CURRENT THERAPEUTIC APPROACHES TO LIPID LOWERING  
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Cardiovascular diseases (CVD) continue to remain the leading cause of morbidity and mortality in the developed world, with coronary heart disease (CHD) being rated as the number one killer, and stroke following as the leading third, in the United States. Over the years, research has established the link between dietary fats (lipids), lipid transport and metabolism in the body, atherosclerosis (the progressive narrowing of the arteries over time), and cardiovascular disease. Lipids present in the blood and tissues of the body include cholesterol, cholesterol esters, triglycerides, and phospholipids.

Since lipids are insoluble in blood (plasma), they must be transported to and from the cells by special carrier molecules, the lipoproteins. Abnormal lipoprotein or lipid metabolism may induce hyperlipidemia, or “high cholesterol” and hypertriglyceridemia known to be etiological factors in cardiovascular disease. Dyslipidemias are defined as disorders of lipoprotein metabolism, including lipoprotein overproduction or deficiency. These disorders are generally manifested as elevated plasma levels of total cholesterol, low-density lipoprotein (LDL) cholesterol and triglyceride concentrations; and a decrease in the plasma high-density lipoprotein (HDL) cholesterol concentration. A condition characterized by small, dense LDL particles, elevated triglycerides, and low HDL, termed the “atherogenic triad”, is characteristic of atherogenic dyslipidemia, often found in people with diabetes, metabolic syndrome and CHD.

High levels of low-density lipoprotein cholesterol (LDL-C) are particularly correlated with atherosclerosis and cardiovascular disease, based on evidence from clinical studies and epidemiological analysis. Multiple risk factors include cigarette smoking, hypertension, diabetes, and a low level of high-density lipoprotein cholesterol (HDL-C). Establishing healthy dietary and lifestyle practices is the first step in the intervention of CHD. Drug therapy is the regimen normally used for those that do not respond to lifestyle interventions, and for those facing a high short-term risk for heart disease. Currently, the statins are the first choice drugs when treating dyslipidemias, especially in patients with hypercholesterolemia alone or accompanied by hypertriglyceridemia.

Most therapeutic approaches target reducing LDL. However, studies in animal models show that over-expression of apolipoprotein (apo) A-1, the major HDL lipoprotein, inhibits progression and induces regression of atherosclerosis. Therefore HDL is an important target for therapeutic intervention, and low HDL-C levels are a modifiable risk factor for cardiovascular disease. Recent clinical studies also reveal that increased HDL-C levels are associated with reduced risk of ischemic stroke in the elderly, and among different racial or ethnic groups. These data add to the evidence relating lipids to stroke and support HDL-C as an important modifiable stroke risk factor. The mechanism by which HDL cholesterol inhibits atherosclerosis is not as yet completely clear.

The National Institutes of Health in the United States, established a public health initiative, the National Cholesterol Education Program (NCEP) in 1985. As part of this effort, the NCEP Adult Treatment Panel I (NCEP-ATP I) developed its first set of guidelines, in 1988, establishing clear goals for patients with lipid abnormalities. These initial recommendations were revised in 1993; with more emphasis on HDL levels, healthy body weight, and physical activity.
A third set of guidelines, was released in May 2001, reflecting changes in calculating coronary risk and in the management of hypercholesterolemia. These changes were necessitated by the fact that earlier guidelines, though fairly aggressive, did not cover the entire group of individuals at risk of CHD. Based on these new guidelines, the number of patients with cholesterol levels that can be classified as abnormal, has now tripled. The guidelines recommend complete lipoprotein profile (total, LDL, HDL, triglycerides) as preferred screening for assessing CHD risk status. LDL remains a primary target of cholesterol-lowering therapy, along with increased emphasis on optimal HDL levels. Diabetics without CHD have been added to the at-risk group and patients with metabolic syndrome (insulin resistance) are advised intensive therapeutic lifestyle changes. The panel presented a revised classification of dyslipidemias and also recommended, and outlined dietary and therapeutic measures, along with thresholds for the initiation of pharmacological therapy. Natural approaches, such as the use of plant sterols/stanols as a therapeutic dietary option to lower LDL cholesterol levels formed part of these recommendations.

