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FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Coupled amyloid self-assembly and guanine crystallization generate hybrid protein–crystal architectures

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Background. Biogenic guanine crystals are widespread across the animal kingdom, from fish to insects, crustaceans and mollusks.[1] Owing to their exceptionally high refractive index, these crystals perform diverse optical functions, including structural coloration and vision enhancement, particularly in aquatic environments.[2,3] Despite their biological importance, little is known about the molecular machinery that orchestrates crystal formation and maintains crystal morphology and organization.[4] Recent evidence suggests that protein matrices seed and spatially organize guanine crystals.[5] In particular, fibrous protein assemblies with amyloid-like structural signatures have been proposed to act as scaffolds for crystal growth and polymorphism, enabling the coherent tissue-level optical properties observed *in vivo*.[6]

Objectives. Here, we investigate the molecular basis of protein–crystal interactions (PCIs) using a reductionist, bottom-up approach. First, we tested lysozyme, a well-characterized amyloidogenic protein, for its ability to form protein–crystal complexes. We then designed a screening strategy to systematically dissect the molecular forces governing protein–crystal crosstalk using peptides as minimal models.

Results. Time-course turbidimetry and Thioflavin T fluorescence revealed a dose-dependent inhibition of guanine crystallization during lysozyme amyloid self-assembly. Confocal microscopy confirmed that lysozyme forms the core of spherulitic guanine crystals, indicating that crystallization and protein self-assembly are mechanistically intertwined. Prompted by these findings, we designed a panel of 12 peptides comprising hexapeptide steric zippers that assemble into rigid amyloid structures and peptide stretches that remain conformationally flexible. Because hydrogen bonding and π–π interactions govern crystalline architecture,[7] we probed aromatically enriched hydrophilic sequences in two structural contexts: (*i*) steric zippers from Sup35, prion, transthyretin and GPNMB to test the effect of periodic aromatic patterning at the fibril interface;[8–10] and (*ii*) flexible, non-fibrillar hexapeptides derived from amyloidogenic and chaperone proteins to determine whether less ordered aromatic interactions can likewise direct crystal morphogenesis. Using SEM, XRD and Raman spectroscopy to assess crystal morphology, structure and composition, we aim to reduce the protein determinants of guanine crystallization to the peptide scale.

Conclusions. Beyond providing a mechanistic framework for protein-guided crystallization, this work aims to decipher the sequence determinants underlying PCIs, enabling the systematic discovery of crystal-interacting proteins across natural proteomes. In addition, it will guide the rational design of peptide-based morphogens for engineering hybrid crystalline biomaterials with programmable structural and optical properties.

[1]L. Addadi, *et al*., *Adv. Mater.* **36**, 2408060 (2024); [2]A. Hirsch, *et al*., *Angew. Chem. Int. Ed.* **56**, 9420 (2017); [3]D. Gur, *et al*., *Adv. Sci.* **5**, 1800338 (2018); [4]R. Deis, *et al*., *Nat. Chem. Biol.* **21**, 383 (2025); [5]A. Wagner, *et al*., *Nat. Commun.* **14**, 589 (2023); [6]Z. Eyal, *et al*., *J. Am. Chem. Soc.* **144**, 22440 (2022); [7]D. Brenman-Begin, *et al*., *Small.* **22**, e10102 (2026); [8]M. Sawaya, *et al*., *Nature* **447**, 453 (2007); [9]L. Saelices, *et al*., *Protein Sc.* **27**, 1295 (2018); [10]L. Goldschmidt, *et al*., *Proc. Nat. Acad. Sci. USA* **107**, 3487 (2010).