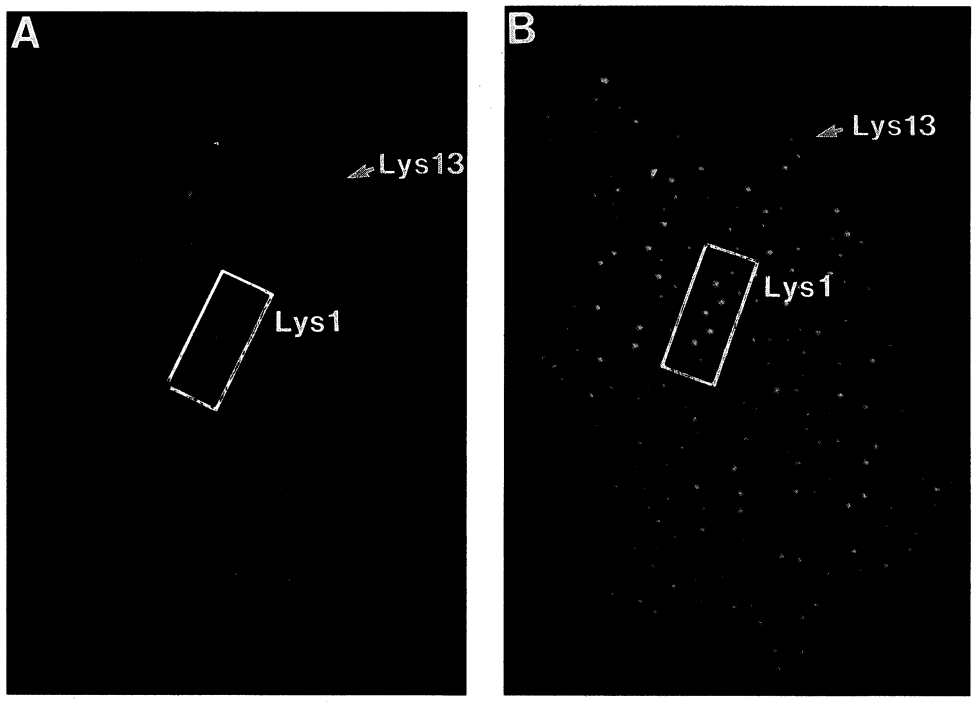

FIG. 5. Unmasking of E3α Ub–protein ligase recognition determinants on lysozyme by Cys-6 Cys-127 disulfide cleavage. Rearrangement of the C terminus in three-disulfide lysozyme was modeled from the native structure (22) by elimination of the Cys-6 Cys-127 disulfide bond and rotation about the N—C_α bond of Gly-126. The spacefilling models depict lysozyme before (*A*) and after (*B*) the disulfide cleavage and bond rotation. The cleft formed by rearrangement of the C-terminal peptide may allow binding of the Ub–protein ligase complex and give access to Lys-13. Side chains for Lys-1 and Lys-13 are indicated, and the C, O, N, and S atoms are colored green, red, blue, and yellow, respectively.

rcm-lysozyme structure will assist in the design of peptide and protein probes to better define these specificity determinants.

We thank J. Setsuda for samples of 6,127-rcm-lysozyme, N. Strynadka and M. James for coordinates to native lysozyme, and D. Eisenberg for his support. This work was supported by National Institute of General Medical Sciences Grant GM 37666 to R.E.C., GM 31299 to the UCLA Structure Group, and Cell and Molecular Biology Training Grant GM 07185.

