

## 84<sup>th</sup> Congress of the European Atherosclerosis Society, 29 May -1 June, Innsbruck, Austria

### The Sunday Report

#### Gene therapy and diet for prevention of CVD: Preludes to EAS Congress

*This year's Congress opened with élan! At the time of the Opening Ceremony, 2,075 delegates from over five continents had registered, carrying on the success of recent EAS Congresses. And what a Congress it will be, covering the range of research interests from genetics, experimental and clinical research.*

The Opening ceremony was of course a highlight (see **report**). But before this, there were two informative EBAC Accredited Sessions, focusing first, on diet and cardiovascular disease (CVD), and second, on gene therapy and lipoprotein lipase deficiency. In an exciting report, **Professor Erik Stroes, (Academic Medical Center, Amsterdam, the Netherlands)** showed that lipoprotein lipase gene therapy based on AAV vectors in more than 30 patients not only reduced triglyceride levels in the first weeks but also reduced the occurrence of pancreatitis. Professor Stroes also presented the novel concept of antisense apolipoprotein CIII therapy for treatment of patients with hypertriglyceridaemia. An interview with Professor Stroes is on the EAS Facebook page

<https://www.facebook.com/EuropeanAtherosclerosisSociety/>

Diet and prevention of CVD is very much centre stage again, with the recent publication of the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice,<sup>1</sup> which emphasize diet and lifestyle as the first fundamental step for prevention of CVD. And one of the remaining key debates is over fat. As reviewed by **Professor Alice H. Lichtenstein (Gershoff Professor of Nutrition Science and Policy Tufts University, USA and senior author on the 2015 US Dietary Guidelines<sup>2</sup>)** there is an extensive evidence-base, dating from the 1950s with observational studies, and more recently, with intervention studies that replacing saturated fat in the diet with polyunsaturated fat reduces low-density lipoprotein cholesterol levels and subsequently CVD. However, in the 21<sup>st</sup> century there has been increasing concern in how this message has been translated. Instead of replacing saturated fat with PUFAs, this message has transmuted to replacement of saturated fat in the diet with a diet low in saturated fat, to a diet low in total fat. As highlighted by recent research, this fails to take account of the importance of dietary patterns; the focus should be on improving diet quality, adopting wherever possible a Mediterranean type diet and restricting intake of red and processed meats, and foods rich in refined grains, starch, added sugars, salt, and trans fat. So with fat back on the agenda, education is a priority for ensuring that clinicians, patients and the wider public recognize the importance of diet quality, especially when it comes to fat. According to Prof. Lichtenstein: *'We need to shift the message back to what is supported by the data.'*

And, according to **Professor Jean-Pierre Després (Laval University, Québec QC Canada)**, the next fight will undoubtedly be sugar, with sugar-sweetened beverages a primary target. Obesity is now a pandemic; in Europe, the prevalence of obesity in many countries has tripled and numbers continue to escalate. One of the key drivers is the consumption of sugar-sweetened beverages; in North America, temporal increases in the consumption of sugar-sweetened beverages have paralleled the rise in obesity. Moreover, the effects go beyond obesity with the possibility of interaction with genetic predisposition to adiposity.<sup>3</sup> Once again, education of clinicians and patients is key: *'We need to change the way in which we educate patients about diet quality; in the case of children, we need to think about*

*switching consumption from sugar-sweetened beverages to water to improve long-term health and prevent CVD and other chronic diseases.'*

With the emphasis on diet quality it is important to think again about the potential impact of individual food components that may impact lipid-lowering, specifically lowering of low-density lipoprotein cholesterol (LDL-C), as discussed by **Professor John Chapman (University of Pierre and Marie Curie and National Institute for Health and Medical Research, Pitié-Salpêtrière Hospital, Paris, France)**. Certainly there is good evidence that fibre (beta-glucan), nuts and soy protein lower LDL-C levels, albeit with variable effects, all of which have been considered in recent guidelines. Added to this, there is also consistent evidence for a role for foods with added plant sterols and stanols (often referred to as phytosterols), which at a daily intake of 2 g/day lower LDL-C by up to 10%. These dietary components have been the focus of a previous EAS Consensus Paper,<sup>4</sup> which critically appraised the evidence for mechanism, efficacy and safety, suggesting that incorporation of foods with added plant sterols/stanols may have LDL-C lowering benefit across the spectrum of cardiovascular risk, with effects that are additive to statins. Moreover, there is evidence of other lipid-lowering benefit, specifically lowering triglycerides, with enhanced triglyceride-lowering of 11-28% in individuals with hypertriglyceridaemia, suggesting application in the setting of metabolic syndrome.<sup>5</sup> Whether incorporation of foods with added plant sterol/stanols reduces CVD remains an unknown, although it is unlikely that such a trial is feasible given the large number of patients required with the magnitude of LDL-C lowering.

Finally, the role of the microbiota in CVD was discussed by **Dr. Jingyuan Yu (University of Groningen, the Netherlands)**. Given recent studies indicating a contributory role for gut microbiota in the development of cardiometabolic disorders, there has been growing interest in how to modulate the gut microbiota as a potential therapeutic strategy for CVD prevention. However, what is lacking is large-scale studies in humans to dissect out associations between cardiovascular risk factors and the gut microbiota. Dr Yu overviewed LifeLines DEEP, a prospective, general population cohort study in the northern Netherlands which aims to provide integrative evidence for translation of information on biomarkers, such as the microbiota, for disease.<sup>6</sup> There is initial evidence from this study that the gut microbiome may play an important role in variability in body mass index and blood lipid levels, independent of age, sex, and host genetics. Although early days, and given the potential confounders, such meta-data will need much dissection before translation to the clinic.

## References

1. Piepoli MF, Hoes AW, Agewall S et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2016; DOI: <http://dx.doi.org/10.1093/eurheartj/ehw106> First published online: 23 May 2016.
2. Millen BE, Abrams S, Adams-Campbell L et al. The 2015 Dietary Guidelines Advisory Committee Scientific Report: Development and Major Conclusions. Adv Nutr 2016;7:438-44.
3. Qi Q1, Chu AY, Kang JH et al. Sugar-sweetened beverages and genetic risk of obesity. N Engl J Med 2012;367:1387-96.
4. Gylling H, Plat J, Turley S et al. Plant sterols and plant stanols in the management of dyslipidaemia and prevention of cardiovascular disease. Atherosclerosis 2014;232:346-60.

5. Rideout TC, Marinangeli CP, Harding SV. Triglyceride-lowering response to plant sterol and stanol consumption. *J AOAC Int* 2015;98:707-15.

6. Tigchelaar EF, Zhernakova A1, Dekens JA et al. Cohort profile: LifeLines DEEP, a prospective, general population cohort study in the northern Netherlands: study design and baseline characteristics. *BMJ Open* 2015;5(8):e006772.