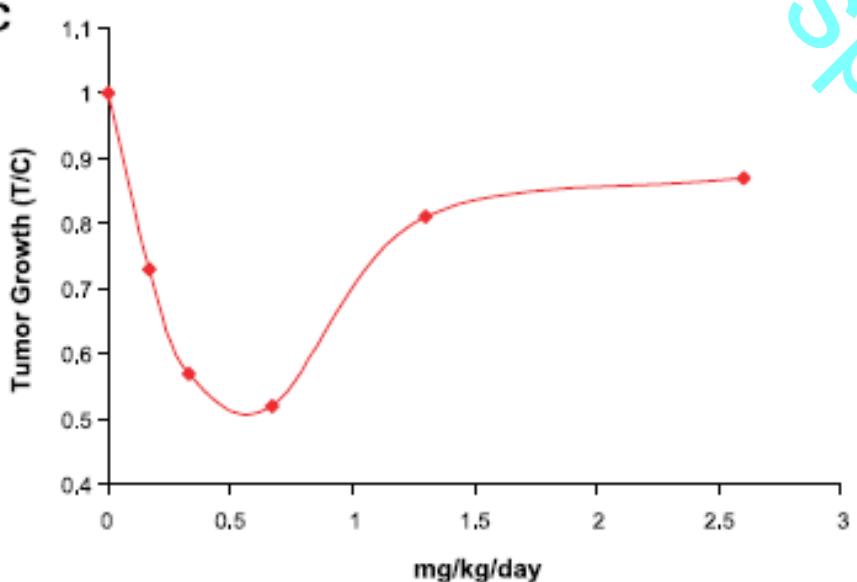
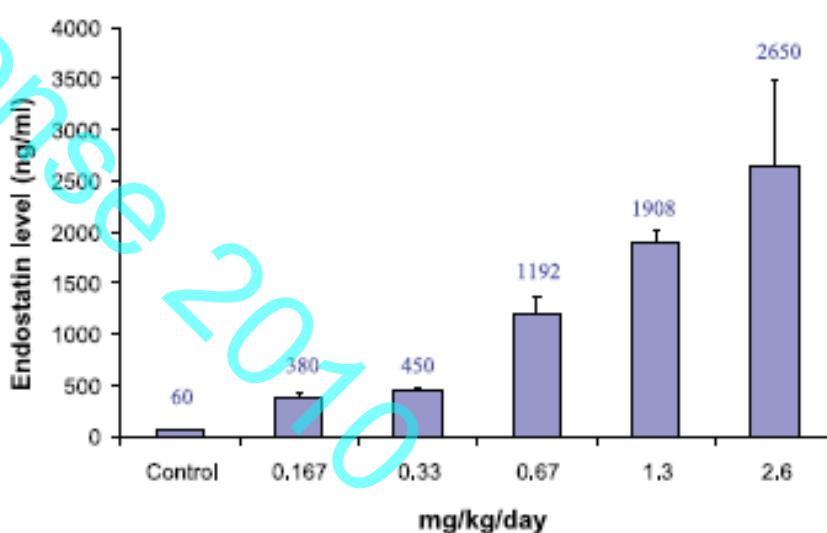
A**B****C****D**

Fig. 2. Treatment of human melanomas (A2058) with hFc-endostatin. Ten SCID mice in each group. S.c. injections were delivered in 0.2 mL volume of PBS once every 6 days; (↓) n = 10. *A*, tumor size as a function of time and concentration of endostatin. The ratio of T/C is shown for each group. *B*, tumor size is plotted as a function of concentration of the delivered protein. The Avastin dose is the same as endostatin at its optimum efficacy (0.67 mg/kg/d). Daily injection of clinical grade endostatin at 0.5 mg per mouse day (20 mg/kg/d). *C*, the U-shaped curve for data of *B*. *D*, ELISA of endostatin 3 days after the last injection.

