iMetabolic Biopharma Corporation

"Restoring Health Through Innovation"

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Lipid Language: The iMBP Corporation Newsletter

Perspective

Dear Friends:

As iMetabolic Biopharma (iMBP) Corporation embarks on its momentous journey into the world of drug discovery and development, the management team wanted to create a platform to share information that would directly benefit each and every one of you. With a fundamental belief in education, our core goals are to provide novel insight and a better understanding of obesity plus its debilitating and deadly comorbidities. For this, we present to you **Lipid Language**, the iMBP Corporation Newsletter. The goal of this Newsletter is to not just simply provide our readers with updates on Company developments, and provide an opportunity to get to know our team, but to also learn more about the evolving science in the field. As we focus on developing solutions to these challenging health problems, we firmly believe as a Company that it's only through education that we can provide an effective solution.

"A true teacher would never tell you what to do. But he would give you the knowledge with which you could decide what would be best for you to do."

-Christopher Pike, "Sati"

Featured Article

*A Particle Look at LDL Cholesterol: When **Size** Really **Does** Matter!*

By: Urban A. Kiernan, Ph.D.

Most of us are familiar with the ordeal of getting a lecture from our primary care physician regarding the dreaded LDL Cholesterol (LDL-c), the "bad" cholesterol, and how we need to do a better job at controlling that number. Common reference ranges define the optimal target goal as < 100 mg/dL, and high levels exceed 160 mg/dL. However, I question how many of us have actually taken the time to understand what that number truly means and how that information could be interpreted in a number of different ways. This question is not a criticism or meant to belittle. It is simply a direct attempt to get you to ponder what in reality is "bad" cholesterol.

From a chemistry view point, cholesterol is an organic molecule that is classified as a sterol fat. It is made by a number of different organs in the body and is a major component of all cell membranes. It is also an essential building block for steroid hormones, such as testosterone & progesterone, and other functional biomolecules such as bile. Cholesterol is transported through the blood in a variety of particles called Lipoproteins **(Figure 1)** which are classically differentiated by density. These lipoprotein particles vary in fat composition (ratio between cholesterol and triglyceride), apolipoprotein components (special proteins that control structure and function of the particles) and ultimately size. It is this

size differential within this variety of "bad" cholesterol that requires additional focus as the cholesterol molecule in itself is neither good nor bad; it's the function and ultimate fate of these lipoprotein particles that define them as beneficial or detrimental.

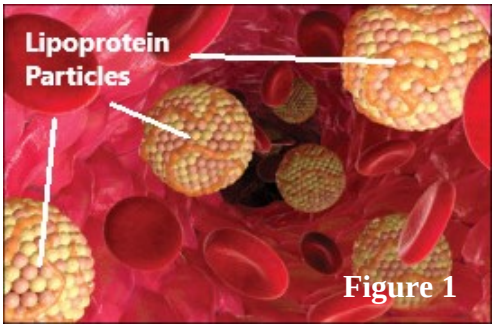

Figure 1

It is here that specific emphasis needs to be placed in the LDL portion of the nomenclature, which stands for Low Density Lipoprotein. What is presented to you and your physician is not truly LDL by itself. The results that are provided are a mix of different lipoprotein subtypes that include LDL. Also included are amounts of Very Low Density Lipoprotein (VLDL) and Intermediate Density Lipoprotein (IDL). For the record, the inclusion of all these particles types into a single data point is referred to as non-high density lipoprotein (HDL). Remember that HDL is your "good" cholesterol, so non-HDL is everything but the "good" cholesterol. The point being made is that size does matter when it comes to lipoproteins. As shown in **Figure 2**, you can have two individuals with the same LDL-c concentration, but depending upon particle size there can be a significant difference in cardiovascular disease risk. Even if you look specifically at LDL particles, there is a lot of different sizes present in the blood. Research has shown that a higher number of smaller LDL particles leads to higher levels of atherosclerosis, leading to an increased risk of heart attack and stroke. However, the less abundant larger partcles have a higher payload of fat thus skewing the plasma concentration to a higher number. So now the question we need to ask how can you tell the difference between these two patient types when the LDL-c concentration numbers being reported are the same?

