



EUROPEAN VASCULAR GENOMICS NETWORK

Linking Europe in the Fight
against Heart Disease

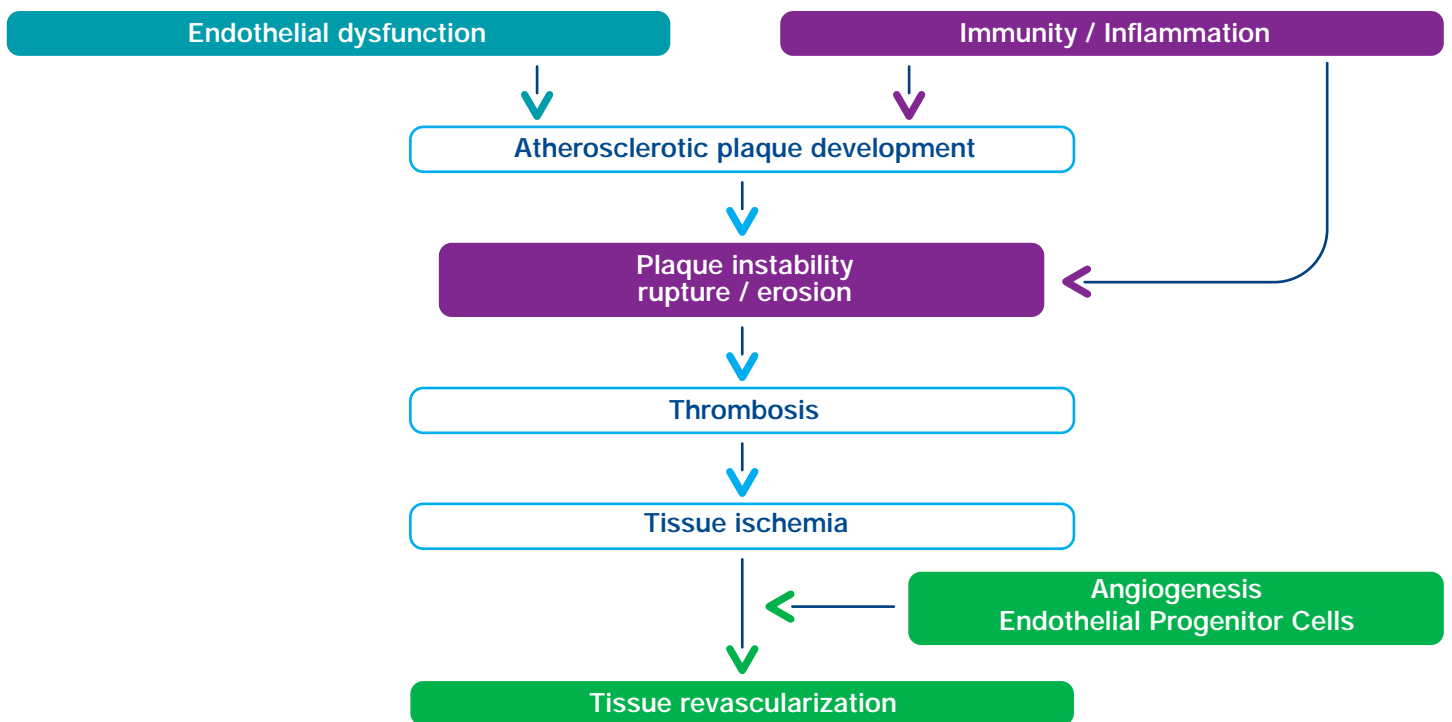
www.evgn.org

The European Vascular Genomics Network (EVGN) is a Network of Excellence funded by the European Commission under the 6th Framework Programme, Priority 1: "Life Sciences, Genomics and Biotechnology for Health". The EVGN assembles the necessary critical mass and promotes multidisciplinary interactions by uniting world-leading basic and clinical groups in Vascular Biology to foster complementary research activities in atherosclerosis. Its research armory spans genomics, proteomics, molecular biology, cell biology, gene transfer and genetic modification in mice, and integrative pathophysiology in human.

► The ultimate goal of EVGN is to reduce the incidence and impact of coronary heart disease in the European population and to help the European healthcare sector to compete internationally.

