Supramolecular World

Edited by Elham Radvar and Dominic Collis

Research highlights for issue 2

Peptide amphiphiles (PAs) as building blocks to construct self-assembling biomaterials

Biomaterials research has witnessed substantial progress in the last two decades and has shifted from traditional biomaterials, such as ceramics, metals and polymers, to biomaterials that are designed rationally with controlled structure and dynamic functionality to integrate with native tissues and promote regeneration. Molecular self-assembly uses non-covalent interactions (hydrogen bonding, π-π stacking metal–ligand interactions, dipole–dipole interactions, hydrophobic forces and electrostatic interactions) and allows control of biomaterial properties from the molecular to the macro-scale.

A number of building blocks have been explored for developing biomaterials by self-assembly, but peptides have gained great attention due to their self-assembly characteristics, relatively simple and well-established synthesis. Utilizing 20 naturally occurred α-amino acids, a variety of designs can be achieved (primary structure) which can then self-assemble into different architectures, such as cylindrical fibers, spheres, lamellae, twisted ribbons, tapes, tubes, and helical ribbons (1). Peptide amphiphiles (PAs) are a class of self-assembling peptides which were first developed in 1995 by Tirrell and co-workers. The design consisted on a peptide sequence conjugated to a dialkyl ester tail (2). The rational in the PAs design relies on having a hydrophobic tail attached to a hydrophilic peptide sequence. Later in 2001, Stupp's laboratory developed a PA design that is able to mimic the fibrous structure of extracellular matrix (ECM). Their design is based on having four regions, including: (i) hydrophobic alkyl chain, (ii) β-sheet sequence, (iii) charged residues and (iv) biological epitope (optional) (3). Due to the β-sheet segment, assemblies of PAs result in fibrous nanostructures with 6-10 nm in diameter and often many micrometers in length (3).

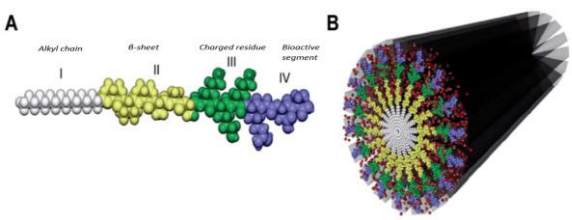

Figure 1 Pictorial representation of PAs assembly into nanofibers[1].

Self-assembly of PAs can be triggered by addition of counter ions or changes in pH, which at certain concentration leads to the formation of a gel. The packing of hydrophobic chain directs the peptide segment towards the aqueous environment and provides a platform to display biological epitopes (3).

One example of using PAs for creating novel biomaterials has been reported by Ferreira and co-workers utilizing bottom-up approaches based on supramolecular self-assembly (4). They developed two-dimensional membranes combining PA and hyaluronic acid (HA), one of the glycosaminoglycans present in the ECM of skin. The PA consists of an alkyl chain (palmitic acid), β-sheet segment (VVVAAA), charged segment (KKK) and fibronectin derived RGDS epitope (4). The membranes showed a nano-fibrous structure resembling the natural ECM architectural features (4). These membranes were used to culture human dermal fibroblasts and their degradation in the presence of enzymes was also analyzed. The results showed that these 2D hybrid membranes can be a potential biomimetic supportive matrix for skin regeneration.

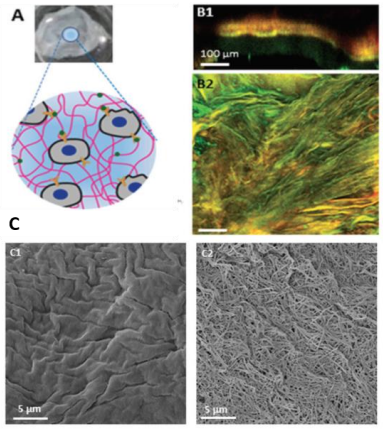

Figure 2 (A) Schematic representation of PA–HA membranes; (B) Confocal microscopy images of the membranes prepared with fluorescein–HA and rhodamine peptide showing the localization of HA (green) and PA (red) over the membrane surface (B2) and cross section (B1). Yellow represents the overlapping of both components. (C) Scanning electron microscopy images of the self-assembled membranes showing the surface on the polymer (C1) and peptide (C2) sides (4).

