Operations of the National Crystallization Center: Two Decades of High-Throughput Crystallization Efforts Fueled by Structural Genomics

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The National High-Throughput Crystallization (HTX) Center at HWI has been operational since the turn of the century and has made significant contributions to NIH's Protein Structure Initiative (PSI) by serving as a screening resource for PSI supported projects, including the Northeast Structural Genomics Consortium (NESG) and others[1]. It quickly became apparent with large-scale crystallographic efforts that crystallization represented the largest hurdle in the gene-to-structure pipeline. Spurred by the need to improve crystallographic pipelines, the HTX Center developed two comprehensive 1536-well screens for soluble and membrane proteins that have since been used to screen over 18,000 samples from over 2000 laboratories[1]. Since its inception, further technological developments at the HTX Center have improved throughput and reproducibility, including robotic liquid handling, automated brightfield and SONICC imaging, and MARCO-enabled crystal identification. Though technological advances enabled by the PSI have allowed for ultrahigh-throughput crystallography pipelines, the cost of the associated instrumentation is prohibitively expensive for individual labs and even university research core facilities, making the HTX Center a valuable resource for the structural biology community beyond the conclusion of the PSI. Here, we give a historical perspective on the HTX Center, contextualize the development of our crystallization pipelines, and consider how the resources and expertise borne of the PSI serve us in today's structural biology world.

{1}. Lynch, M. L., Snell, M. E., Potter, S. A., Snell, E. H. & Bowman, S. E. J. 20 years of crystal hits: progress and promise in ultrahigh-throughput crystallization screening. Acta Crystallographica Section D: Structural Biology 79, 198–205 (2023)