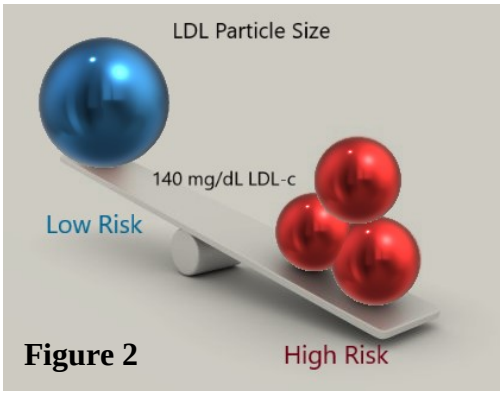

Figure 2

The simple answer is you can't. That is if you stick with the same analytical and decision making processes applied as a part of the status quo. It should be noted that a 2009 national study conducted by Fonarow (David Geffen School of Medicine at UCLA) et al showed that 50% of patients admited to hospitals for heart attacks and 50% of patients with heart disease had normal to low LDL-c levels as a part of a standard lipid panel (total cholesterol, LDL-c, High Density Lipoprotein (HDL)-c and Triglycerides). Since then the clinical guidelines for cardiovascular disease have changed, but the most recent iteration still do not provide clear guaidance on how to address such issues. Advancements in cardiovascular disease research have resulted in the development of the Verticle Auto Profile (VAP) test. This test provides enhanced lipid profile information. This includes a more accurate direct measurment of LDL, LDL pattern density which establishes particle size ranges, measurement of all the lipoprotein subclasses and Lipoprotein(a). Nonetheless, there is a catch to the VAP test and that is cost. The tests available are extremently expensive with current technologies and most issuance programs will not cover these tests.

However, don't dispare as there is a viable answer that enhances the current lipid panel data while cost effective. This answer is Apolipoprotein B100 (ApoB). To quickly explain, lipoprotein particles contain a number of different apolipoproteins which dictate both form and specific function. All "bad" cholesterol, the traditionally viewed LDL-c particles, contain one molecule of ApoB per particle, **Figure 3**. Your "good" cholesterol, HDL-c, does not contain any ApoB. Therefore, by simply measuring the fasting concentration of ApoB, the number of LDL particles can be estimated. Using this calculated number of particles, along with the conventional LDL-c concentration, a comparable estimation of particle size can easily be established. Some will argue that the calculation of non-HDL is a good surogate marker of

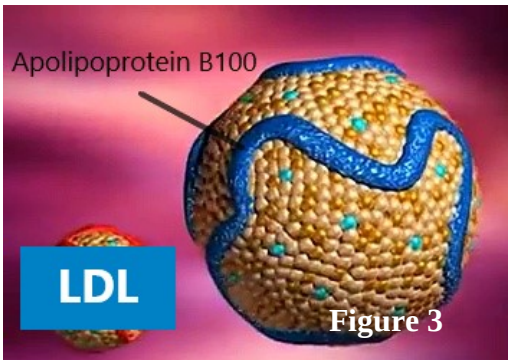

Figure 3

particle size. However, that is a topic of debate that still warrants asking the question if a ApoB meaurement would be helpful as a part of a standard screening. Even better in support of this ApoB story is that tests are already availble at most service labs and have reimbursment codes accepted by most insurnace providers. Yet this test is not included as a part of routine patient screening, treatment determination or included in clinical guidelines.

As cardiovascular disease is America's number one cause of premature death, and a tremendous expense on the American population at a cost of > $1 Billion per day, improvement over the status quo is justified. I will concede that such changes do take time, but this nouveau thinking around the effects of fat in the body (including triglyceride), disease detection and improved patient population segregation have now been around for over a decade. Arming patients with sufficient information to ask educated questions is the first step in refining cardiovascular disease care, improving patient compliance through understanding and ultimately preventing unnecessary tragedy.

Next issue…….the featured article will discuss the LDL particle life cycle and where disease related problems may lie.

