Scholarly Research Journal for Humanity Science & English Language,
Online ISSN 2348-3083, SJ IMPACT FACTOR 2016 = 4.44, www.srjis.com
UGC Approved Sr. No.48612, DEC-JAN 2018, VOL- 5/25

PEPTIDE BASED SELF-ASSEMBLED NANOSTRUCTURES

Acharya Diptesh Satish

Abstract

Self-assembly of biomolecules facilitates the creation of a diverse range of hierarchical nanostructures from a wide range of polymeric and non-polymeric materials. Peptides and specifically short peptides are very attractive in this respect due to their unmatched biocompatibility, ease of synthesis, function ability as well as tunable bioactivity along with the availability of rich chemistry for fine-tuning the structure and function of peptides according to environmental conditions. Self assembled peptide based nanostructures such as tubes, filaments, fibrils, hydrogels, vesicles; monolayers have been studied by many research groups and found application as three-dimensional cell growing scaffolds, dental implants, neural tissue engineering scaffolds and as carriers for drugs, proteins and genes, nucleotides. Nanostructures are also being developed from designed or modified amino acids to have enhanced cellular as well as in vivo stability. These modified nanostructures showed enhanced drug delivery properties both under in vivo and in vitro conditions.

Keywords*: Nanostructures, peptides, drug delivery, tissue engineering, self-assembly.*

Introduction:

Self-assembly is defined as the autonomous organization of components into ordered patterns or structures.1 Living cells consist of many self-assembling systems that work in synchronization to achieve a defined goal. Self-assembly, as a process contributes significantly in biology such as maintaining the cell integrity, performing important cellular functions as well as inducing abnormalities that cause disease.1 Thus, understanding life necessitates a better understanding of self-assembly. Concepts of self-assembly have also been used in many disciplines for constructing useful materials. Molecular self-assembly is in fact a very practical way of making ensembles of nanostructures. The ubiquitous existence of self-assembly processes in living systems along with the prevalence of various non-covalent interactions (van der Waals, electrostatic, and hydrophobic metal—ligand, π-π stacking interactions, hydrogen and coordination bonds) in biology, have resulted in rapid development of self-assembling biomaterials as a promising research area.2-4 Self-assembly provides the flexibility of developing novel materials with tailored morphologies and desired functions through single-molecule design and engineering. This results in controlling the bulk properties of the resultant material by modulating individual monomeric building blocks.

Thus, by modulating structural changes in constituent molecules it becomes possible to dictate the behavior of the end product. In recent past, many self-assembling nanomaterials are being generated from various organic polymers, carbohydrates, nucleic acids, proteins etc. either to gain a better understanding of the phenomenon or to use them for applications ranging from molecular devices to delivery systems or scaffolds.

Research Methodology:

MaterialsandMethods

Peptide Synthesisand Purification

Detailed procedures have been described in Chapter2. All^{13}C-labeled N-and C-capped AP (16-22) an alogs were synthesized on a Rain in Symphony QUARTET multiplex solid-phase peptidesyn the sizer. Final purity and identity was confirmed by MALDI-TOF.Thesinglemassunitdifferenceconfirmedboth Clabelincorporation and sample purity (data not shown).

Freezing process optimization

CD spectrum minimum shifts were used to compare the protection efficiency.

(1) Freezingtemperatureoptimization

Mature Ap (16-22) nano tube solution 20μL wereflash-frozeninliquidN2(-200°C),methanol/dryicebath (--80°C) and acetonitrile/dryicebath (--40°C) respectively. The frozen solutions were allowed to thaw gradually at room temperature and CD spectra were me a sured after the solutions were completely thawed. The lower the freezing temperature was, the more nano tube damages were observed.

(2) Freezingrateoptimization:

Mature AP (16-22) nano tube solution 20μL was firstly in cubatedat-4 ^{0}C for equilibrium and then gradually cooled to- 7^{0}C before ice crystal formation occurred (Studelska2003). The sample was then plunge din to- 80^{0}C baths for complete freezing. Afterthawing,thesolutionwasanalyzedbyCD.Noobviousnanotube protectionwasobserved.

(3) Cry oprotectant optimization

PEG concentration optimization. Nano tube solution 20μLwas mixed with 20 μL excipient 40% acetonitrile/water (pH2) solution having different PEG concentration from 0% to 40%. Freeze the solution sat-40 ^{0}C and thawgraduallyat room temperature. 1% PEG was enough to protect then a no tubes.

Trehalose concentration optimization. Nano tube solution 20 J..lL was mixed with20J..Ll of excipient 40% acetonitrile/water (pH2) solution having1% PEG and different concentration oftrehalose from 0 to 200 m M. Freeze the solution sat-40 oc and thawgraduallyat room temperature. 30 mM was the optimized trehalose concentration.

Dextran concentration optimization. Nanotubesolution20J..lL was mixed with 20J..l Lofexcipient 40% acetonitrile/water (pH2) solution having 1% PEG, 30 mMtrehalose and different concentration of dextran (70kDaand500kDa) from 0to10 mg/ml. Freeze the solutions at-40 oc and thawgradually at room temperature. 0.67 mg/mldextran was chose nas the protectant.

Objectives:

- The main objectives of the study are as follows:
- To obtain the important peptide registry information using IE-I Randss-NMR techniques.
- To check out the peptide organizationswithintheP-sheet.
- To find out the difference between peptideregistry of Nano tube satpH2 and fibrilsatp H6.
- Whether the electrostatic interactions between K and E, together with maximizing the hydrophobic packing, can stabilize the fibril architecture or not.
- To study whypH13nano tube sadopt the in-register antiparalle lP- sheet structure after the depro to nation of the lysines instead of using the favorable packingaspH2nanotubes.
- With the same peptide registry, why AP (16-22) forms fibrilsinpH6, however, nano tubes in pH 13? Understanding the sequestions will further the understanding of the amyloidfibril structures.
- To find peptideregistry whetherthesameordifferentinnanotubesandfibrils?
- What determines the supra molecular organization in nano tubes *vs* fibrils?
- Energetically,whatcontrolstheassemblypathway?

