Drug Discovery and Design from Marine Organisms Such as Slugs: Implications for the Perception of an Omniscient Engineer

by C. Shipman, Marine Biologist and Educator

The boundless knowledge we can acquire from God's creation is astonishing. Chemicals from marine organisms and their potential use in medicine are immeasurable, since it is believed that most marine life is not yet discovered, and the majority of known marine life still requires chemical study. These chemicals, known as marine natural products, can be used to explore the complex processes of cells at the molecular level. Incredibly, they also possess the ability to treat diseases such as cancer and AIDS. Research

into marine natural products and its relevance to pharmacology, the study of drugs, is a fairly new scientific discipline that is advancing medicine. Its emergence demonstrates the progress of science, an innovative and creative process, which only works because it is studying a created nature.

Algae, bryozoans, and sponges, in addition to the vast array of other marine

continued on page 3



Figure 1. Stypopodium sp., genus of brown marine algae (Suringar, 1870). https://en.wikipedia.org/wiki/Stypopodium

RNA Viruses as Examples of Evolution

by Dr. Kevin Anderson

The SARS-CoV-2 pandemic has dramatically raised public awareness of viruses. The evolutionist community has sought to leverage this increased attention to tout certain variations in viral activity as a clear example of evolution. Falling back on their simplistic definition that evolution is merely *change*, they point to the mutational changes of viral envelope proteins as "evolution in action."

Virus Structures

Animal and human viruses are obligate, invasive entities. They can only reproduce by infecting cells and using the cell's metabolic machinery to replicate their genome and synthesize their proteins. Once replicated, these viral genomes and

proteins are assembled into new viruses during the maturation step (Figure 1).

Enveloped viruses obtain their outer layer by a process of budding. This event surrounds the newly formed virus with a portion of the infected cell's membrane as the virus exits the cell. Once released from

Math Matters

A Grain of Sand

by Don DeYoung, PhD

"To see a world in a grain of sand, and heaven in a wild flower, Hold infinity in the palm of your hand, and eternity in an hour..."

So begins the poem *Auguries of Innocence* by William Blake (1757–1827). In 132 lines of verse, Blake describes the infinite details of creation. His point is that small everyday objects in nature are a window on what lies beyond. An augury is a sign of what is about to happen, and the poem describes the results of poor stewardship of nature.

As William Blake suggests, let us consider a grain of sand. The typical size is a millimeter, larger than silt particles and smaller than gravel. The chemical composition of sand is usually silicon dioxide, SiO₂, also called quartz. This common mineral has unusual hardness and is a common product of rock disintegration.

Suppose a sand grain has a mass of 0.01 gram, 250 times less than a penny. The grain contains about 10²⁰ quartz molecules arranged in an elegant 3-dimensional hexagon structure. If one could see within this sub-microscopic world, the sand grain interior would resemble a vast stadium filled with an orderly array of silicon and oxygen atoms. Here and there occur atom vacancies resulting in crystal defects. There also are stray impurity

Contents



atoms including iron, aluminum and manganese. With this vast crystalline structure of quartz molecules and atom variables, no two sand grains on earth are identical on the micro scale.

How many total sand grains exist on all the shorelines of planet earth? One estimate is 10^{22} , or ten billion trillion sand grains

(DeYoung, p. 118). There is something curious about this vast number: It is also an approximation for the total known stars in the physical universe.

The numerical comparison between stars and sand grains provides a good illustration of the vastness of the heavens. The next time you walk along a sandy shoreline, perhaps you can imagine moving among the countless stars. Consider also that each grain of sand has an interior world of complexity.

A special promise given to Abraham was that his descendants would number as "the stars of heaven and as the sand on the seashore..." (Genesis 22:17). This implies that the offspring of Abraham are beyond numbering. The family of God is large and growing.

Reference

DeYoung, Don B., 2010, *Astronomy and the Bible*, BMH Books, Winona Lake, IN. Available from CRS Books.