As NCEP guidelines have been changed to include a global measure for CHD risk, risk status and treatment measures adopted for some patients, may be different as compared to the earlier guidelines. Essential approaches to combat a leading killer disease through helping patients achieve the new target levels include continued educational efforts, improvements in clinical practice, as well as effective and safe therapeutic agents, supported by adequate lifestyle and dietary interventions.

Lipoproteins, dyslipidemias, and CVD risk:

The six major classes of plasma lipoproteins are

- **Chylomicrons**: that transport dietary cholesterol and triglycerides to muscles and other tissues.
- **Very low-density lipoproteins** (VLDL): Particles synthesized by the liver that transport triglycerides to muscles and to fat tissue.
- **Intermediate density lipoproteins** (IDL): Particles formed when the triglyceride portion of the VLDLs are removed. IDLs are either converted to LDLs or directly taken up by the liver.
- **Low-density lipoproteins** (LDL): Particles that are the primary plasma carriers of cholesterol. LDL is also known as the "bad cholesterol" because excess LDL cholesterol in the blood with other substances can form atherosclerotic plaques
- **High-density lipoproteins** (HDL): HDL is known as the "good cholesterol" because it mediates the removal of cellular cholesterol carrying it away to the liver for subsequent excretion A high HDL level is associated with a lower risk for coronary heart disease (CHD).
- **Lipoprotein (a) (Lp(a))**: Particle similar in composition to LDL with an additional apoprotein, apo(a), covalently linked to apo B. Lp(a) is called the "deadly cholesterol" reported to be 10 times more dangerous than low-density lipoprotein (LDL) and 15 times more potent than total cholesterol. Factors influencing Lp(a) levels include race, ethnicity, and genetics. Compared to LDL, Lp(a) preferentially deposits in the human atherosclerotic tissues, restricting blood flow and encouraging clots.

Hyperlipoproteinemias are classified into different types depending upon the nature of abnormality (Table 1).
Table 1: Classification of Hyperlipoproteinemias

<table>
<thead>
<tr>
<th>Type</th>
<th>Major Lipoprotein Abnormality</th>
<th>Elevated Lipoprotein</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hypertriglyceridemia (familial hyperchylomicronemia)</td>
<td>chylomicrons</td>
<td>Lipoprotein lipase deficiency</td>
</tr>
<tr>
<td>IIa</td>
<td>Hypercholesterolemia (familial hypercholesterolemia)</td>
<td>LDL</td>
<td>Genetic deficiency of LDL or Apo A/B receptors</td>
</tr>
<tr>
<td>IIb</td>
<td>Hypercholesterolemia and, to a lesser extent, hypertriglyceridemia (familial combined dyslipidemia)</td>
<td>LDL, VLDL</td>
<td>High Apo B synthesis and defective Apo E</td>
</tr>
<tr>
<td>III</td>
<td>Hypertriglyceridemia and, to a lesser extent, hypercholesterolemia (familial dysbetalipoproteinemia)</td>
<td>IDL</td>
<td>Abnormal IDL metabolism</td>
</tr>
<tr>
<td>IV</td>
<td>Hypertriglyceridemia (familial hypertriglyceridemia)</td>
<td>VLDL</td>
<td>Abnormal VLDL metabolism</td>
</tr>
<tr>
<td>V</td>
<td>Hypertriglyceridemia (Familial mixed hypertriglyceridemia)</td>
<td>VLDL, chylomicrons</td>
<td>Abnormal VLDL and chylomicrons metabolism</td>
</tr>
</tbody>
</table>

The NCEP ATP III report issued a revised classification for blood lipid levels and outlined the three risk categories with set plasma lipid thresholds for initiating drug therapy.