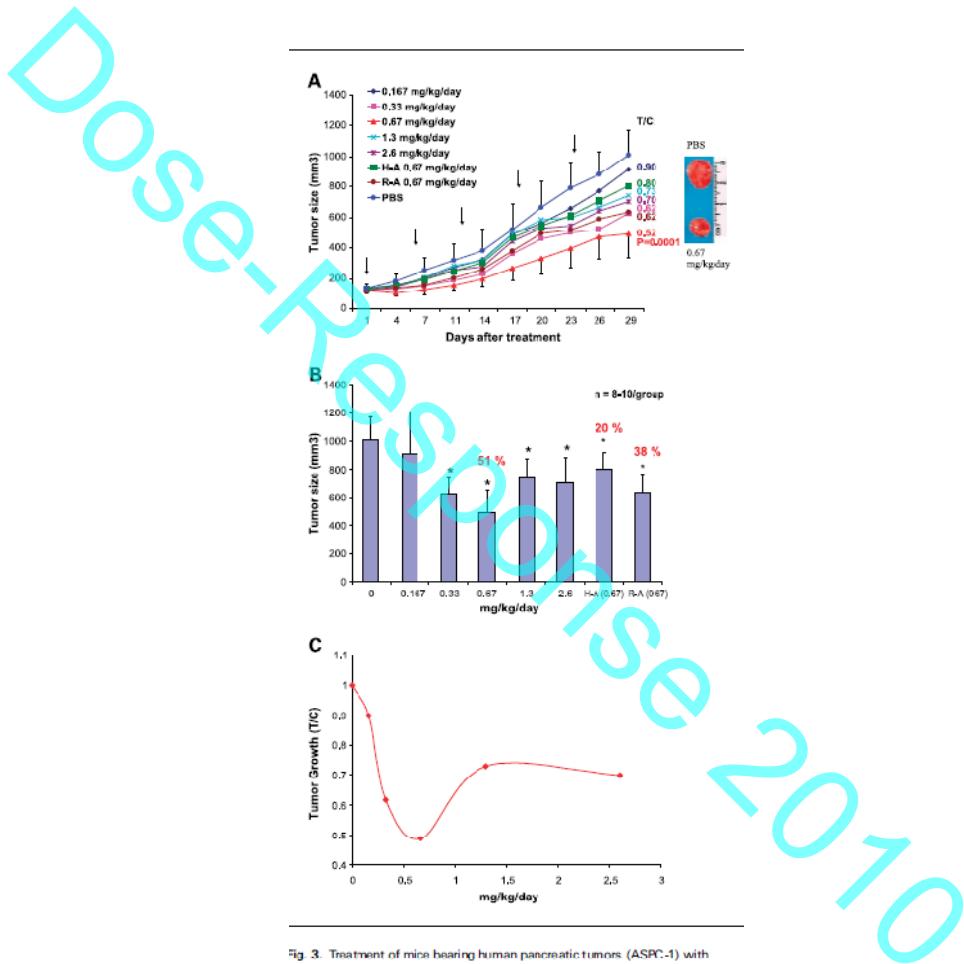
