



The Power of Peptides: The Precision Molecules of Life

John A Catanazaro^{1*}

Abstract

This review briefly discusses peptides, polypeptides, and their self-assembly architecture as a diverse platform for precision and personalized medicine. Self-assembly is a vital force of nature. The self-assembly process of the peptide chains is dynamic — reassembly repeatedly occurs in a self-healing manner. The interactions that happen to reassemble peptide structures include van der Waals forces, ionic bonds, hydrogen bonds, and hydrophobic forces. These forces also facilitate the molecular recognition function that the peptides encompass.

Keywords: Immunotherapy, Cancer, Neoantigen, personalized vaccine, peptide vaccine,

More Powerful Than DNA

One of the most potent discoveries that have changed the course of science and have affected every aspect of life on this planet is DNA discovery. DNA was first identified in the late 1860s by Swiss chemist Friedrich Miescher. In the decades following Miescher's discovery, other scientists, notably Gregor Mendel, Albrecht Kossel, Walter Sutton, and Theodor Boveri. Phoebus Levene and Erwin Chargaff conducted a series of research efforts that revealed additional details about the DNA molecule, including its primary chemical components and how they joined. Without the scientific foundation provided by these pioneers, Watson, Crick, Wilkins, and Franklin may never have reached their groundbreaking conclusion of 1953: that the DNA molecule exists as a three-dimensional double helix.

Though DNA and RNA are powerful discoveries and both essential to life, a far more complex arrangement of molecular networking coordinates every form of energy. Peptides, polypeptides, proteins, and genes are terms we may all be familiar with and are the essential programming features integrated into every living thing. An intricate network of continual evolutionary adaptation that codes, recodes, edits, re-edits, assembles, and self-assembles to coordinate the unseen world's higher processes.

Self-Assembly A Vital Process

Self-assembly is a vital force of nature. The self-assembly process of the peptide chains is dynamic — reassembly repeatedly occurs in a self-healing manner. The interactions that happen to reassemble peptide structures include van der Waals forces, ionic bonds, hydroge-

Significance | Peptides showed pivotal potency in precision individualized medicine design.

*Correspondence: John Catanazaro at Neo7bioscience, 539 W. Commerce St #2886 Dallas, TX 75208. Email: john.catanazaro@neo7bioscience.com

Edited by Aman Shah Abdul Majid, Quest International University, Malaysia. And accepted by the Editorial Board Dec 20, 2020 (received for review Dec 01, 2020)

Author Affiliation:

¹ Neo7bioscience, 539 W. Commerce St #2886 Dallas, TX 75208

Please cite this article:

John Catanazaro. (2021). The Power of Peptides: The Precision Molecules of Life. *Journal of Precision Biosciences*, 3(1), 1-6.

The 'One Gene – One Polypeptide' Rule

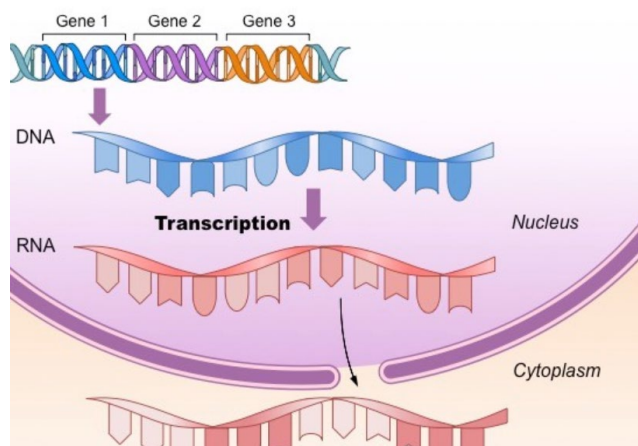


Figure 1. peptides and their pivotal role in protein synthesis and complexities in sustaining life, we discover that “one gene-one protein” is a very simplistic hypothesis.