Table 2. Classification of Blood Lipids by Adult Treatment Panel III

<table>
<thead>
<tr>
<th>Lipid Type</th>
<th>Serum Lipid Concentration (mg/dL)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL cholesterol</td>
<td>&lt;100</td>
<td>Optimal</td>
</tr>
<tr>
<td></td>
<td>100-129</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td></td>
<td>130-159</td>
<td>Borderline high</td>
</tr>
<tr>
<td></td>
<td>160-189</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>&gt;/=190</td>
<td>Very high</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>&lt;200</td>
<td>Desirable</td>
</tr>
<tr>
<td></td>
<td>200-239</td>
<td>Borderline high</td>
</tr>
<tr>
<td></td>
<td>&gt;/=240</td>
<td>High</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>&lt;40</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>&gt;/=60</td>
<td>High</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt;150</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>150-199</td>
<td>Borderline high</td>
</tr>
<tr>
<td></td>
<td>200-499</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>&gt;/=500</td>
<td>Very high</td>
</tr>
</tbody>
</table>
Ever since Fredrickson and Lees proposed a system for phenotyping hyperlipoproteinemia in 1965, clinical laboratories use electrophoresis to determine the risk level for coronary heart disease. Lipoproteins can be electrophoretically separated into alpha (HDL), pre-beta (VLDL), and beta (LDL) lipoproteins, with a distinct chylomicron band sometimes visible. Most HDL-C is carried by alpha-lipoproteins, most LDL-C is transported by beta lipoproteins and most endogenous triglyceride is carried by pre-beta lipoproteins. Thus in most cases, beta is increased with high LDL cholesterol levels, and pre-beta is increased with high endogenous triglyceride levels, indicating increased risk for cardiovascular disease.

C-reactive protein originally discovered in the serum of pneumonia patients and so named because it binds to a polysaccharide in pneumococcal cell walls, is an acute phase reactant used as an index of inflammation in clinical laboratory testing. This protein is produced by the liver in response to acute inflammatory conditions. Both C-reactive protein and low-density lipoprotein (LDL) cholesterol levels are elevated in persons at risk for cardiovascular events. Recent studies suggest that blood levels of myeloperoxidase (MPO) are elevated as well.6

Current medical opinion considers inflammation of atherosclerotic plaques, and the subsequent formation of blood clots on the surface of these plaques, as critical events that lead to most atherosclerosis induced cardiovascular events. A recent clinical study revealed that CRP test appeared to correlate more closely with already established cardiovascular disease risk factors than did the LDL test alone.7

Current therapeutic agents:

The role of therapy is to enable the patient to achieve target blood lipid and lipoprotein levels based on the ATP III guidelines. Drugs are administered if lifestyle and dietary approaches alone do not suffice. A therapeutic or nutraceutical agent essentially serves to modulate lipid absorption or affects lipid or lipoprotein metabolism, at different points in the metabolic pathway. An overview of therapeutic and dietary agents that are currently available to address lipid lowering is presented here.

Statins:

Most current therapeutic approaches seek to lower LDL-C. The discovery of statins was a major milestone in lipid lowering therapy. Statins are competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the rate limiting enzyme that catalyzes the conversion of HMG CoA to mevalonate in the liver cells. Mevalonate is the precursor molecule for cholesterol, Coenzymes Q and squalene (an intermediate in cholesterol synthesis). The decrease in cholesterol intracellular level induces a higher surface expression of LDL receptors which consequently increases the clearance of plasma LDL cholesterol. Intermediate-density lipoproteins and very low-density lipoprotein (VLDL) remnants are removed as well, contributing to lowering triglyceride-rich lipoprotein levels.8

The original statin molecule is mevastatin (as the name signifies, arresting mevalonate synthesis), isolated in 1980 from the fungus Penicillium citrinum. Simvastatin as well as lovastatin are also of a fungal origin (Aspergillus terreus), whereas pravastatin was obtained after chemical modification of the bacteria Nocardia
autotrophica. Fluvastatin, cerivastatin, atorvastatin and rosuvastatin (the most recently approved statin drug in the United states) are synthetic.

Statins are the most powerful drugs for lowering LDL, facilitating dose-related reductions in LDL ranging from 20-60%. Fluvastatin is reported to be the least potent, decreasing LDL levels by only 22-36% at the maximum recommended dosage. The new member, Rosuvastatin is reported to be the most potent, reducing LDL levels by up to 65% (in a dose range of 20-80 mg/day), in clinical studies. Statins also have moderate effects on HDL, raising levels by approximately 5%, and decrease triglyceride concentrations to a maximum of about 30%. Statins show remarkable efficacy in reducing major coronary events and mortality rates in patients with CHD.