Newsroom

Mr. Bobby Mikkelsen and Kitt Falk Petersen, M.D. join the iMetabolic Biopharma Corporation team. Mr. Mikkelsen joins the management team as the Vice President of Finance while Dr. Petersen is an outstanding addition to the Medical Advisory Board.

The iMBP Corporation of Seed Round funding is still open for accredited investors. Visit the Investment Opportunity page on our website for more information.

Health Facts

Did you know that 1 in 3 of all Americans is clinically obese. This disease prevalence carries over into the cardiovascular world in multiple ways. One specific area is with hypertension, which is observed in 1 in 3 Americans as well. However, according to the Agency for Healthcare Research and Quality (https://www.ahrq.gov) men are 24% less likely than a woman to visit a doctor on an annual basis and 22% more likely to have neglected their cholesterol tests. This might not be surprising to some, but this fact does have a real world effect on our families and society as whole. Maybe it's time for you and your family to sit down and discuss your annual checkup scheduling.

In the Spotlight

To help you better understand iMetabolic Biopharma Corporation, this issue features company Founder, President and Chief Executive Officer (CEO); Urban A. Kiernan, Ph.D.

With a career that spans almost two decades, Dr. Kiernan has authored over 45 peer reviewed publications, four book chapters and over a dozen patent applications (four currently issued). After earning his Ph.D. from Arizona State University, he pursued his passion in the health and life sciences/ biotechnology industry. After graduation he immediately joined the early stage start-up company Intrinsic Bioprobes, Inc (IBI-Tempe, Arizona). One of the many aspects of IBI was the identification and development of novel diagnostics for a variety of disease states such as type 2 diabetes (T2D) and heart disease. During the course of his 11 year tenure at IBI he rose up the ranks to Director of Biomarker Discovery and was awarded over $3.5 Million in National Institutes of Health (NIH) grant funding. With a core research focus on T2D, he spearheaded one of the most successful Small Business Innovative Research programs in the country. This success culminated in a biomarker licensing deal with Johnson & Johnson, but more importantly it was during this time that Dr. Kiernan conceived the premise of iMBP Corporation.

Over the course of the following decade, IBI was acquired by Thermo Fisher Scientific (Waltham, MA), where Dr. Kiernan quickly transitioned over into the business world. He was recognized for his natural leadership skills, drive, and strong sense for strategy. This lead him to be promoted into a Global Business Development role, where he was able to develop strong personal relationships with many key players in the

biopharma sector while providing the experience necessary for him to establish his own CEO management style. During all this time, Dr. Kiernan stood fast in his belief in making iMBP Corporation a reality which has now started to take root.

This 14 year long journey began, not with a great "Eureka" moment, but a casual observation of a unique mass spectrometric signature that statistically correlated with the presence of T2D. Even though the discovery was subtle, the significance was pronounced. What Dr. Kiernan was observing was Apolipoprotein CIII (ApoCIII), an obscure protein and component of both VLDL and HDL (See Featured Article above). By observing these changes as related to disease, Dr. Kiernan was placed on a path leading him on a journey to learn more about this protein and establishing a knowledge network linking it to a number of different cardio metabolic pathologies. As random as this path may sound, he established a single commonality that links these diseases together, and that is obesity. The plague of westernization, 70% of Americans are now either overweight or obese, significantly driving up both rates and the severity of all comorbidities. As the years progressed Dr. Kiernan did not simply perform an academic game of connect the dots, but he established enough experimental data to demonstrate that ApoCIII was a drugable target that demonstrated improved lipid metabolism functionality in human tissues. With the establishment of iMetabolic Biopharma Corporation, Dr. Kiernan has committed himself to developing iMBP-001(the early stage lead candidate drug) into a viable product that will eventually help tens of millions of people around the world treat the compounding detrimental effects that obesity and its comorbidities inflicts on its sufferers.

Outside of his career, Dr. Kiernan is a devoted family man. He is happily married and the proud father of three children. He is a firm believer in the ancient Greek philosophy around the necessity of strong body, mind and spirit...and practices what he preaches.

Reminders

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