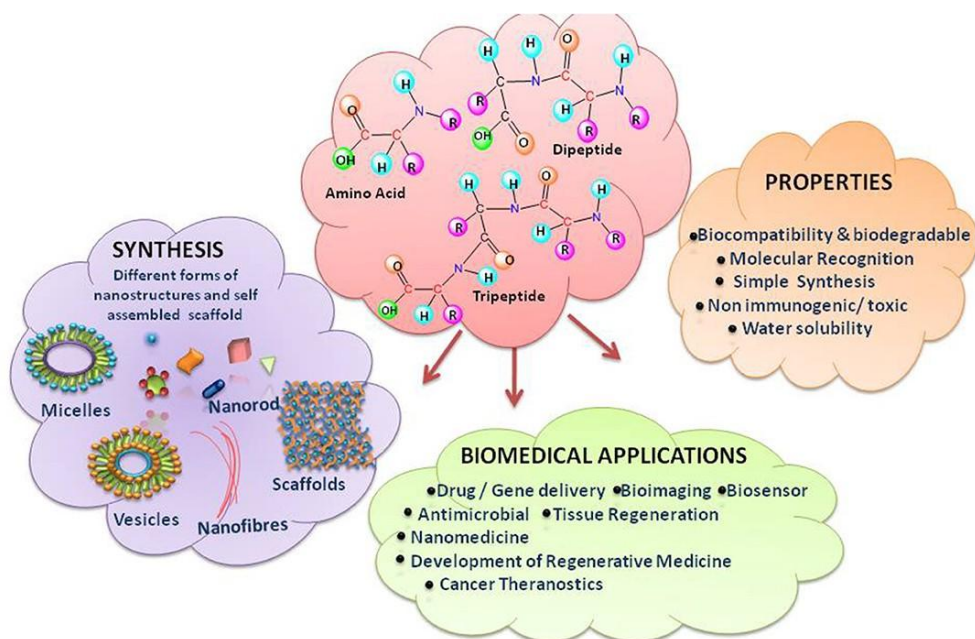


Figure 2. Different forms of peptide nanostructures within the self-assembly model are possible. These peptides can have an impact on many critical areas in the precision or personalization medicine world.

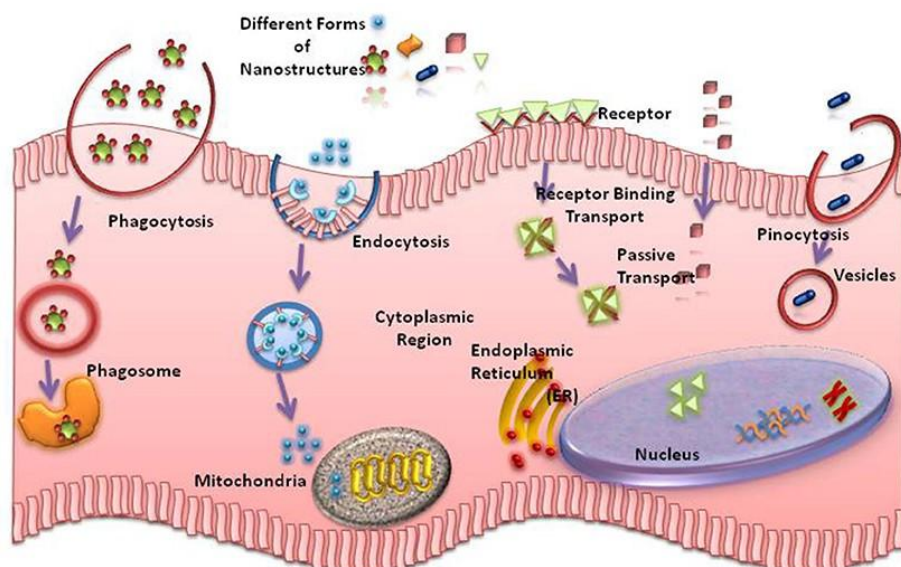


Figure 3. Diverse Cell Delivery of Short Peptide Self-Assembly. Enhanced delivery for every cell structure component and function is necessary to assure transport and desired target action.

-n bonds, and hydrophobic forces. These forces also facilitate the molecular recognition function that the peptides encompass.

Polypeptides are self-assembly sequences that are elementary in the architecture of proteins and are pivotal in protein-protein interactions (PPIs).

An in-depth study of any gene/protein construct reveals the lattice of amino acids involved in the intricate polypeptide assembly's existing engineering. Our current understanding of Genes is that they code for self-assembly polypeptides and are called protein-coding genes. However, not all genes determine self-assembly polypeptides. The challenges to existing gene/protein theory are; is the gene coding for the self-assembly of polypeptides, or is the self-assembly of polypeptides coding for the gene? The science of protein building, structure, and formation continues to evolve as we develop advanced deep-learning technology of proteins. We understand that translation is the overall big picture in protein building. The translation is essential for most living cells to stay alive.

Translation is the process that takes the information passed from DNA as messenger RNA and turns it into a series of amino acids bound together with peptide bonds. It is essentially a translation from one code (nucleotide sequence) to another code (amino acid sequence). One gene-one polypeptide hypothesis is that each gene synthesizes a single polypeptide. It was initially stated as the one gene-one enzyme hypothesis by the US geneticist George Beadle in 1945 but later modified when it discovered that genes also encoded non-enzyme proteins and individual polypeptide chains. It is now known that some genes code for various types of RNA involved in protein synthesis.

