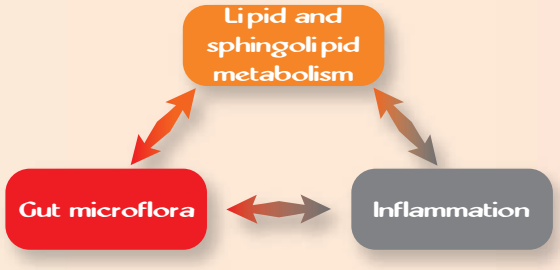
THE PROBLEM

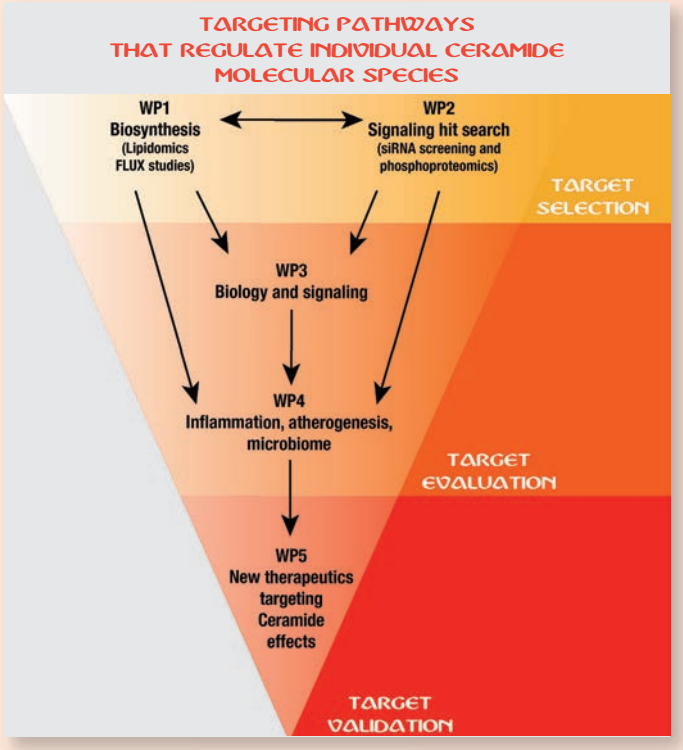
Cardiovascular disease (CVD) causes much of the disease burden in Europe, claiming each year 4.3 million lives in Europe, 2.0 million in the EU (European Heart Network; www.ehnheart.org). The main forms of CVD are **coronary artery disease** (CAD) and **stroke.** CAD by itself is the single most common cause of death in Europe: accounting for 1.8 million deaths in Europe and 681,000 deaths in the EU per year (European Heart Network; www.ehnheart.org). Lipid lowering is the only therapeutic approach targeting the root cause of CVD, with statins achieving an impressive event reduction compared to other lipid lowering agents. Yet patients on high doses of statins still have a high residual CV risk, sparking attempts to mitigate this risk. However, alternatives and adjuncts to statins are difficult to develop, and complex problems were revealed whilst targeting the cholesteryl ester transfer protein (CEPT) pathway. **New therapeutic targets in CVD are thus urgently required.**

Athero-Flux builds on the lipidomics findings that a class of lipids (SLs) that is currently untargeted is associated with significant CVD risk. Data generated by the "AtheroRemo" FP7 Consortium (www.atheroremo.org) have revealed that specific **sphingolipids (SLs)** are associated with CV risk while others appear to be protective. Remarkably, **their levels are a better predictor of clinical outcome than traditional risk factors such as low-density lipoprotein-cholesterol.**
SLs are implicated in significant biological activities including cell survival, inflammation, and metabolic diseases. Moreover, their levels in metabolic diseases are modulated by previously unrecognized factors such as the gut microflora. Thus, we hypothesize that by controlling **SL metabolism** a better primary and secondary prevention of CVD events than with statins alone can be achieved.



ATHERO-FLUX FOCUS AND OUTCOME

The **Athero-Flux Consortium** intends to generate **new therapeutic targets** and tools to address a hitherto unrecognised imbalance in lipid metabolism importantly linked to CV risk. It builds on the **strengths of leading European SMEs** with know-how in lipid metabolism and RNAi while giving them access to state-of-the-art models of disease and biological readouts and a whole **new pipeline** of therapeutic targets aligned with their priority areas. The Academic beneficiaries benefit from collaboration with SMEs with strong regulatory experience to accelerate the translation of their results into clinical applications.



The Consortium creates a translational opportunity to turn lipidomics findings in large-scale clinical studies **into new therapeutics** for CVD. It also elucidates the complex interaction between dyslipidaemia, atherosclerosis and inflammation essential for designing new therapeutic strategies for patients at risk or suffering from CVD.

ATHERO-FLUX ALLIANCE

Athero-Flux consortium consists of eleven partners from nine EU countries (UK, Denmark, Finland, Germany, Italy, Sweden, Greece, France and Israel), and brings together experts in **atherosclerosis, lipidomics, SL metabolism, high-throughput RNAi screening, LNA technology and gut microflora** in a true multidisciplinary effort to achieve **better treatment for CVD beyond hypolipidemic drugs.**
The **Athero-Flux** workflow enables close integration between the Academic and SME capacities. The planned Academic and SME partnership will feed potential targets into the SME pipeline. The Academia provides knowledge and experience in SL biology and state-of-the-art *in vitro* and *in vivo* models of atherosclerosis. The SMEs in turn offer high-throughput lipidomics and screening technologies as well as LNA validation tools with a proven translational pipeline.

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Targeting novel lipid pathways for treatment of cardiovascular disease

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EC Contribution: € 5.987.700

Duration: 60 months

Starting date: 01/09/2013

SEVENTH FRAMEWORK PROGRAMME

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