Creation Matters

ISSN 1094-6632 Volume 25, Number 4, Fall 2020

Copyright © 2020 Creation Research Society
All rights reserved

Editor: Jean K. Lightner

Design Services: Cindy Blandon, cblandon@aol.com

Creation Matters is a publication of Creation Research Society, 6801 N. Highway 89, Chino Valley, AZ 86323-9186, www.creationresearch.org

Article submissions and inquiries for *Creation Matters* can be addressed to CMeditor@creationresearch.org

Articles published in *Creation Matters* represent the opinions and beliefs of the authors, and do not necessarily reflect the official position of the CRS.

Drug Discovery

continued from page 1

animals lacking a backbone, are rich sources of compounds lethal to various mouse, rat, and human cancer cell types. Stypopodium zonale (Figure 1), a Caribbean brown marine algae, contains the natural product stypoldione (Figure 2), which disrupts spindle formation, ultimately stopping cancer cell division. Spindles are cellular structures needed to separate the duplicated DNA of the

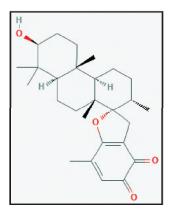


Figure 2. Stypoldione, from Stypopodium zonale, stops cancer cell division (PubChem). https:// pubchem.ncbi.nlm.nih.gov/compound/ Stypoldione

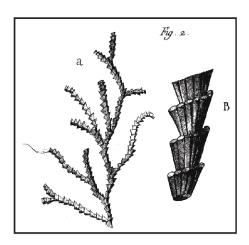


Figure 3. The bryozoan Amathia convoluta (Lamouroux, 1816). http://www.bryozoa.net/ctenostomata/vesiculariidae/amatcon.html

parent cell into two daughter cells. The bryozoan Amathia convoluta (Figure 3) contains convolutamide A (Figure 4), a chemical successfully utilized to treat mouse leukemia, a blood cancer, and human epidermoid carcinoma, a cancer of thin, flat cells of the skin and lining of hollow organs. The deep-water sponge Dercitus sp. (Figure 5), of the Bahamas, comprises dercitin (Figure 6), a compound which extends the life span of mice with leukemia tumors. It also is effective against human melanoma, a cancer of the pigment-manufacturing cells, melanocytes. Dercitin also attacks small cell Lewis lung carcinoma, a lung cancer affecting mice. It likely functions by blocking DNA replication in these cancer cell types.

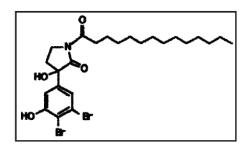


Figure 4. Convolutamide A from Amathia convoluta (Zhang et al. 1994). https://www.sciencedirect.com/science/article/abs/pii/ S004040200181752X



Figure 5. Dercitus (Halinastra) luteus, a sponge in the genus Dercitus (Photo taken by Rob van Soest). http://www.marinespecies.org/porifera/porifera. php?p=image&pic=11446

The chemical compounds within marine organisms act as a blueprint for chemists to design and build replicate copies of these chemicals in the lab. Chemical design in the lab inspired from nature is persuasive, logical evidence that nature itself was designed. Since humans were made in the image of God, we continue to exhibit His creativity and copy His engineering to develop the medical and pharmaceutical sciences.

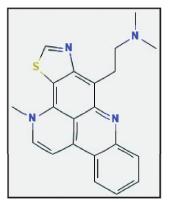


Figure 6. Dercitin from a sponge, Dercitus sp., is effective against human melanoma and small cell Lewis lung carcinoma (PubChem). https://pubchem.ncbi.nlm.nih.gov/compound/ Dercitin#section=Structures



Figure 7. Dolabella auricularia contains the anticancer compound Dolastatin 10 (Photo taken by Baron Joshua). https://aquafauna. fandom.com/wiki/Dolabella_auricularia