1. Goldberg, A. L. & St. John, A. C. (1976) *Annu. Rev. Biochem.* **45,** 747–803.
2. Olson, T. S. & Dice, J. F. (1989) *Curr. Opin. Cell Biol.* **1,** 1194–1200.
3. Rivett, A. J. (1990) *Curr. Opin. Cell Biol.* **2,** 1143–1149.
4. Stadtman, E. R. (1990) *Biochemistry* **29,** 6323–6331.
5. Goldberg, A. L. (1992) *Eur. J. Biochem.* **203,** 9–23.
6. Finley, D. & Chau, V. (1991) *Annu. Rev. Cell Biol.* **7,** 25–70.
7. Varshavsky, A. (1992) *Cell* **69,** 725–735.
8. Hershko, A. & Ciechanover, A. (1992) *Annu. Rev. Biochem.* **61,** 761–807.
9. Gonda, D. K., Bachmair, A., Wünning, I., Tobias, J. W., Lane, W. S. & Varshavsky, A. (1989) *J. Biol. Chem.* **264,** 16700–16712.
10. Reiss, Y., Kaim, D. & Hershko, A. (1988) *J. Biol. Chem.* **263,** 2693–2698.
11. Reiss, Y. & Hershko, A. (1990) *J. Biol. Chem.* **265,** 3685–3690.
12. Heller, H. & Hershko, A. (1990) *J. Biol. Chem.* **265,** 6532–6535.
13. Bartel, B., Wünning, I. & Varshavsky, A. (1990) *EMBO J.* **9,** 3179–3189.
14. Hershko, A., Heller, H., Eytan, E. & Reiss, Y. (1986) *J. Biol. Chem.* **261,** 11992–11999.
15. Bachmair, A. & Varshavsky, A. (1989) *Cell* **56,** 1019–1032.
16. Dunten, R. L. & Cohen, R. E. (1989) *J. Biol. Chem.* **264,** 16739–16747.
17. Dunten, R. L., Cohen, R. E., Gregori, L. & Chau, V. (1991) *J. Biol. Chem.* **266,** 3260–3267.
18. Radford, S. E., Woolfson, D. N., Martin, S. R., Lowe, G. & Dobson, C. M. (1991) *Biochem. J.* **273,** 211–218.
19. Denton, M. E. & Scheraga, H. A. (1991) *J. Protein Chem.* **10,** 213–232.
20. Bernstein, F. C., Koetzle, T. F., Williams, G. J. B., Meyer, E. F., Jr., Brice, M. D., Rodgers, J. R., Kennard, O., Shimanouchi, T. & Tasumi, M. (1977) *J. Mol. Biol.* **112,** 535–542.
21. Abola, E., Bernstein, F. C., Bryant, S. H., Koetzle, T. F. & Weng, J. (1987) in *Crystallographic Databases—Information Content, Software Systems, Scientific Applications*, eds. Allen, F. H., Bergerhoff, G. & Sievers, R. (Data Commission of The International Union of Crystallography, Bonn), pp. 107–132.
22. Strynadka, N. C. J. & James, M. N. G. (1991) *J. Mol. Biol.* **220,** 401–424.
23. Brünger, A. T. (1992) XPLOR Manual (Yale Univ., New Haven, CT), Version 3.0.
24. Jones, T. A. (1985) *Methods Enzymol.* **115,** 157–171.
25. Pickart, C. M. & Vella, A. T. (1988) *J. Biol. Chem.* **263,** 12028–12035.
26. Chen, Z. & Pickart, C. M. (1990) *J. Biol. Chem.* **265,** 21835–21842.
27. Banerjee, S. K. & Rupley, J. A. (1973) *J. Biol. Chem.* **248,** 2117–2124.
28. Pace, C. N. & McGrath, T. (1980) *J. Biol. Chem.* **255,** 3862–3865.
29. Hodson, J. H., Brown, G. M., Sieker, L. C. & Jensen, L. H. (1990) *Acta Crystallogr. Sect. B Struct. Sci.* **46,** 54–62.
30. Ramanadham, M., Sieker, L. C. & Jensen, L. H. (1990) *Acta Crystallogr. Sect. B Struct. Sci.* **46,** 63–69.
31. Chau, V., Tobias, J. W., Bachmair, A., Marriott, D., Ecker, D. J., Gonda, D. K. & Varshavsky, A. (1989) *Science* **243,** 1576–1583.