

Supporting Information

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hGzmA 1 I I G G N E V T P H S R P Y M V L L S L D R K T - - - - I C A G A L I A K D W V L T A A H C N L N K R S Q V I L G A H S I T R E E P T K Q I
hGzmB 1 I I G G H E A K P H S R P Y M A Y L M I W D Q K - S I K R C G G F L I Q D D F V L T A A H C - W G S S I N V T L G A H N I K E Q E P T Q Q F
mGzmC 1 I I G G N E I S P H S R P Y M A Y Y E F L K V G G K K M F C G G F L V R D K F V L T A A H C - K G R S M T V T L G A H N I K A K E E T Q Q I

hGzmA 67 M L V K K E F P Y P C Y D P A T R E G D L K L L Q L T E K A K I N K Y V T I L H L P K K G D D V K P G T M C Q V A G W G R T H N S A S W S D
hGzmB 69 I P V K R P I P H P A Y N P K N F S N D I M L L Q L E R K A K R T R A V Q P L R L P S N K A Q V K P G Q T C S V A G W G Q T A P L G K H S H
mGzmC 70 I P V A K A I P H P D Y N P D D R S N D I M L L K L V R N A K R T R A V R P L N L P R R N A H V K P G D E C Y V A G W G K V T P D G E F P K

hGzmA 137 T L R E V N I T I I D R K V C N D R N H Y N F N P V I G M N M V C A G S L R G G R D S C ~ N G D S G S P L L C E G V F R G V T S F G L E N K
hGzmB 139 T L Q E V K M T V Q E D R K C E S D L R H Y Y D - - - S T I E L C V G D P E I K K T S F ~ K G D S G G P L V C N K V A Q G I V S Y G R N - -
mGzmC 140 T L H E V K L T V Q K D Q V C E S Q F Q S S Y N - - - R A N E I C V G D S K ~ I K G A S F E E D S G G P L V C K R A A A G I V S Y G Q T - -

hGzmA 206 C G D P R G P G V Y I L L S K K H L N W I I M T I K G A V
hGzmB 202 - - N G M P P R A C T K V S S - F V H W I K K T M K R Y -
mGzmC 203 - - D G S A P Q V F T R V L S - F V S W I K K T M K H S -
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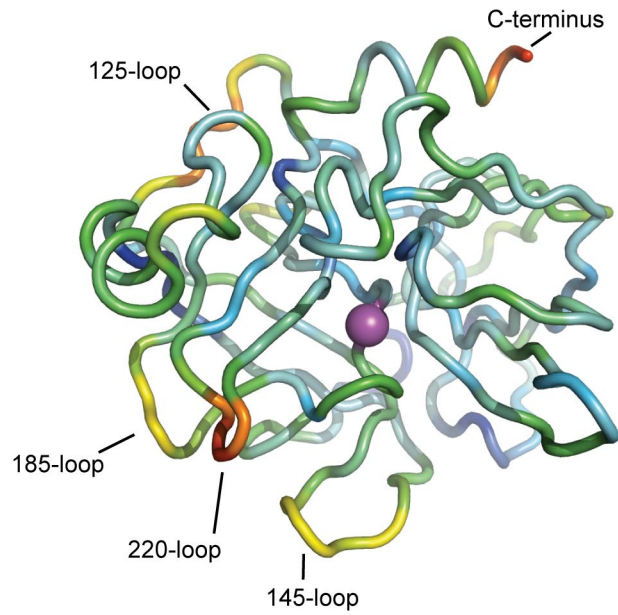


Fig. S1. Register shift in granzyme C. Structural alignment of granzyme C with human granzyme A and granzyme B. Amino acids are colored by hydrophobicity: orange, hydrophobic; green, polar; blue, basic; red, acidic; magenta, cysteine. Residues involved in the gzmC register shift are background colored and are aligned based on the structure. Arrow indicates the direction of register shift.

A



B

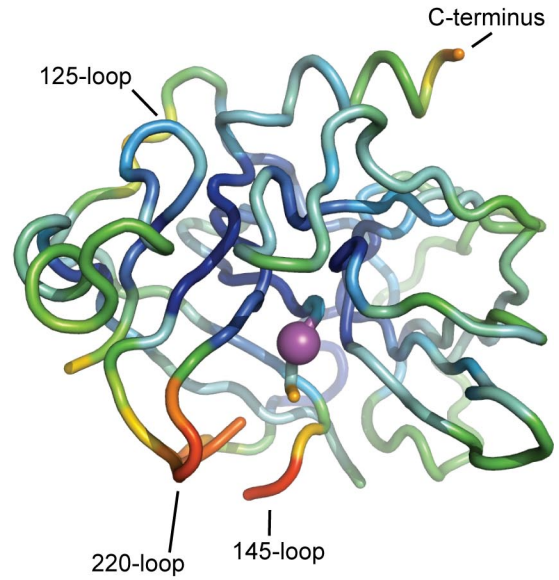


Fig. S2. Granzyme C *B* factors. (A) Representation of WT granzyme C colored according to *B* factor from 40 Å² (blue) to 70 Å² (red). The active-site Ser-195 is shown as a magenta ball, and regions of high *B* factor are labeled. (B) Representation of granzyme C E192R/E193G mutant colored according to *B* factor from 20 Å² (blue) to 65 Å² (red). The active-site Ser-195 is shown as a magenta ball. Note that the 145- and 185-loops could not be fully modeled.

Other Supporting Information Files

[Table S1 \(PDF\)](#)