Drug Discovery

continued from page 3

Opisthobranchs, or marine slugs, contain astounding biochemical capacities to safely acquire defensive compounds from their food (i.e. algae, bryozoans, and sponges), which they can modify as necessary to produce toxic compounds that protect them against predators. The bright warning colors of many slugs alert predators to the fact that they are poisonous. As a result, they do not need a shell

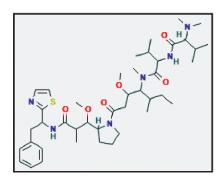


Figure 8. Dolastatin 10, an anticancer compound from the marine slug Dolabella auricularia, which inhibits microtubule assemblage and arrests mitosis (PubChem). https://pubchem.ncbi. nlm.nih.gov/compound/dolastatin-10#section=Structures

to protect their soft bodies, or some have a reduced shell.

With over 5,000 species, each potentially containing undescribed natural products, marine slugs are a promising source for the discovery and extraction of novel anticancer agents. Researchers already have isolated anticancer compounds (Figures 8, 10, and 12) from the marine slugs Dolabella auricularia (Figure 7), Elysia rufescens (Figure 9), and Jorunna funebris (Figure 11).

The discovery of advantageous chemicals within marine organisms highlights the

value of the ocean and its life to humanity. Protection and conservation of fragile marine ecosystems, such as diversityrich coral reefs, is vital since the cure for cancer, AIDS, and other diseases could be unearthed from organisms occupying these underwater jungles. With this scientific knowledge, we are reminded of our call to steward God's creation so we can continue to reap benefits from these natural chemicals, which can assist us in treating diseases that resulted from mankind's fall and the dysfunction of the original, perfect biological creation.



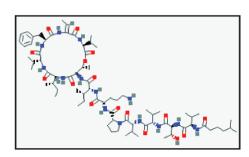


Figure 10. Kahalalide F, a cytotoxic marine natural product from Elysia rufescens (PubChem). https:// pubchem.ncbi.nlm.nih.gov/compound/ Kahalalide-F

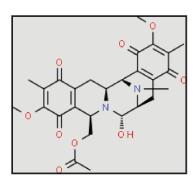


Figure 12. Jorumycin, the cytotoxic chemical derived from the marine slug Jorunna funebris (ChemSpider). http://www.chemspider.com/ Chemical-Structure.10478273.html



Figure 9. Elysia rufescens contains the anticancer compound Kahalalide F (Photo taken by Philippe Bourjon). https://commons.wikimedia.org/ wiki/Category:Elysia_rufescens#/media/File:Elysia_ rufescens_R%C3%A9union.jpg



Figure 11. Jorunnα funebris harbors the anticancer chemical jorumycin found within the drug Zalypsis® (Photo taken by Chaloklum Diving). https://commons. wikimedia.org/wiki/File:Jorunna_funebris,_Koh_Phangan. jpg

RNA Viruses

continued from page 1

the cell, the virus retains a portion of this membrane as its envelope (Figure 1).

This viral envelope contains cell membrane proteins, as well as certain viral proteins. These viral proteins are expressed from genes on the virus' genome, and are transported and inserted into the cell's membrane prior to the virus' exit. Since they are encoded on the viral genome, these specific envelope proteins are unique to a particular family or even strain of virus.

Several of these viral proteins protrude from the envelope to form structures called spikes. Some spikes are involved in viral attachment to the cell's surface prior to entering the cell. Different viral spikes have a binding affinity for different cell surface proteins (Shang et al., 2020; Wilen et al., 2012). In part, this determines not only what animal species the virus can successfully infect, but even the specific cells of that species. Hence, some human viruses can only infect our blood cells and others only infect our epithelial cells.

Some viral envelope proteins may also serve as an antigen, which the immune system will use to detect and identify the virus. As long as the protein remains chemically unaltered, it will continue to serve as an antigen for that specific strain of virus. The immune system will retain a "memory" (sometimes for decades) of this antigen, and respond more quickly to subsequent infections by this particular virus. Known as "acquired immune response," this is the general basis of all vaccines.

