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Searching for Silver Bullets: An Alternative Strategy for Crystallizing Macromolecules. Bob Cudney¹, Alexander McPherson², ¹Hampton Research, 34 Journey, Aliso Viejo, CA 92656-3317, ²Univ. of California, Dept. of Molecular Biology & Biochemistry Irvine, CA 92697-3900.

Based on a hypothesis that various small molecules might establish stabilizing, intermolecular, non covalent cross links in protein crystals and thereby promote lattice formation, we carried out three separate experiments. We assessed the impact of more than 200 chemicals on the propensity of 81 different proteins and viruses to crystallize. The compounds were formulated as 115 overlapping reagent mixes, each containing 1 to 20 individual components. The experiments were comprised of 18,240 vapor diffusion trials. A salient feature of the experiments was that, aside from the inclusion of the reagent mixes, only two fundamental crystallization conditions were used, 30% PEG 3350, and 50% Tacsimate™ at pH 7. Overall, 65 proteins (85%) were crystallized. Most significant was that 35 of the 65 (54%) crystallized only in the presence of one or more reagent mixes, but not in control samples lacking any additives. Based on these experiments, we propose that an alternate approach to crystallizing proteins might be developed, which employs a limited set of fundamental crystallization conditions combined with a broad screen of potentially useful small molecule additives.