1. Dankers PY, Meijer E. Supramolecular biomaterials. A modular approach towards tissue engineering. Bulletin of the Chemical Society of Japan. 2007;80(11):2047-73.
2. Berndt P, Fields GB, Tirrell M. Synthetic lipidation of peptides and amino acids: monolayer structure and properties. Journal of the American Chemical Society. 1995;117(37):9515-22.
3. Pérez CMR, Stephanopoulos N, Sur S, Lee SS, Newcomb C, Stupp SI. The Powerful Functions of Peptide-Based Bioactive Matrices for Regenerative Medicine. Annals of biomedical engineering. 2015;43(3):501-14.
4. Ferreira DS, Marques AP, Reis RL, Azevedo HS. Hyaluronan and self-assembling peptides as building blocks to reconstruct the extracellular environment in skin tissue. Biomaterials Science. 2013;1(9):952-64.

MHAtriCell Group

Past Research Students

Since the last issue, we have had two master students under the Erasmus programme from the *Universidade Católica Portuguesa do Porto*, *Escola Superior de Biotecnologia (Portugal)* for 5 months' placement.

Ana Faria	Oct 2015 - Feb 2016	Novel hyaluronan-based hydrogels obtained by supramolecular crosslinking with peptides
Rita Doria	Oct 2015 - Feb 2016	Design and synthesis of self-assembling peptides with binding affinity to hyaluronan

Group Photo (January 2016): Left to Right; Jayati, Helena, Clare, Rita, Dominic, Yeijao, Ana, Elham

Presentations at national and international conferences/meetings

The MHAtriCell group has been very active in attending and presenting work in conferences across the UK and internationally.

Clare O'Malley	Joint Stem Cell Workshop London, UK 14th March 2016	Using phage display as a method to discover novel peptides that specifically bind cancer stem cells in head and neck squamous cell carcinoma – Poster presentation
Dominic Collis	2nd London Polymer Symposium London, UK 13th April 2016	Design and synthesis of biomimetic graft glycopolymers based on hyaluronic acid – Poster presentation
	Self-Assembling Materials for Biomedicine Shinfield Grange Berkshire, UK 14th April 2016	Design and synthesis of hyaluronan based glycopolymers for self-assembly with hyaluronan binding peptides – Poster presentation
	10th World Biomaterial Congress (WBC) Montreal, Canada 17th-22nd May 2016	
Yeijao Shi	Self-Assembling Materials for Biomedicine Shinfield Grange Berkshire, UK	

	14th April 2016 10th World Biomaterial Congress Montreal, Canada 17th-22nd May 2016	Rational design of multifunctional peptide amphiphiles for micelle self-assembly and intracellular delivery – Poster presentation
Elham Radvar	2nd London Polymer Symposium London, UK 13th April 2016	Three-dimensional nanofibrous peptide-polymer scaffolds for hydroxyapatite mineralization – Poster presentation
	Self-Assembling Materials for Biomedicine Shinfield, Berkshire, UK 14th April 2016	
	10th World Biomaterial Congress Montreal, Canada 17th-22nd May 2016	Self-assembled peptide-polymer hydrogels as a 3D nanofiber substrate for biomimetic hydroxyapatite mineralization – Poster presentation
Helena S. Azevedo	10th World Biomaterial Congress Montreal, Canada 17th-22nd May 2016	Self-assembled bioactive membranes for bone regeneration – Oral presentation
		Hyaluronan-based multifunctional hydrogels formed via enzyme-mediated crosslinking – Oral presentation
		Starting a competitive academic lab - Lunch & Learn session

Travel Grants

The MHAtriCell group was also successful in securing funding to support the participation of the members at national and international conferences. We thank the funding organisations for their kind support.