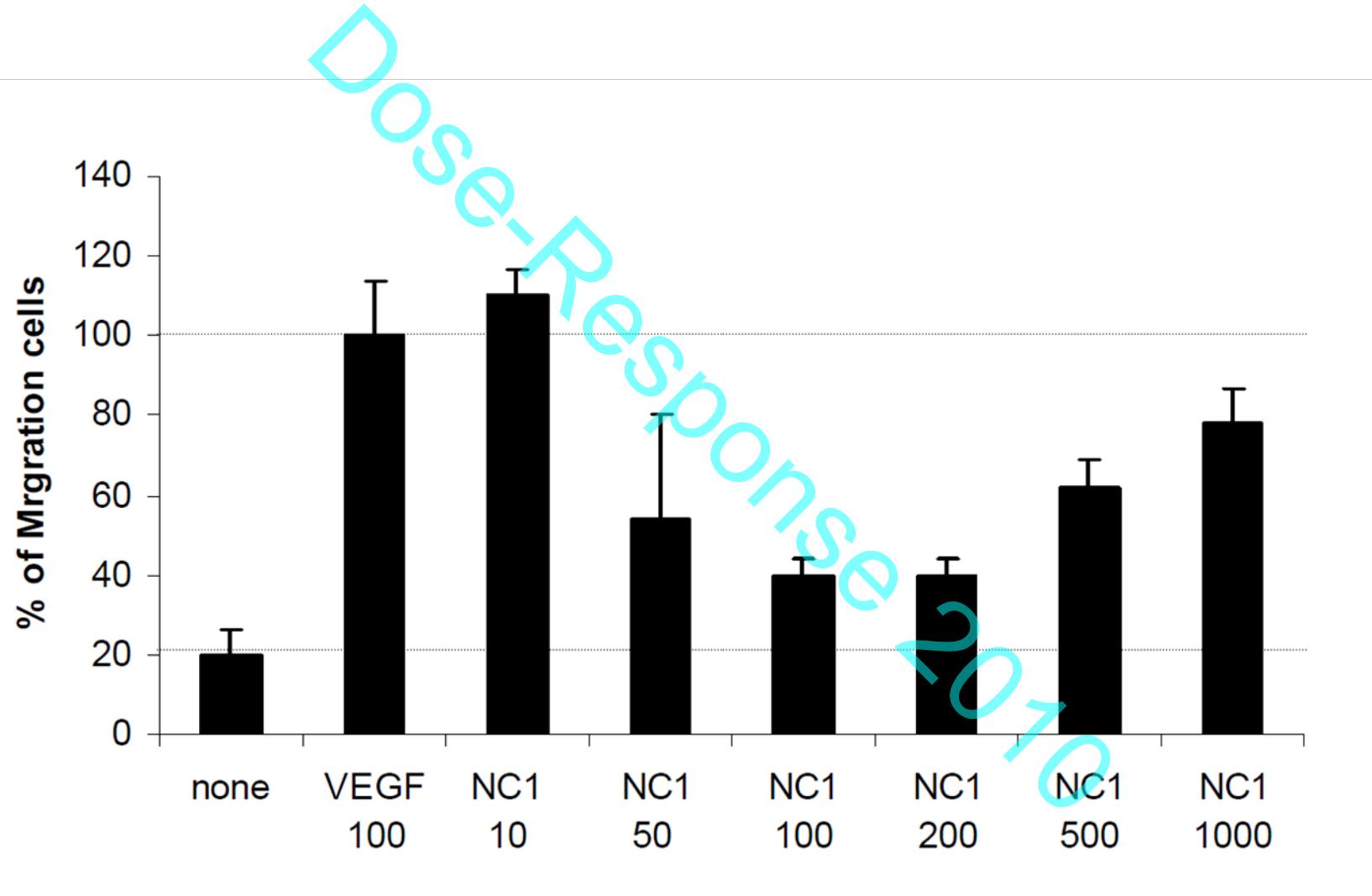
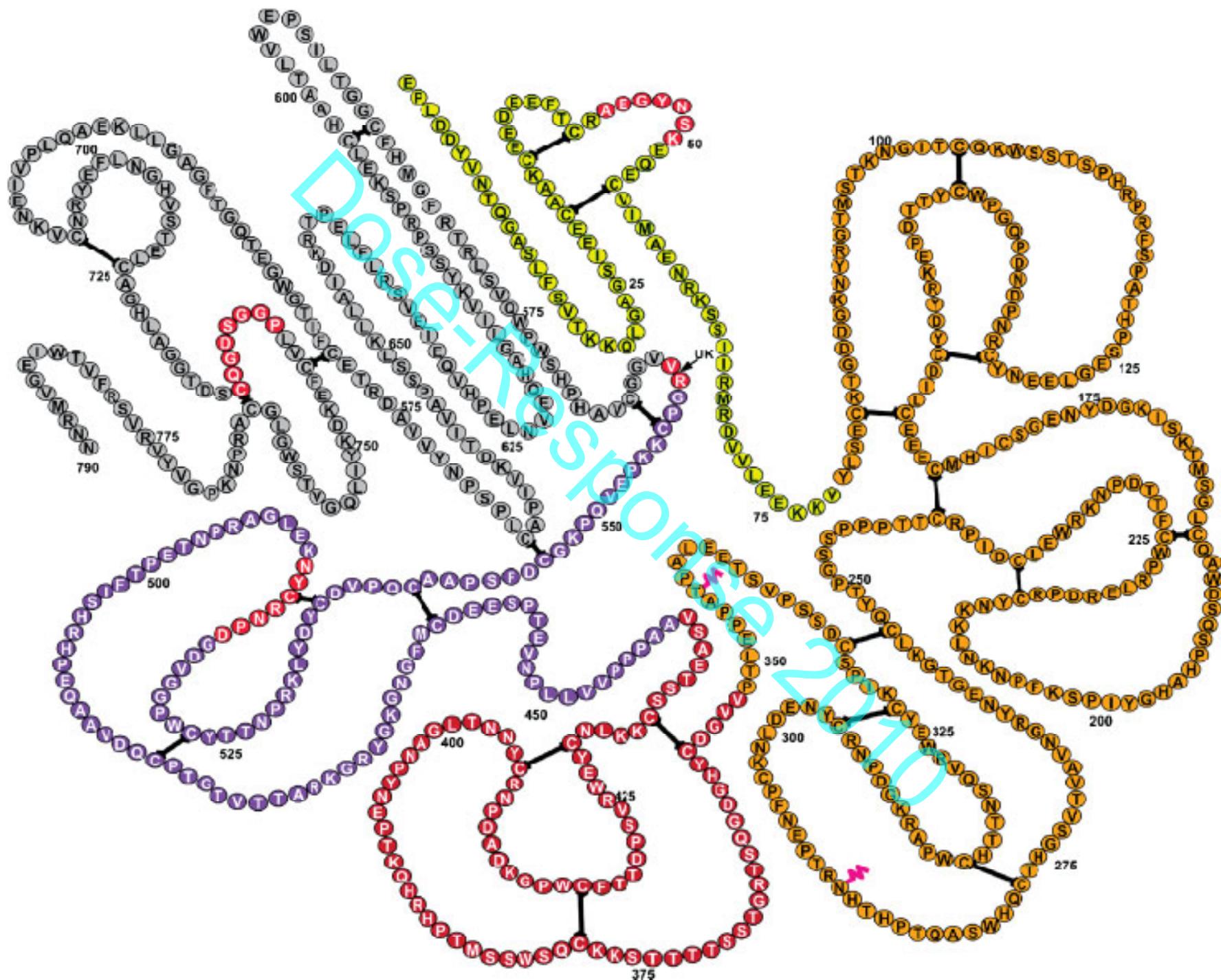