Ever Changing Viral Proteins

Many enveloped viruses, such as influenza viruses and coronaviruses, possess

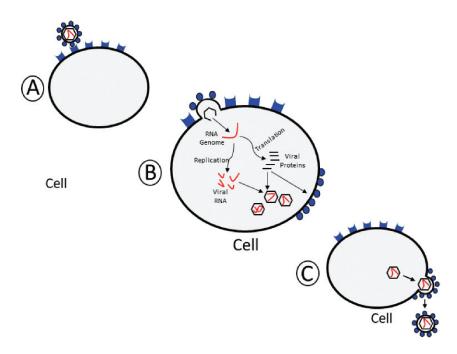


Figure 1. General overview of the infection and replication stages of an enveloped RNA virus. A) Viral spike proteins bind to specific cell surface proteins as a first step of infection. B) Upon entering the cell, the virus' RNA genome is replicated and also translated into viral proteins. Some of these viral proteins are used to form new viruses (a process called maturation). Other viral proteins are inserted into the cell's membrane. C) Following maturation, new viruses use a "budding" process to exit the cell. As part of "budding," a portion of the cell's membrane becomes the viral envelope. This envelope contains both cell membrane proteins and viral proteins (illustrated as blue circles).

genomes of RNA rather than DNA. Upon infecting a cell, these RNA genomes are replicated via a specialized virus enzyme: RNA-dependent RNA polymerase. This enzyme uses a strand of RNA as the template and makes a complementary strand of RNA.

However, most of these viral RNA polymerases are very mutation-prone (i.e., low fidelity) with no repair system for these mutations (Drake and Holland, 1999)—coronaviruses appear to be one of the few exceptions (Cyranoski, 2020). As a consequence, mutations are occasionally introduced into the viral RNA genome. If a mutation occurs in the genomic region that codes for an envelope protein, the mutation may alter the protein's amino acid sequence. In

turn, this may change the protein's conformational structure as it is placed into the cell's membrane. Following budding, the virus' envelope will now contain this structurally altered protein.

If the altered protein serves as a viral antigen, potentially this alteration could affect its antigenic properties (resulting in "antigen variation"). The immune system may not recognize this altered structure, thereby diminishing the organism's acquired immune response. Simply stated, immunity is lost or dramatically weakened. The virus can now re-infect a host and more successfully evade that host's immune system.

RNA Viruses

continued from page 5

Mutational change of the envelope spikes may also alter the virus' ability to bind to a cell. This could reduce or even eliminate cell binding. Since binding to the cell surface is an essential first step of viral infection, any mutation that eliminates this binding will render the virus inert.

On the other hand, some conformational changes can alter a protein's binding specificity, enabling a viral spike to bind to different cell surface proteins. As a consequence, the virus may now bind to cells of a different species. A species jump from animal to human is known as zoonosis. This zoonotic jump appears to have occurred with several coronaviruses, including SARS-CoV-2 (Anderson et al., 2020).

In addition, many RNA-enveloped viruses frequently engage in recombinational gene swapping (Pérez-Losada et al., 2015). This can occur if a cell is simultaneously infected by at least two different viral RNA genomes (Figure 2). During the maturation step, portions of these different genomes may recombine, shuffling the genes of the different viruses.

While the resulting recombined genome may weaken viral activity, it typically imparts little impact on the virus. How-

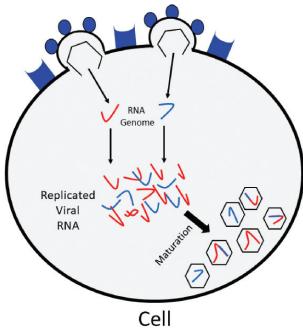


Figure 2. RNA virus recombination. Different RNA viruses simultaneously infect the same cell. Each virus' RNA genome is replicated, resulting in a pool of different viral genomes inside the cell (represented by different colors). During maturation, copies of the different genomic RNA are packaged together, forming a hybrid strain of virus.

ever, sometimes this recombination alters viral antigens, causing an antigenic shift (Zambon, 1999). Like the mutational changes previously discussed, this shift can interfere with the immune system's recognition of particular viruses. This is one reason why seasonal influenza vaccines vary in effectiveness.