Dominic Collis	IBCarb Travel Grant	£200	The money is linked to the Glycobiotechnology 2016-IBCarb Glycobiotechnology conference in Manchester to help support Dominic Travel to Manchester.
	Royal Society of Chemistry Travel Grant	£650	The money is aimed to support Dominic travel to Canada for the WBC2016, where Dominic will present a poster.
Elham Radvar	Royal Society of Chemistry Material Division	£500	The money is aimed to support Elham travel to Canada for the WBC2016, where Elham will present a poster.

15th Iberian Peptide Meeting

This year, the 15th Iberian Peptide meeting was held in Porto, Portugal. The conference include presentations in the field of peptides. Dr Helena Azevedo and Sofia Ribeiro were among the presenters for the event. Helena delivered one of the keynote presentations titled: "The use of peptides for self-assembling biomaterials: instructive building blocks for constructing complexity and functionality in biomaterials". Sofia presented her work titled "Peptide design for interfacial self-assembly of biomaterials for bone regeneration." The conference had speakers from academia as well as industry from companies such as CEM, who delivered a talk on "An improved coupling method for peptide synthesis at elevated temperature." The presentations were enjoyed by those who attended, including past-students in the MHAtriCell group, Filipa Duarte and Carla Cunha.

Upcoming Publications

- Y. Shi, R. Lin, H. Cui, H. S. Azevedo, Multifunctional self-assembling peptide-based micelles for targeted intracellular delivery: design, physicochemical characterization and biological assessment, in Biomaterials for Tissue Engineering: Methods and Protocols, Ed. K. Chawla, Methods in Molecular Biology.
- A. Mata, H. S. Azevedo, J. Connelly, J. Gautrot, Bioengineering complexity and tuneability in hydrogels, in Hydrogels: Design, Synthesis & Application in Drug Delivery & Regenerative Medicine, Eds. T. R. R. Singh, G. Laverty, R. Donnelly, Science Publishers.
- H. S. Azevedo, Engineering hyaluronan (HA) hydrogels with bioactive and mechanical signals, in Hydrogels: Design, Synthesis & Application in Drug Delivery & Regenerative Medicine, Eds. T. R. R. Singh, G. Laverty, R. Donnelly, Science Publishers.
- J. Banerjee, E. Radvar, H. S. Azevedo, Self-assembled peptides for tissue regeneration and repair, in Peptides and proteins as biomaterials for tissue regeneration and repair, Eds. M. A. Barbosa, C. L. Martins, Elsevier Woodhead.
- "Self-assembling biomaterials: molecular design, characterization and application in biology and medicine", Editors: Helena S. Azevedo and Ricardo M. P. da Silva, Elsevier Ltd

Conferences

International Events

- Self-Assembly & Supramolecular Chemistry - 17-22 May 2016, Lucca, Italy Link
- 10th World Biomaterials Congress - 17-22 May 2016, Montreal, Canada. Link
- ISMSC-2016 - 10-14 July 2016, Seoul, Korea. Link
- ACS International Carbohydrate Symposium - 17-22 July 2016, New Orleans, USA Link

- ICCESC 2016 : 18th International Conference on Chemical Engineering and Supramolecular Chemistry – 22-23 Aug 2016, Paris, France Link
- 6th EuCheMS Chemistry Congress – 11-15 September 2016, Seville, Spain. Link
- International Conference on Applied Chemistry – 17-18 October 2016, Istanbul, Turkey. Link

UK Events

- Glycobiotechnology 2016 – IBCarb Mid-Term Showcase Event – 4-5th April 2016, Manchester
- London Polymer Group 2016 – 13th April 2016, London
- Self-Assembling Materials for Biomedicine – 14th April 2016, Reading
- International Symposium on Macrocyclic and Supramolecular Chemistry (ISMSC) in conjunction with ISACS: Challenges in Organic Materials & Supramolecular Chemistry – 2-6th July 2017, Cambridge

For more conferences visit: http://www.chemistry-conferences.com/topics/

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