Unfortunately, the mechanism of action of statins through inhibition of the mevalonate pathway inhibits the biosynthesis of vital biochemical products of this loop, including coenzyme Q10 (CoQ10). In humans, CoQ10 or ubiquinone (2,3-dimethoxy-5-methyl-6-decaprenyl-1,4-benzoquinone), is a major participant in electron transfer during oxidative phosphorylation in the mitochondria, a potent antioxidant and free radical scavenger, and a membrane stabilizer that preserves cellular integrity. These functions are particularly relevant to cardiovascular health, leading to the logical conclusion that patients on long-term statin therapy should receive supplemental CoQ10.

Statins in general are well tolerated with a low risk of adverse drug reactions (<0.1%) and few drug-drug interactions. According to literature reports, myalgia and myopathy occur in 2% and 0.5% of patients, respectively, with less than 0.1% of cases progressing into rhabdomyolysis, which may be associated with acute renal failure. Myopathy appears to affect 0.1-0.3% of patients treated with lovastatin, atorvastatin, or simvastatin and less than 0.1% treated with pravastatin and fluvastatin. The risk is higher with cerivastatin, which was withdrawn from the market in August 2001 after reports of 31 deaths from rhabdomyolysis, most often in elderly patients who were also taking fibrates. The U.S. Food and Drug Administration (FDA) labeling information recommends liver function testing before and 12 weeks after starting statin therapy.

Other lipid-lowering agents:

Besides statins, other current lipid-altering agents that lower LDL-C primarily through increased hepatic LDL receptor activity include, bile acid sequestrants/resins and cholesterol absorption inhibitors such as ezetimibe. Natural approaches such as plant stanols/sterols, polyphenols, as well as nutraceuticals such as oat bran, psyllium and soy proteins are also reported to lower LDL-C.

Fibrates (including bezafibrate, gemfibrozil and fenofibrate) are a group of lipid lowering drugs that have been in existence for over 40 years. They are usually used in patients with mixed or combined hyperlipidemia and hypertriglyceridemias. Fibrates are reported to decrease plasma triglycerides by decreasing their hepatic synthesis and increasing their catabolism. They decrease the triglyceride-VLDL synthesis through enhancing beta-oxidation of fatty acids in the liver and increase the plasma triglyceride catabolism by inducing lipoprotein lipase gene transcription and decreasing the apoC-III gene transcription. Fibrates are reported to increase high density-lipoprotein (HDL)-cholesterol by increasing apoA-I and apoA-II gene transcription.

Other current agents that are proven to beneficially affect lipid metabolism include nicotinic acid (niacin), acipimox, high-dose fish oils, antioxidants and policosanol. Drug combinations (fixed-dose) such as extended-release niacin/lovastatin
are available, and current and future lipid-altering drugs may include anti-obesity agents which could favorably affect lipid levels, as well.\textsuperscript{17}

**A note on Niacin in lipid lowering:**

Studies reveal that both healthy patients and those with type II, III, IV, or V hyperlipoproteinemia, characterized by high lipid levels in the blood, can benefit from a daily dose of niacin greater than one gram. Niacin was able to reduce serum levels of total-cholesterol, LDL-cholesterol, VLDL-cholesterol, and triglycerides, while increasing serum levels of high-density lipoprotein (HDL). Additionally, apolipoprotein B (apo B), lipoprotein (a), and phospholipid serum concentrations were reduced by niacin and apolipoprotein A-I (apo AI) increased in these patients.\textsuperscript{19}

Thus, niacin regulates all circulating lipoproteins in the appropriate direction and may also help to improve them qualitatively. The beneficial lipid-regulating effects of niacin are believed to be mediated through several potentially interrelated effects on lipid and lipoprotein metabolism. These include:

1. inhibition of lipolysis in adipose tissues;
2. reduction of triacylglycerol formation in the liver;
3. increase in lipoprotein lipase (LPL) activity;
4. inhibition of the synthesis and secretion of apo B-100 and of hepatic VLDL;
5. impairment of cholesterol biosynthesis, and reduction of the fractional catabolic rate of HDL-apo A-I.

Apo A-I, an activator of lecithin cholesterol acyl transferase (LCAT) plays a major role in the complex process of reverse-cholesterol transport. Because HDL3 is a primary substrate for LCAT, the elevation in A-I levels due to niacin therapy probably stimulates the esterification of HDL3 cholesterol, thereby enhancing its rate of conversion to HDL.

