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Perils of Pseudosymmetry Combined with Merohedral Twinning. Schuermann, J. P., Rodriguez, A. J., Taylor, A. B., Hart, P. J., Univ. of Texas Health Science Center at San Antonio, San Antonio, TX.

The structure determination of a human copper-zinc superoxide dismutase (SOD1) mutant that causes amyotrophic lateral sclerosis (ALS) was complicated by a combination of nearly perfect hemihedral twinning and pseudosymmetry. Twinning was suspected when refinement stalled at R and R-free values of 0.25 and 0.29 in space group $C222_1$. The shape of the cumulative intensity distribution plot appeared to support this suspicion. The diffraction data were reprocessed in space group P3 and uploaded to the Merohedral Crystal Twinning Server, which returned a twin fraction (α) of 0.47 for each of the 3 possible twin laws. Brute force molecular replacement was performed in all 18 possible space groups (6/mmm, 6/m, 3m1, 31m). Four candidates (P622, P6, P321, P312) returned reasonable statistics and crystal packing. In each of these space groups, the packing consists of a six-fold "honeycomb" looking down the *c* axis (Figure 1A). The correct space group was eventually determined to be P321 (and not P312) with the help of a native Patterson. Mature SOD1 is an enormously stable homodimer with two metal ions and a disulfide bond within each subunit. In this case, the aysmmetric unit contains four pathogenic SOD1 subunits. Two associate to form a canonical SOD1 homodimer, but the remaining two lack metal ions and the disulfide bond. Metal- and disulfide-free SOD1 is known to be monomeric. These dimers and "pseudodimers" pack in alternating bilayers and generate two sets of pseudo-two-fold axes (Figure 1B). The structural differences between these forms of this pathogenic SOD1 mutant have profound implications for both SOD1 maturation and the etiology of SOD1-linked ALS. These differences, and the insight derived from them, would have been completely missed had the twinning issues not been detected and handled properly.