Hypothesis

We have to conduct a hypothesis test about the research proportion. This approach consists of four steps:

(1) State the hypothesis

(2) Formulate an analysis plan

(3) Analyze sample data

(4) Interpret results.

H0: The discovered PNTs possess remarkably similar structural elements to those of the normal as sembledamyloid fibrils, such ascross-Pdiffraction pattern, CR binding and P-sheet secondary structures.

H1: Differently, they differ from the fibrils by extending the laminationfromthe6sheetsof Ap(l0-35) fibrilsto130sheetsof AP{l6-22) nano tubes.

Scope of the study:

Life couldnot exist without proteins. These large bio polymers fold in to a variety of structures and perform various functions in nature. Unfortunately, upto this point, the understanding of how sequence dictates structure remains elusive. Protein folding cannot be fully predicted and controlled. Several basic forces, such as electric interactions, hydrophobic interactions, hydrogen bonding and vander Waals interactions, have been identified to be crucial to as table 3 -Dstructure. Inaddition, protein folding is sensitive to the environment, for example, ionic strength, temperature and pH, makingthe process even more complicated as the local conditions change during folding. Proteins associated with the conformational diseases, including the no torious Alzheimer's disease, are normally soluble and fold normally, but for some reason, populate an alternate structure that allows self- association into fibrous arrays in tissues. Given that understanding the driving forces and me chanisms for prote in folding will be essential not only forde signing in hibitors/drugs butal so to fabric atenovelbio materials with defined structures, these amyloidmodelsmay facilitate the assignment of the sepath ways.

Conclusion:

Self-assembly is a marvelous strategy to make ensemble of nanostructures. Small peptide-based self-assembled nanostructures, due to their inherent biocompatibility, easy tunability, simple and cost-effective synthesis could offer a myriad of potential uses in biomedical applications. Peptides could spontaneously self-assemble into tubular or fibrillar or vesicular nanostructures. The nanostructures have been shown to entrap a wide range of bioactive molecules with a controlled release pattern. Peptide based hydrogels with nanofibrillar morphology has been shown to support 3D growth of various cell types along with promoting cell differentiation in many cases. Thus small peptides have tremendous potential to be developed as intelligent biomedical scaffolds with many biomedical applications. Thus

peptide self-assembly is emerging as a new area of research and has spurred intense interest in the fabrication of nano scale devices and demand for miniaturization in both academia and industries necessitate progress in this area.

References:

G. M. Whitesides and B. Grzybowski, Science, 2002, 295, 2418-2421.
S. Zhang, Nat. Biotechnol., 2003, 21, 1171-1178.
S. Stupp, Nano Lett., 2010, 10, 4783-4786.
G. M. Whitesides, J. P. Mathias and C. T. Seto, Science, 1991, 254, 1312-1319.
Z. Liu, Y. Jiao, Y. Wang, C. Zhou, Z. Zhang, Adv. Drug Deliv. Rev., 2008, 60, 1650–1662.
K. A. Janes, P. Calvo, M. J. Alonso, Adv. Drug Deliv. Rev., 2001, 47, 83–97.
M. Prabaharan, J.F. Mano, Drug Deliv., 2005, 12, 41–57.
D.G. Kim, Y.I. Jeong, C. Choi, S.H. Roh, S.K. Kang, M.K. Jang, J.W. Nah, Int. J. Pharm., 2006, 319, 130–138.
Z.R. Cui, R.J. Mumper, J. Control. Rel, 2001, 75, 409–419.
A. Zahoor, S. Sharma, G.K. Khuller, Int. J. Antimicrob. Agents, 2005, 26, 298–303.
J. W. de Vries, F. Zhang, A. Herrmann, J. Control. Rel., 2013, 172, 467–483.
D. Kim, Y.Y. Jeong, S. Jon, ACS Nano, 2010, 4, 3689–3696.
J.I. Cutler, E. Auyeung, C.A. Mirkin, J. Am. Chem. Soc. 2012, 134, 1376–1391.
N.L. Rosi, Science, 2006, 312, 1027–1030.
J.J. Storhoff, R. Elghanian, R.C. Mucic, C.A. Mirkin, R.L. Letsinger, J. Am. Chem. Soc., 1998, 120 1959–1964.
M.D. Costioli, I. Fisch, F. Garret-Flaudy, F. Hilbrig, R. Freitag, Biotechnol. Bioeng., 2003, 81, 535–545.
M. Safak, F.E. Alemdaroglu, Y. Li, E. Ergen, A. Herrmann, Adv. Mater., 2007, 19, 1499–1505.
F.E. Alemdaroglu, K. Ding, R. Berger, A. Herrmann, Angew. Chem. Int. Ed., 2006, 45, 4206–4210.
M. Kwak, J. Gao, D.K. Prusty, A.J. Musser, V.A. Markov, N. Tombros, M.C.A. Stuart, W.R. Browne, E.J. Boekema, G. ten Brinke, H.T. Jonkman, B.J. van Wees, M.A. Loi, A. Herrmann, Angew. Chem. Int. Ed., 2011, 50, 3206–3210.
P. Guo, J. Nanosci. Nanotechnol., 2005, 5, 1964–1982.
S. Guo, N. Tschammer, S. Mohammed, P. Guo, Human Gene Ther. 2005, 16, 1097-1109.
A. Khaled, S. Guo, F. Li, P. Guo, Nano Lett., 2005, 5, 1797-1808.