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Vault Domains: Advancing Beyond 48-fold NCS Phasing. Daniel H. Anderson^{1,2}, Stuart Sievers³, Valerie Kickhoefer⁴, Leonard Rome², David Eisenberg^{1,2}, ¹HHMI, ²Medical School, ³Biochem., ⁴Biol.Chem. at UCLA.

Vaults are large cytoplasmic ribonucleoprotein structures, and one of the largest discrete objects to crystallize and diffract. A vault structure may lead to its unknown biological function, and would facilitate exploitation of vaults as nanocapsules. 96 Copies of Major Vault Protein self-assemble into a 9 megaDalton vault shell. 9Å Phases resulted from single-axis 48-fold NCS averaging within a cryo-EM envelope. Though not uniform, the map patterns show that most of the vault monomer is built from autonomously folded domains. The chains likely braid to 24-fold symmetry at the base of the C-terminal cap region. The chains divide into two layers of 24 as the structure constricts in the last 35-40 cap residues. 25 Plausible N-terminal residues were built from fragments. Using homology and *ab initio* modeling methods we predict tertiary structure for many modules, subject to density restraints. For example, a model for residues 26-87 fits its envelope of density, and if correct would form plausible NCS contacts including a testable salt bridge. Module fold prediction will be refined as we distribute masses. With model atoms in the envelopes of density, we will improve the NCS masks and the phases, and generate testable hypotheses of where to insert ligand binding loops.