(SD2015-321) Method For Fabricating Two-Dimensional Protein Crystals

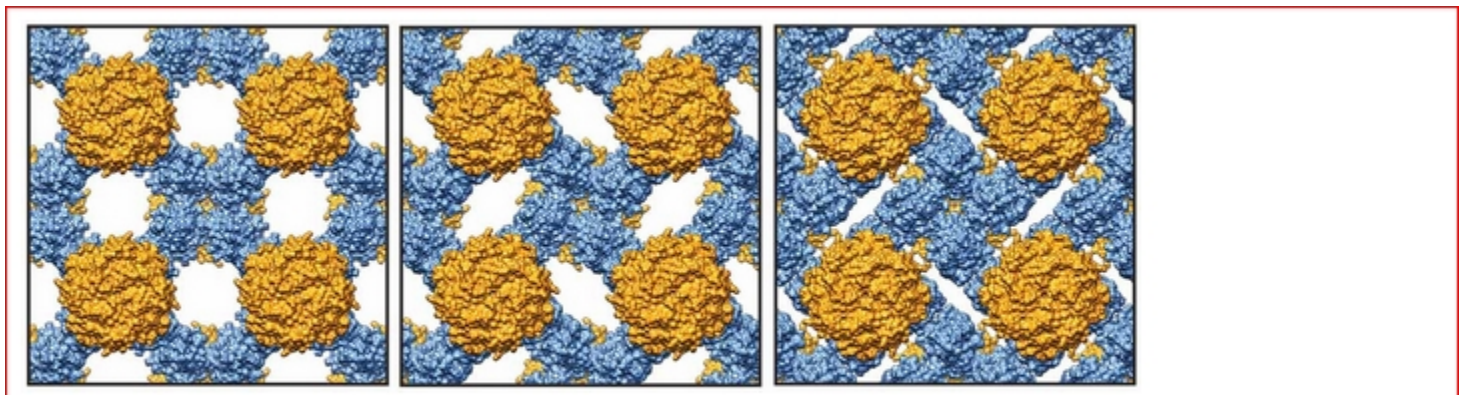
Tech ID: 25324 / UC Case 2015-321-0

BACKGROUND

2D crystalline materials possess high surface area-to-volume ratios, light and can be very porous. These properties have rendered synthetic 2D materials immensely attractive in applications including electronics, sensing, coating, filtration and catalysis. The rational design of self-assembling 2D crystals remains a considerable challenge and a very active area of development. The existing methods for the bottom-up fabrication of biological or non-biological 2-D crystalline materials are not generalizable and scalable. 2D protein design strategies, in particular, require extensive computational work and costly protein engineering. In addition, these strategies have low success rates, the resulting materials contain large defects, and are multi-layered and therefore not appropriate for scaling or materials-applications. Moreover, these strategies often require the presence of lipids for supported assembly.

TECHNOLOGY DESCRIPTION

Scientists at UC San Diego have developed and patented a highly efficient/expeditious design strategy for the fabrication of single layered, ultra-low defect 2D crystalline materials out of protein building blocks. The 2D crystalline materials are essentially defect-free and self-assemble in an unsupported fashion in solution. They also offer a better strategy because of their simplicity, low cost nature, effectiveness, and potential generalizability.



The bonds in the protein tiles allow them to rotate to open spaces after a compression has been applied. Yuta Suzuki and Timothy Baker, UC San Diego

APPLICATIONS

The 2D crystalline protein materials generated have diverse potential applications including the following:

1) Fabrication of self-assembled, chemically dense, lab-on-a-chip platforms for sensing, diagnostics, vaccine development, and drug delivery,

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OTHER INFORMATION

KEYWORDS

fabrication, protein crystals, 2D, Aldehyde-Lyases, Crystallization, Disulfides, Mutant Proteins, Pliability, Protein Conformation, Thermodynamics

CATEGORIZED AS

- **Biotechnology**
  - Other
- **Materials & Chemicals**
  - Biological
  - Other

RELATED CASES

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2) Fabrication of molecular membranes for sieving and filtration,

3) Fabrication of molecular templates that provide 5-100 nm spatial resolution for patterning and deposition (which is a length scale that is hard to attain with diffraction-based methods),

4) Stabilization of enzymes and proteins of commercial value, and

5) Fabrication of crystalline molecular scaffolds for macromolecular structure determination by 2D crystallography and electron microscopy.

INTELLECTUAL PROPERTY INFO

Claims in the issued patent include:

1. A non-naturally occurring symmetrical polypeptide building block comprising two or more RhuA proteins, wherein each subunit of the RhuA protein comprises a cysteine residue at position 98, and wherein the RhuA proteins of the polypeptide building block are coupled by formation of disulfide bonds between some or all of said plurality of cysteine residues of different RhuA proteins to facilitate formation of 2D crystals.

4. The polypeptide building block of Claim 1, wherein at least one of said cysteine residues has been introduced into said polypeptide building block through genetic engineering.

5. The polypeptide building block of Claim 1, wherein said polypeptide building block is generated via solid phase synthesis.

8. The polypeptide building block Claim 1, further comprising an additional polypeptide modification selected from the group consisting of functional groups, tags, other polypeptides, peptide tags, detectable labels, fluorophores, and nanoparticles.

18. The polypeptide building block of Claim 1, wherein the polypeptide building block is chemically modified with inorganic nanoparticles or one or more organic functional groups including a fluorophore, a metal chelating group or a host complex.

23. A 2D crystalline material comprising two or more RhuA proteins, wherein each subunit of each RhuA protein comprises a cysteine residue at position 98, wherein disulfide bonds are formed between some or all of said cysteine residues.

24. The 2D crystalline material of Claim 23, wherein said 2D crystalline material is auxetic.

25. The 2D crystalline material of Claim 23, wherein the 2D crystalline material comprises a Poisson's ratio of at least -1.

28. The 2D crystalline material of Claim 23, wherein the 2D crystalline material is chemically modified with inorganic nanoparticles or one or more organic functional groups including a fluorophore, a metal chelating group or a host complex.

32. The 2D crystalline material of Claim 23, wherein the 2D crystalline material can be genetically modified/fused with functional proteins and peptides.

148. The 2D crystalline material of Claim 23, wherein the 2D crystalline material is free of defects.

149. The 2D crystalline material of Claim 23, wherein the 2D crystalline material allows dynamic interconversion between an open conformational state and a closed conformational state.

RELATED MATERIALS

- Material that thickens when stretched may lead to better body armor. By Michael Franco - 05/03/2016
- Suzuki Y, Cardone G, Restrepo D, Zavattieri PD, Baker TS, Tezcan FA. Self-assembly of coherently dynamic, auxetic, two-dimensional protein crystals. Nature. 2016 May 19;533(7603):369-73. doi: 10.1038/nature17633. Epub 2016 May 2. - 05/02/2016

▶ Chemically Directed Self-Assembly of Protein Superstructures. F. Akif Tezcan. Biomolecular Materials Principal Investigators' Meeting–2015, August 3–5, 2015, Hilton Washington DC North/Gaithersburg, Gaithersburg, MD. p221.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20180354988	12/13/2018	2015-321
Patent Cooperation Treaty	Published Application	2017011705	01/19/2017	2015-321

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