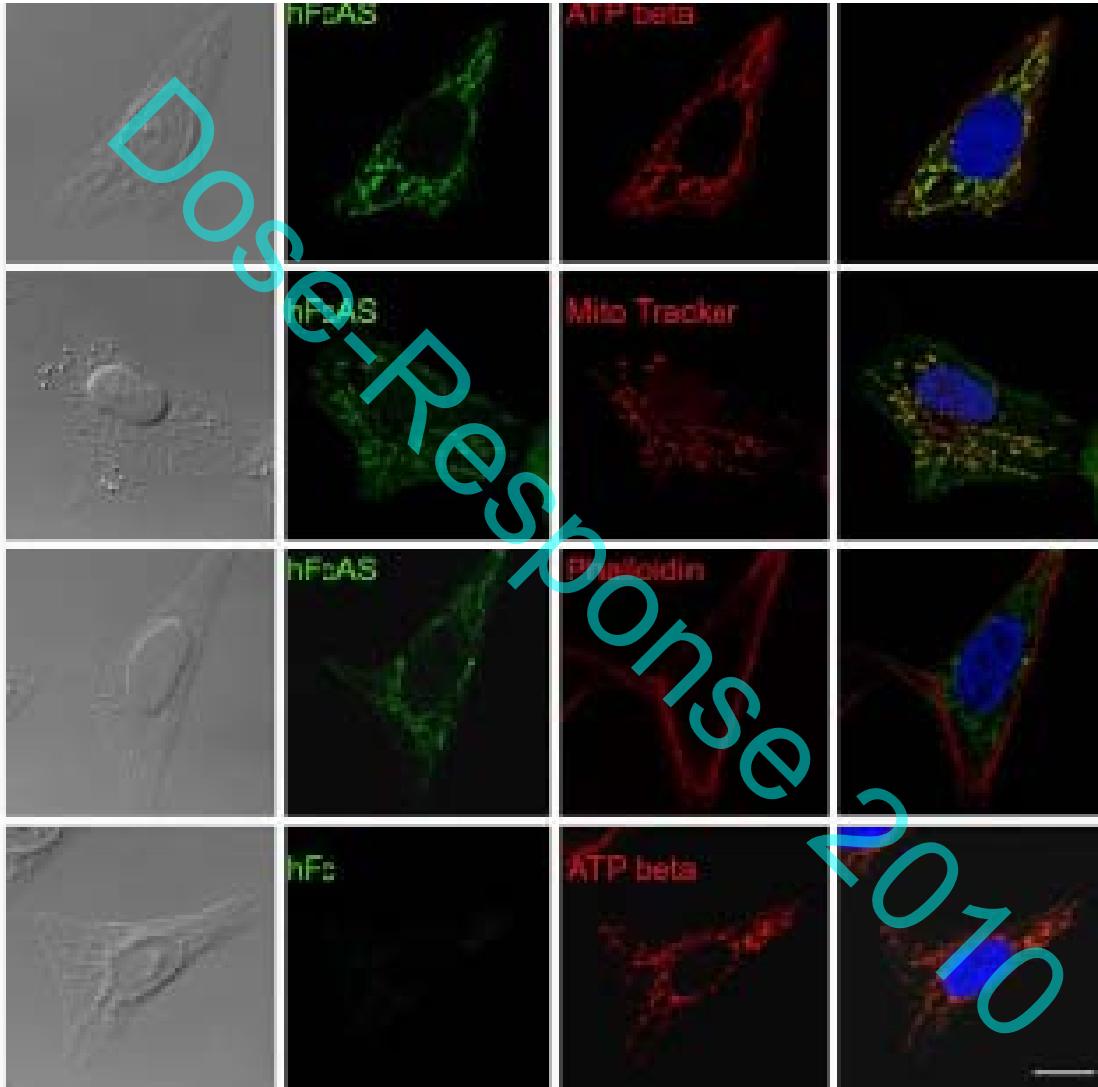