Niacin is the only commonly used agent that has positive effects on the complete lipid profile. It is therefore an attractive treatment option for mixed dyslipidemia, especially when used in combination with other lipid-modifying drugs. Niacin's LDL-C lowering is linear, but its effect on triglycerides and HDL-C is curvilinear, meaning that low dosages can significantly alter triglycerides and HDL, and significant LDL reduction becomes apparent as dosage increases.\textsuperscript{19} Niacin also converts small, dense LDL particles to larger, more buoyant, and less atherogenic LDL particles, further contributing to its impact on the total lipid profile. It is reported to decrease LDL (5-25%), triglycerides (20-50%), and lipoprotein (a) (38%), and is effective in increasing HDL levels (15-35%).\textsuperscript{20}

As with statins, niacin helps in the regression of atherosclerotic lesions, decreases coronary events, and reduces mortality in patients with CHD. Additionally, niacin inhibits mobilization of free fatty acids from peripheral adipose tissue to the liver, consequently reducing hepatic synthesis of both VLDL and triglycerides. Niacin increases HDL by blocking uptake of apolipoprotein A-I in the liver.

Almost all patients treated with immediate-release (IR) niacin experience flushing and up to 20% of them discontinue therapy as a result. Tolerance to this adverse effect does appear to develop with continued therapy. Sustained-release (SR) niacin was developed to decrease flushing associated with niacin IR. However, although flushing is reduced, niacin SR is associated with a high rate of adverse hepatic side effects, sometimes leading to hepatic failure. Extended release niacin preparations taken at bedtime help to avoid this problem.\textsuperscript{16}
Historically, niacin was avoided in patients with diabetes due to its potential to increase blood glucose levels. Two recent studies, however, suggest that lipid-modifying dosages of niacin can be given safely to patients with diabetes and that the drug may be considered an alternative to statins or fibrates in those in whom these agents are not tolerated or who have high triglyceride or low HDL levels despite therapy. Niacin potentially improves all components of the atherogenic triad, often present in patients with diabetes.16

**Phytonutrient approaches to lipid lowering:**

Plant sterols/stanols,20 polyphenols, natural antioxidant herbal extracts such as curcuminoids from turmeric21, viscous fiber such as oat bran22, saponin-rich seed extracts from fenugreek23, and seed proteins such as soy protein24 have also been shown to be beneficial in lipid lowering.

In a landmark study reported in 2002,25 US researchers unraveled the potential mechanism of action of guggulsterones, the biologically active components of the resin of guggul (*Commiphora mukul*) used in traditional Ayurvedic medicine to treat inflammation, arthritis, cardiovascular conditions and obesity. Guggulsterones were shown to be antagonist ligands for the bile acid receptor FXR, which is an important regulator of cholesterol homeostasis in the body. Scientific studies on guggul began almost 40 years ago when an Indian researcher, G.V. Satyavati was intrigued by the strong parallels between modern concepts on the etiology of atherosclerosis and obesity, and descriptions in the *Sushruta Samhita* written in the 5th to 4th century B.C.

Policosanol26 is a natural mixture of higher aliphatic alcohols, found in plant waxes. Sugarcane wax is the common source. The components of policosanol include 1-octacosanol, 1-dotriacontanol, 1-tetracosanol, 1-tetraatriacontanol, 1-hexacosanol, 1-heptacosanol and 1-nonacosanol. This mixture of alcohols is clinically proven to be effective in maintaining normal cholesterol levels.

*In vitro* studies, studies on animal models and clinical studies published in literature reveal that Policosanol beneficially affects cholesterol metabolism. In clinical studies, Policosanol was shown to be effective in lowering both total cholesterol and LDL-C and increase the levels of HDL-C. Other beneficial effects include inhibition of platelet aggregation, which in turn is helpful in maintaining cardiovascular health. A comparative study with the commonly used Lovastatin on subjects suffering from intermittent claudication revealed the superior benefits of policosanol.