Genome recombination also may have imparted CoV-2 with an ability of coopting a cellular enzyme to increase its proficiency of cell entry (Cyranoski, 2020). This makes CoV-2 more infectious than other coronaviruses. A similar enzyme coopting is found in several highly virulent RNA viruses, such as HIV, Ebola, and influenza.

What is Evolution?

If evolution is only defined as "change," then clearly alterations of viral envelope proteins are examples of evolution. These alterations involve changes to both the genotype and phenotype of the virus. Thus, presumably, this offers a perfect example of evolutionary transformation.

However, defining evolution as merely "change" is not very scientifically useful. What type of change? How much change? Changes at what level? This simplistic definition does not provide any explanatory power regarding the origin of any species, let alone the origin of all species. Plus, this definition does not differentiate evolution from a creation model, which also allows for life to undergo certain levels of change.

Instead, current theories of evolution propose to explain the origin and diversity of all life on Earth. Thus, to serve as a theory of origins, all teachings of evolution must encompass more than mere biological change. Evolution must explain how life arose to its current levels of complexity and structure.

As part of this explanation, teachings of evolution propose some form of "universal common descent," the claim that all life shares a common ancestry (Woese, 1998). This level of descent seeks to describe the massive transformations predicted by evolution; e.g., how vertebrates derived from invertebrates and how reptiles mutated into mammals. Such massive transformations require very specific and large-scale changes, not just a generic type of change. Therefore, the more appropriate question is whether changes observed in viral proteins give any genetic insight into the massive transformations driving universal common descent.

¹ While the literature frequently identifies these viral events as recombination, they are non-reciprocal exchanges (more appropriately identified as gene conversion). As such, viral recombination does not involve the same events as recombination in sexually reproducing organisms. However, the use of the word "recombination" has become so established in virology that it is unlikely the terminology will be changed.

RNA Viruses

continued from page 6

Virus Evolution?

Broadening the viral spike's affinity for certain cell surface proteins is actually a reduction of protein specificity (Bone, 1989). The broader a protein's binding affinity, the less specified is the protein's activity. Thus, reduced specificity is biochemically degenerative. While this reduced specificity may enable the virus to infect a wider range of cells, it comes at the expense of a pre-existing specificity of the protein. These types of events have been described as antagonistic pleiotropy, a beneficial adaptation due to the loss of a pre-existing function or system (Schneider and Lenski, 2004). Such pleiotropy does not provide a genetic mechanism for the origin of protein specificity, only its demise. A mountain climber does not reach the peak of a mountain by descending (Anderson and Lightner, 2016). Thus, this level of viral change offers no genetic insights into a mechanism for universal common descent.

By the same token, mutational alteration of antigenic proteins may be beneficial for the virus' ability to evade the immune system. However, decreasing the antibody binding affinity for a viral antigen reveals nothing about how that precise affinity originated. What aspect of this mutation provides any genetic insight into the origin of proteins, let alone the origin of viruses, membranes, or cells?

The recombination of viral RNA may alter the virus' phenotype. For many influenza viruses, this recombination can result in antigenic shift. In the case of CoV-2, this recombination appears to have increased its ability to enter human cells. For the virus, altering antigens or increasing the efficacy of cell entry is beneficial. However, as with other forms of horizontal gene transfer, RNA virus

recombination incorporates genomic sequences from one viral RNA genome into a different RNA genome. This genetic exchange involves pre-existing genomic sequences. New sequences of viral RNA are not formed. Thus, viral recombination does not provide genetic insight into the origin of the recombined segments, only their transfer within the biological world.

Altering binding specificity of proteins, structural changes of antigen binding sites, or rearranging various envelope antigens illustrates how limited adaptive variation can occur within the virus world. However, these variations fail as examples of genetic events required for universal common descent. Consequently, it is misleading to cite such viral changes as "evolution in action." By using such phrasing, evolutionists are attempting to disguise these limited variations to imply that they are part of a mechanism driving universal descent of all life.

