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28DEC2022

Ross Youngs
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Dear Ross:

Many thanks for the long discussion re Biosortia and the attachments demonstrating some of the potential of what I might call “The Freshwater Cyanobiome”.

Over the last fifteen or so years, microbiologists and scientists from other disciplines have begun to investigate the human microbiome and by analogy, the microbiome of other organisms, many of which are from areas that people have not even considered as being a “Microbiome”. Examples of which would be the as yet uncultured microbes that exist inside of marine invertebrates, in particular sponges which I know that Guy Carter may well have been “mentioning these areas as future targets”. I should add that as yet uncultured microbes have had their active compounds traced back to beetles, so Mother Nature is rather promiscuous as to where she places bioactive molecules.

However, what Biosortia has done and effectively on a shoestring, is to take advantage of the freshwater cyanobacteria blooms that occur in inland lakes, and demonstrate that these naturally occurring blooms can contain previously unknown bioactive compounds, that though not usually a drug entity, can direct talented chemists towards a naturally occurring chemical structure that has potential in a variety of disease states.

What is well-known in drug discovery pathways is that combinatorial chemistry “shot its bolt” many years and countless millions of dollars ago, without producing more than three to four approved drugs in the USA/EU. Yes, Combichem is magnificent for developing an active structure, but is useless as a discovery tool.

What Biosortia has is effectively a relatively unlimited source of potentially bioactive structures. These can be manipulated to tease out the bioactive portion(s) of a novel structure and provide it as a lead for optimization via chemists working closely with biologists. Their ultimate aim being to produce a series of potential leads that contain the “active center(s)” of the isolated compounds.

Another advantage of the Biosortia approach is that it basically starts with the technologies necessary to isolate structures that were previously unknown and/or not recognized, as the number of scientists involved in utilizing what is effectively a large-scale natural resource. Yes, as climate changes occur, the materials found in any one specific place of freshwater cyanophyte blooms will change, but the “real gold” is in the determination of the “bioactive centers”.

One can argue that a “laundry list” of novel compounds is not what the pharmaceutical discovery platforms want as they are often tied to what natural products chemists call the “bioactive isolation paradigm” where only a bioactive agent is initially identified. This has definitely proved to be very fruitful in the earlier days of antibiotic discovery and other drug areas, but requires resources that Biosortia does not have. However, linking in with the new “biological DARPA aka ARPA-H” where Biosortia’s novel chemical compounds can be tested in a large variety of relevant models is a potential route to developing your discoveries.

Just to demonstrate how a peptidic natural product led to both a treatment for diabetes 2 and antiobesity drugs that are “flying off the shelves, one only has to look at the current story of the peptidic semaglutide and tirzepatide both based on peptidic natural products as antiobesity drugs even though first approved for treatment of Type 2 diabetes. This effect was not predicted initially but is now quite real. The lesson from the above is that you really do not know everything that can occur with a particular structure.

The topic above brings up an area that Guy and myself would have always been against in “earlier lives”, the technique that natural product chemists used to call “grind and find” which was, and still is, responsible for the vast number of natural products reported over the last 90 plus years mainly from plant sources. However, the structures reported by Biosortia are quite different from those “G&F” sources, even though it is probable that a significant number of those agents are the product of microbes in, on or around the plant and its rhizosphere.

In addition, the Biosortia compounds are also different from the compounds reported by scientists who collect cyanophytes and then ferment them to produce materials that are then subjected to bioactivity isolation in their “disease of choice”. Biosortia’s product(s) are from multiple interactions between cyanophytes and other organisms in the water column from which they were isolated.

Thus, one may argue that these compounds are the “ultimate product(s) from multiple interactions” that have occurred with the organisms in, on or around the source watershed.

You can use any part of this that you wish in discussions with other companies / organizations etc. I will add, for their benefit, that this letter was drawn up without any financial arrangements either discussed or in place with Biosortia.

Sincerely,

David J. Newman, DPhil, FRSC, FRSB

Principal, Newman Consulting LLC