Fig. 3. Treatment of mice bearing human pancreatic tumors (ASPC-1) with ¹Fc-endostatin. The protocol was identical to that in Fig. 2 except a different tumor cell line was used. H-A, endostatin mutants H1A and H3A; R-A, endostatin mutants R27A and R139A.



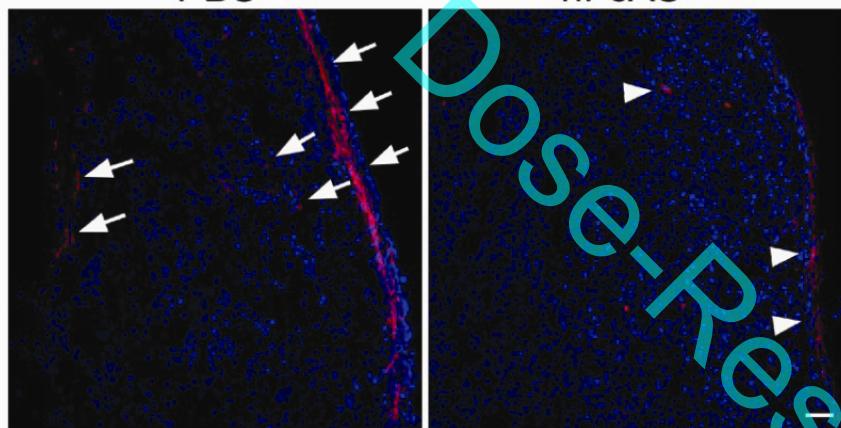




A

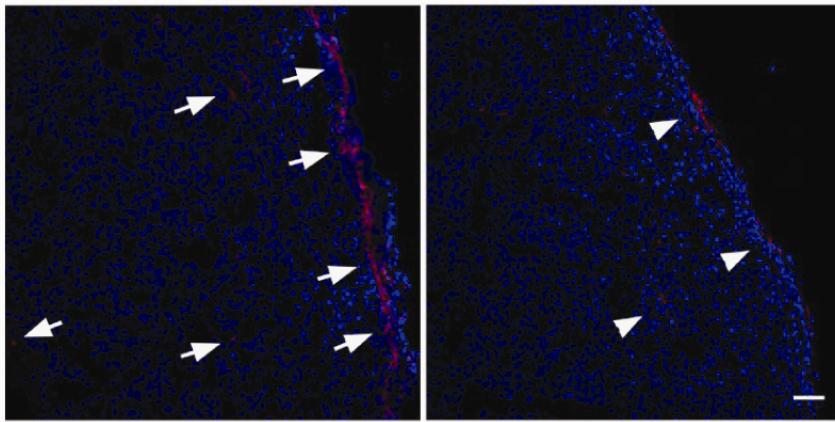
PBS

hFcAS

CD
11b**B**

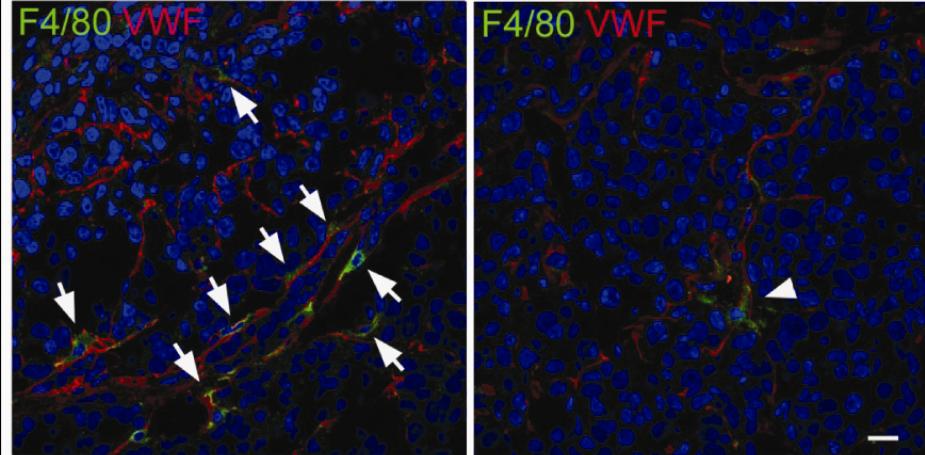
PBS

hFcAS

CD
45**C**

PBS

hFcAS

**D**

F4/80 positive area (pixels)

PBS

hFcAS