As we advance in our understanding of peptides and their pivotal role in protein synthesis and complexities in sustaining life, we discover that "one gene-one protein" is a very simplistic hypothesis (Figure 1). It seems more probable that spontaneous evolution began with a peptide backbone with nucleic acid coupling, translating into the code of life. I discuss this briefly below.

Peptides and Nucleic Acids

In an article re-published by Scientific American, "one of the greatest chicken-or-the-egg questions is: Which came first?—?proteins or nucleic acids like DNA and RNA? Four billion years ago or so, basic chemical building blocks gave rise to longer polymers that could self-replicate and perform functions essential to life: storing information and catalyzing chemical reactions. For most of life's history, nucleic acids have handled the former job and proteins the latter. Yet DNA and RNA carry the instructions for making proteins, and proteins extract and copy those instructions as DNA or RNA. Which one could have originally handled both jobs on its own?" Life's First Molecule Was Protein, Not RNA, New Model Suggests?—?Scientific American

The article further points out that the favored molecule for decades is RNA. RNA is complex, extraordinarily touchy, and under harsh conditions, making it less likely a candidate to have spontaneously arisen. In this case, there is a call for a more stable nucleic structure and a new hypothesis of the dynamic feasibility of a nucleopeptide. An existing genetic replication machinery upon the existing DNA / RNA construct does not explain the origin of the DNA-polypeptide duplication system.

RNA World, Protein World, Nucleopeptide

Before defining peptides and their essential role in human life, we must attempt to understand their true origin. Simply embracing DNA and RNA as the ruling order constructs for life is not enough to satisfy the complexity of interactions with peptides, which contain vital communication sequence coding that can influence virtually every functional protein, cell, and human system.

Evolutionary science continues to investigate the cataclysmic effects of the primordial period. The primordial period bore frequent meteorite hits on the earth's surface. These collisions are assumed to have destroyed all unstable molecules on earth, demolishing life processes' origin. The uniformity of the biochemistry and the genetic code in all living organisms implies that all modern organisms that eventually followed these elimination processes descend from a common ancestor (CA). A unique CA's existence suggests there was only a single successful path from which life evolved, thus giving the mechanisms of early chemical evolution a key role. A fundamental question regarding CA's development is how biological organizations became from an abiotic supply of small organic molecules. Two theorems are known to explain this problem: the "RNA world" and the "protein world" theorems.

The "RNA World"

The "RNA world" hypothesis is the chemical functionality of short RNA fragments, on the one hand, and their remarkable information storage capacity. Short RNA aptamers can specifically bind various chemical entities, and RNA ribozymes can act as efficient catalysts.

Combining these qualities can give rise to aptazymes acting as sophisticated chemical switches. These RNA molecules could have served as their genes and would have been simpler to duplicate than proteins. But the "RNA world" theory suffers from an Achilles heel: the instability of the RNA bases in the primordial earth conditions and the instability of the ribose sugar even under moderate chemical and thermal environments. Under these limitations, it has RNA that could not sufficiently accumulate to allow RNA-based chemical evolution. An alternate hypothesis suggests there were ancestor polymers to RNA and that these polymers later evolved into RNA.

This approach is problematic, first because any minute change in the RNA structure would directly and significantly affect the enzymatic activity of the ribozymes, hence leaving us again with the problem of trying to fill the gap between the pre-RNA world and the existing RNA. Second, since there is no known relic for such a molecule in today's biological systems, there are no leads regarding such a molecule. In light of these obstacles, we should examine peptides' possible roles as a starting point for the origin of life problems should be discussed in a new manner.

The "Protein World"

The "Protein World" hypothesis can satisfy the above considerations. Present research of self-assembly peptides explains similar short peptides' ability to bind and recognize with high specificity nucleotides, the central role for simple peptide self-assembled structures in stabilizing RNA early chemical catalysis. This scenario could later lead to the formation of RNA polymerase as one of the earliest protoenzymes. The involvement of short self-assembling peptides in the origin of life has potential micelle-forming units (The self-assembly of amphiphilic molecules forms micelles. The structures contain a hydrophilic/polar region (head) and hydrophobic/nonpolar region (tail)). Short peptides can form ordered structures or specifically bind nucleotides. Forming the self-assembled structures by the di- and tripeptides is an incredibly intriguing quest for life's origin. The first demonstration that could undoubtedly form peptides under primordial conditions has all the molecular information to assemble into well-defined encapsulated structures. (Carny and Gazit, 2005)