Effects on cholesterol metabolism and antioxidant effects that prevent the oxidation of LDL-cholesterol, are reported to be responsible for its healthful effects of policosanol. In vitro studies revealed that policosanol may inhibit cholesterol synthesis in the liver but direct inhibition of the hydroxy-methylglutaryl-coenzyme A reductase (which is the mechanism of action of statins) is unlikely. Animal studies suggest that LDL break down may be enhanced, but the precise mechanism of action has not as yet been completely elucidated.

At doses of 10 to 20 mg per day, policosanol was found to lower total cholesterol by 17% to 21% and low-density lipoprotein (LDL) cholesterol by 21% to 29% and raise high-density lipoprotein cholesterol by 8% to 15%. Daily doses of 10 mg of policosanol were shown to be equally effective in lowering total or LDL cholesterol as the same dose of simvastatin or pravastatin, although it did not affect triglyceride levels. Policosanol was found to effectively lower platelet aggregation with efficacy comparable to aspirin at
a dose level of 20 mg, with a combination of Policosanol and aspirin being more efficacious. At dosages of up to 20 mg per day, policosanol is reported to be safe and well tolerated, even in long-term studies.

**Emerging therapies:**

A new statin drug pitavastatin, currently under development, is reported to have brought 86 percent of dyslipidemic patients to NCEP LDL cholesterol target levels. Other drugs in development that modify lipid levels through novel mechanisms may prove useful as mono- or adjunctive therapy. These include bile acid transport inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, acyl-CoA cholesterol acyl-transferase (ACAT) inhibitors, gemcabene, lifibrol, pantothenic acid analogues, nicotinic acid-receptor agonists, anti-inflammatory agents, peroxisome proliferator-activated receptor (PPAR) agonists, and functional oils. Although the potential for additional CHD risk reduction exists with such agents detailed clinical studies are needed before they can be recommended or approved.

Emerging investigational drugs targets include liver X receptor (LXR), farnesoid X receptor (FXR) and sterol-regulatory element binding protein (SREBP). Investigational agents that would potentially modulate HDL-C blood levels or flux include cholesteryl ester transfer protein (CETP) inhibitors (such as torcetrapib), CETP vaccines, various HDL 'therapies' and upregulators of ATP-binding cassette transporter (ABC) A1, lecithin cholesterol acyltransferase (LCAT) and scavenger receptor class B Type 1 (SRB1), as well as synthetic apolipoprotein (Apo)E-related peptides.

In this context, ApoA-I Milano is a variant of apolipoprotein A-I identified in individuals in rural Italy who exhibit very low levels of HDL. Infusion of recombinant ApoA-I Milano-phospholipid complexes produces rapid regression of atherosclerosis in animal models. A recent double-blind, randomized, placebo-controlled multicenter pilot trial comparing the effect of a recombinant ApoA-I Milano/phospholipid complex (ETC-216) or placebo, administered intravenously in 5 doses at weekly intervals to human volunteers, on coronary atheroma burden, as measured by intravascular ultrasound (IVUS). Significant regression of coronary atherosclerosis was observed in these volunteers, although larger clinical studies need to be undertaken to study the effect of this treatment on morbidity and mortality due to cardiovascular disease.

Combination drugs such as atorvastatin/amlodipine, ezetimibe/simvastatin, atorvastatin/CETP inhibitor, statin/PPAR agonist, extended-release niacin/simvastatin and pravastatin/aspirin are also under development.

**New tools for prevention and treatment:**

In light of the phenomenal advances in pharmacogenomics, Biotechnology would play an important role in developing preventive measures and therapeutic modalities to combat abnormal lipid metabolism. A study on individuals with exceptional longevity, and their offspring revealed that these individuals have significantly larger HDL and LDL particle sizes. This phenotype is associated with a lower prevalence of hypertension, cardiovascular disease, the metabolic syndrome, and increased homozygosity for the I405V variant in CETP. These findings suggest that lipoprotein particle sizes are heritable, and encourage a healthy aging phenotype. In recent years, the hypothesis that peroxidation of
LDL may be an initial step in the atherosclerotic process and the discovery of the body’s inherent antioxidant enzyme, paraoxanase, principally associated with HDL, has triggered a whole new area of research. Perhaps it would be possible to beneficially manipulate the induction and activity of this enzyme? From this perspective, genomic tools would enable individualized approaches to the management of lipid disorders through lifestyle, pharmacological and nutraceutical interventions, in the years to come.

References