On the other hand, this level of variation fits within a biblical creation model. God endowed organisms the ability to multiply and fill the earth (Gen. 1:22) including the post-flood earth (Gen. 8:17). This post-flood world possesses a wide array of environments and weather conditions (including areas of extreme hot and extreme cold). To fulfill God's command, organisms must possess the capability of adapting to these different environments. A range of physiological, genetic, and epigenetic mechanisms can enable this adaptation.² Yet, this level of adaptation involves limited changes to organisms and does not support the extensive and dramatic changes required by universal common descent.

References

Anderson, K. and J. Lightner. 2016. The challenge of Mount Improbable. Creation Research Society Quarterly 52:244-248.

Anderson, K.G., A. Rambaut, W.I. Lapkin, E.C. Holmes, R.F. Garry. 2020. The proximal origin of SARS-CoV-2. Nature 26:450-452.

Bone, R., J.L. Silen, and D.A. Agard. 1989. Structural plasticity broadens the specificity of an engineered protease. Nature 339:6221:191-195.

Cyranoski, D. 2020. Profile of a killer virus. Nature 581:22-26.

Drake, J.W., and J.J. Holland. 1999. Mutation rates among RNA viruses. Proceedings of the National Academy of Sciences 96:13910-

Pérez-Losada, M., M. Arenas, J.C. Galán, F. Palero, and F. González-Candelas. 2015. Recombination in viruses: Mechanisms, methods of study, and evolutionary consequences. Infection, Genetics and Evolution 30:296-307.

Schneider, D. and R.E. Lenski. 2004. Dynamics of insertion sequence elements during experimental evolution of bacteria. Research in Microbiology 155:319-327.

Shang, J., Y. Wan, C. Luo, G. Ye, Q. Geng, A. Auerbach, and F. Li. 2020. Cell entry mechanisms for SARS-CoV-2. Proceedings of the National Academy of Sciences 117(21):11727-11734.

Wilen, C.B., J.C. Tilton, and R.W. Doms. 2012. HIV: Cell binding and entry. Cold Spring Harbor Perspectives in Medicine 2:a006866.

Woese, C. 1998. The universal ancestor. Proceedings of the National Academy of Sciences 95: 6854-6859.

Zambon, M.C. 1999. Epidemiology and pathogenesis of influenza. Journal of Antimicrobial Chemotherapy 44(Supp B):3-9.



The Society's eKINDS project is studying a variety of mechanisms that can account for rapid adaptation and diversification following the Genesis Flood. For more information, see https://www.creationresearch.org/ekindsexamination-kinds-natural-diversificationspeciation

Creation Matters

Creation Research Society 6801 N. Highway 89 Chino Valley, AZ 86323-9186 USA

Address Service Requested

NON-PROFIT U.S. POSTAGE PAID TUCSON, AZ PERMIT NO. 271

Prayer Matters

Praise: We thank God for each one of you who contributes through prayer, finances, and service as we seek to glorify God through understanding His Creation.

Prayer: The Creation Research Society (CRS) has recently announced our move to the campus of Arizona Christian University. This strategic move comes with some substantial one-time expenses, to prepare the building for our use. Please pray for God to guide us, and stir the hearts of His people to contribute to this venture, as we together seek to honor God, our Creator. We at CRS want to effectively proclaim the deeds of the LORD to the next generation (Psalm 78:4).

Thanks Again!

CRS is moving!

The Creation Research Society is moving our operation center and research laboratories to the campus of Arizona Christian University, Glendale, AZ. The new facility will provide the Society with:

- High-profile location and increased visibility for the Society
- Modern research laboratory
- Easily accessible walk-in bookstore
- · Modern office space
- · Increased laboratory space

For more information or to help support the move: (928) 636-1153 www.creationresearch.org

