

CARDIOVASCULAR DISEASES - THE PROBLEM

Cardiovascular disease (CVD) causes nearly half of all deaths in Europe (48%), costing a dramatic €196 billion a year. Despite the reduction in mortality that has been achieved over the past decades, 70% of cardiovascular (CV) events cannot be prevented with the treatment of known risk factors. Aggressive glucose metabolism control in Type 2 Diabetes did not automatically result in CVD prevention and lipid-lowering agents beyond statins have not yet delivered the expected reduction in CV events highlighting a **complex relationship between inflammation and hyperlipidaemia**.

NEW INSIGHTS INTO THE PATHOGENESIS OF CVD

Recent studies indicate that **B cells may carry out both pro- and anti-atherogenic functions and that these dual roles are executed by different B cell subsets in CVD**. Thus, as in many other immune disorders, **B cells contribute to both CVD pathogenesis as well as to protection from CVD**. Yet, our ability to discern between pro- and anti- atherogenic B cell subsets and to exploit their functions is limited by our lack of knowledge on their surface markers, master regulators and antigen specificity. Moreover, current therapies targeting B cells are limited to antibodies for B cell depletion that do not discriminate the B cell subsets and are associated with risks of immunosuppression that would be unacceptable in the CVD population. Refining therapeutic strategy to address defined subsets of B cells has the potential to avoid risks of immunosuppression.

ATHERO-B-CELL FOCUS AND STRATEGY

Athero-B-Cell Project sets to overcome the limitations of existing therapeutics by targeting only defined B cell subsets with specific pathogenic or regulatory functions. **The experimental platform of Athero-B-Cell Project will permit the identification of differences in B cell effector subsets relevant to atherosclerosis and investigate how these differences can be used to develop new CVD therapeutics.**

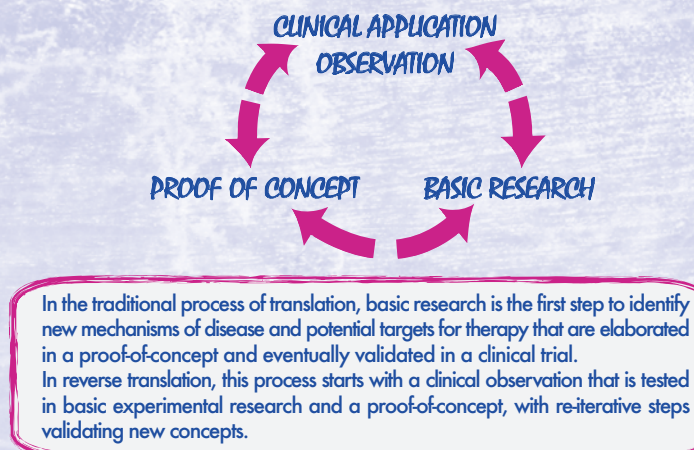
This will be achieved by combining the multidisciplinary knowledge and expertise of **Athero-B-Cell Project Consortium members** on B cells in inflammation and atherosclerosis with the data mining and therapeutic targeting platforms of world leading SMEs.

Athero-B-Cell is an exemplary SME-Academic collaboration that aims to generate a new pipeline of therapeutic targets whose potential will be realised by the SMEs.

Athero-B-Cell project is split into 3 basic research areas encompassing the following objectives

- To define targets to reduce activation of pathogenic B cells and antibodies in CVD
- To identify enhancers of atheroprotective B regulatory cell populations and antibodies in CVD.
- To validate molecular and miRNA targets to modulate B cell behavior in CVD with innovative locked nucleic acid (LNA) based antisense platforms

The traditional track of translational research starts with the discovery of a potential therapeutic target in an experimental or basic research setting and ends with a drug being developed and validated in the clinic. Athero-B-Cell embraces more recent models of **translational research** by starting with extensive clinical data, which will be then fed back into experimental or basic research for further mechanistic insight (**Reverse Translational Research**).

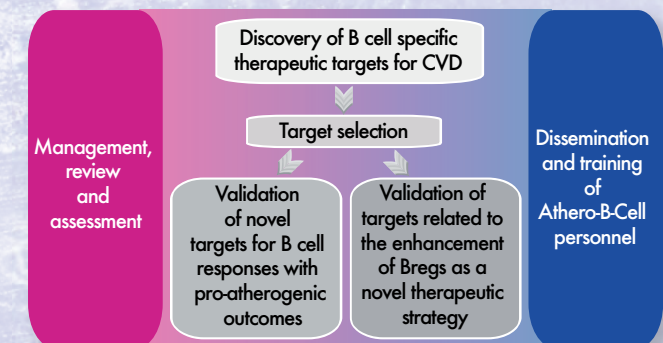


ATHERO-B-CELL ALLIANCE

The Athero-B-Cell Consortium is made up of eleven Beneficiaries, of which three are research-performing SMEs. The Beneficiaries are from seven EU countries (UK, Denmark, The Netherlands, Italy, Sweden, Switzerland and France) and are a well-balanced team of cardiologists, immunologists, clinicians, bioinformaticians, statisticians, biologists and physicians with expertise in cardiovascular diseases, proteomics, transcriptomics, data integration and immunoregulatory cell function.

The Consortium benefits from a significant number of clinical studies (**Circulating Cells; UCORBIO; AtheroExpress; Genoa; APACE; Ferrara; SPUM; SPUM; MDC-CVD and MAMI**), including a total of 16.871 patients.

Due to its strong foundations, **the Athero-B-Cell Consortium** has the exceptional capacity to **mine B cell-specific omics data sets from large-scale clinical studies including live PBMC biobanks**. Combining this omic data with measurement of humoral responses will provide, for the first time, the characterization of pathogenic versus protective B cell responses in CVD. This knowledge is instrumental in the rational design of future therapies and vaccines to control atherosclerosis and CVD development.





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STARTING DATE: 01/09/2013



Targeting and
exploiting
B cell functions
for treatment
in cardiovascular
diseases