The "Nucleopeptide" IDA

The "Nucleopeptide" IDA (Initial Darwinian Ancestor) hypothesis is a self-replicating theory that aligns with living cells' spontaneous evolution. There is sufficient evidence that early life's essential elements on Earth consisted of amino acids, ribose, and deoxyribose, among others. They were resurrecting the Dead (Molecules) (nih.gov). , for a nucleopeptide IDA to qualify, there must be both a nucleic acid and peptide component. Both are obligatory, but it does not necessarily follow that their contributions are equal in the process.

According to Bernard M.A.G. Piette and Jonathan G. Heddle, "the RNA World is challenged by the fact that a self-replicating RNA polymerase ribozyme has yet to be demonstrated and that little evidence for its existence is seen in life today as well as problems in how the transition from RNA-only to RNA-protein world could have occurred. A molecular replicator with two components –RNA and peptide—overcomes these problems and maybe a better fit."

Regulators of Self-Assembly

Self-assembling peptides are short peptides that undergo spontaneous assembling into ordered nanostructures. These peptides have attracted interest in nanotechnology for their potential for application in

biomedical nanotechnology, tissue cell culturing, molecular electronics, and more. Effectively self-assembling peptides act as building blocks for various material and device applications. The essence of this technology is to replicate what nature does: to use molecular recognition processes to form ordered assemblies of building blocks capable of conducting biochemical activities. Peptide self-assemblies are the lattice of 20 amino acids assembled in number, type, sequence, and side-chain groups. These nanostructures are customizable by incorporating modified amino acids in the peptide design to have superior building properties and enzymatic stability.

Different forms of peptide nanostructures within the self-assembly model are possible (Figure 2). These peptides can impact many critical areas of precision/personalization medicine. In contrast to small molecule drugs, mRNA-derived drugs, and antibodies, short-chain self-assembly peptides have many benefits, including the ability to bind to molecular targets in hard-to-reach places. They are non-toxic, biocompatible, biodegradable, easy to manufacture, and have broad applications and uses.

The Power of Peptides: The Precision Molecules of Life

Amino acids are the building blocks of peptides and polypeptides. Peptides are short and medium-chain, between two and fifty amino acids linked by peptide bonds. Polypeptides are long-chain peptides linked by peptide bonds. A polypeptide that contains more than approximately fifty amino acids is known as a protein.

According to the Handbook of Biologically Active Peptides, some groups of peptides include plant peptides, bacterial/antibiotic peptides (also known as antimicrobial peptides AMP), antiviral peptides (AVP), antifungal peptides (AFP), invertebrate peptides, amphibian/skin peptides, venom peptides, cancer/anticancer peptides (also known as neoantigens), vaccine peptides, immune/inflammatory peptides, brain peptides, endocrine peptides, ingestive peptides, gastrointestinal peptides, cardiovascular peptides, renal peptides, respiratory peptides, opiate peptides, neurotrophic peptides, and blood-brain peptides.

The Multi-Mechanistic Action and Application of Short Peptides

The action and application of short peptides as self-assembly molecules continue to gain significant recognition as a promising delivery in many precision medicine areas, including cancer, autoimmune disease, infectious disease (viral and antimicrobial), neurodegenerative disease, inflammation, and regenerative medicine. Considerable attention to short peptides and their chemistry of various non-covalent interactions has led to a swift development of self-assemblies as drug carriers. (Huang et al., 2013; Panda and Chauhan, 2014; Iglesias and Marchesan, 2017; Amit et al., 2018; Raza et al., 2018; Mishra and Jyoti Panda, 2019).

PBIMA – SOLVx inhibition sites on viral replication cycle

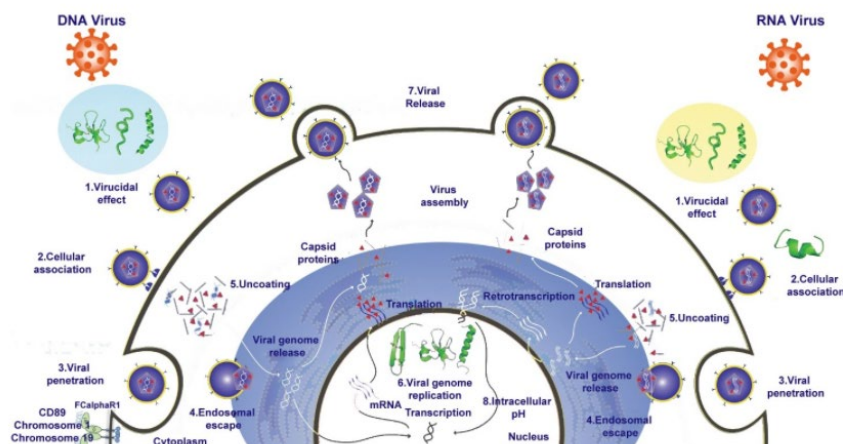


Figure 4. Pooled-peptide therapeutic strategy against multiple viral proteins

Short peptides are direct cell-penetrating peptides (CPPs), carriers for intracellular transport cargoes (siRNA, nucleic acids, proteins, various nano-particulate pharmaceutical carriers, liposomes, micelles). Self-assembly peptides are known to enhance the delivery of small molecule therapeutic agents and use as MRI contrast agents (Guidotti et al., 2017; Hoffmann et al., 2018; Panigrahi et al., 2018; Ramaker et al., 2018; Vánová et al., 2019) since these are internalized by cells in an exceedingly effective manner.

Self-Assembled Short Peptide Enhanced Cell Delivery

What makes short peptides so appealing is their extensive ability and action to facilitate crucial molecular signaling and programming within living cells (Figure 3). This action is especially promising in health and longevity as these signaling and programming capabilities can change the course of adverse molecular changes associated with the disease. Enhanced delivery for every cell structure component and function is necessary to assure transport and desired target action.

Short Peptide Delivery In Immune Defense Against Viral Pathogens

Considering the diverse range of short self-assembly peptides described above, another promising application is in defense against microbes and viruses (Figure 4). These short peptides can effectively initiate favorable actions in bacterial and viral infections. The figure below is an example of a viral replication cycle. A multi-sequence short peptide engineered pooled assembly design was studied on a Sars-CoV2 mutant strain and found to be 99,8% effective as a treatment in eradicating the virus. The design’s viral eradication action is due to multi-mechanistic activity on the viral replication cycle’s inhibition sites. As stated above, research further establishes the value of a diverse delivery to living cells. One of the shortfalls of

essential in combating any disease to have the promise of target / multi-target delivery. Self-assembly short peptides offer robust options in this arena.

Conclusion

The short peptide self-assembly can be potent molecules, particularly in the precision / personalized medicine arena. Diverse applications can prove extremely valuable in developing treatments with minimal toxicity and significant efficacy in improving and sustaining health.

Author Contribution

J.C. wrote and reviewed the manuscript.

Acknowledgment

None declared.

Competing financial interests

The author is working in Neo7bioscience.

References

G. W. Beadle and E. L. Tatum, Genetic Control of Biochemical Reactions in Neurospora, (1941, 27 (11), 499-506, <https://doi.org/10.1073/pnas.27.11.499>)

Jordana Cepelewicz, (2017), Life’s First Molecule Was Protein, Not RNA, New Model Suggests, Quanta Magazine.

Carny, O., and Gazit, E. (2005). A model for the role of short self-assembled peptides in the very early stages of the origin of life. FASEB J. 19, 1051–1055. doi: 10.1096/fj.04-3256hyp

Zauchna J, Heddle JG. Resurrecting the Dead (Molecules). Comput Struct Biotechnol J. 2017 May 30;15:351-358. doi: 10.1016/j.csbj.2017.05.002. PMID: 28652896; PMCID: PMC5472138.

Bernard M.A.G. Piette, Jonathan G. Heddle, (2020), A Peptide–Nucleic Acid Replicator Origin for Life, *Trends in Ecology & Evolution*, 35(5), 397-406.

Gupta Seema, Singh Indu, Sharma Ashwani K., Kumar Pradeep, (2020), Ultrashort Peptide Self-Assembly: Front-Runners to Transport Drug and Gene Cargos, *Frontiers in Bioengineering and Biotechnology*, 8

Catanzaro JA, Yuryev A, Sultan Khan MS Treatment using SOLVx-COVID-19 in a preclinical animal model with a broad-surveillance pooled-peptide therapeutic strategy against multiple viral proteins of SARS-COV2 mutant, ASGCT (published in 2021, Cell Press, *Molecular Therapy Journal*)

Submit your next manuscript to *Journal of Precision Biosciences* published by Eman Research Ltd

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in Australian National Library and Google Scholar
- Both Open (80-100% subsidized APC by ER) & non-open access option

Submit your manuscript at
<https://publishing.emanresearch.org>