EVGN concentrates on three major areas of cardiovascular disease and therapy

1. **Endothelial dysfunction** that plays a crucial role in the development of atherosclerosis
2. **Instability of the atherosclerotic plaque** that is the main cause of arterial thrombus (blood clot) formation leading to coronary artery occlusion and heart attack
3. **Therapeutic angiogenesis** that opens avenues for novel treatment of heart disease meant to improve cardiac oxygenation and reduce heart failure



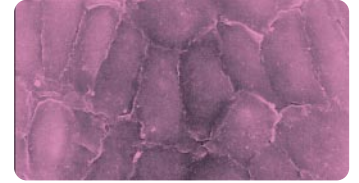
EVGN acts as an interface between basic scientists and clinician scientists to promote and accelerate the transition of knowledge in Vascular Biology to improve diagnosis and treatment of atherothrombotic diseases.

- EVGN is actively involved in training - education and dissemination activities in Vascular Biology through :
- the organization of an annual congress, the European Vascular Biology Research Conference
 - the building up of an annual Summer School in Vascular Biology
 - the promotion of exchange of expertise via an Exchange Programme
 - the promotion of gender equality and gender issues in cardiovascular research via its Gender Action Plan



Endothelial Dysfunction

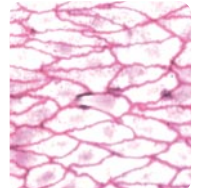
The endothelium is a thin layer of flat cells that line the inner walls of blood vessels (veins and arteries). These cells play an important role in the mechanics of blood flow. In case of damage to the endothelium, the walls of the arteries may become hard and thick, thus reducing the supply of blood - with its oxygen and nutrients - to the tissues.



Endothelial dysfunction is key to the atherosclerosis progression. It is an early prognostic marker and an important pathological mechanism underlying the development of atherosclerosis.

Endothelial dysfunction reflects a state of endothelial cell activation in which, for example, the bioavailability of nitric oxide (NO) is decreased, generation of reactive oxygen species is increased, and expression of a number of pro-inflammatory proteins is enhanced.

The maintenance of endothelial cell function (prevention of endothelial cell activation) is expected to delay the vascular inflammation associated with clinical symptoms.



Microscopic images of endothelium

A major goal of the EVGN is to develop new diagnostic tools and means to correct endothelial dysfunction, which could have a major impact on atherosclerosis prevention.

Endothelial (dys)function is regulated by a series of major factors/enzymes, including endothelial NO synthase, endothelial-derived hyperpolarizing factor (EDHF), NADPH oxidases, cytochrome P450, renin-angiotensin system, kallikrein-kinin system. New tools (adenovirus constructs, fusion expression plasmids) are being generated for studying their role. In addition, several genetic and biological markers, including endothelial microparticles, are being measured in patients with coronary artery disease, and associations between gene variants and vascular dysfunction assessed *in vivo* are being established.



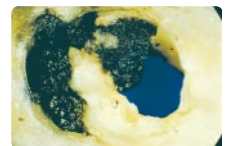
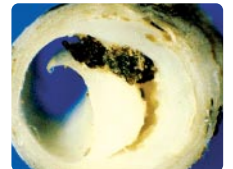
The global strategy of the EVGN is based on the use of differential gene expression techniques, transgenic animals, pharmaceutical tools, and patients from clinical trials in whom endothelial dysfunction is assessed in the coronary artery tree.

Plaque Instability

Atherosclerosis is a chronic inflammatory disease of the arteries and is characterized by the accumulation of lipids, cells and extracellular matrix in the vessel wall. The result of this accumulation phenomenon is known as "atherosclerotic plaque". Although advanced atherosclerotic plaques can grow sufficiently large to occlude the lumen of the vessel wall, the majority of clinical events, like myocardial infarction and stroke, predominantly arise from rupture or surface erosion of a pre-existing atherosclerotic plaque (a consequence of a phenomenon now referred to as "plaque instability") and subsequent thrombus formation.



Measuring endothelial dysfunction



Unstable plaques



The EVGN is aimed at identifying the genes that mediate plaque instability in humans, designing diagnostic tests to identify high-risk individuals and developing drugs to decrease risk of rupture. It is developing unique animal models of atherosclerosis to decipher molecular and cellular mechanisms of plaque rupture.

Also, the EVGN is actively involved in analyzing the role of innate and adaptive immunity in atherosclerosis, with the ultimate goal to develop novel anti-inflammatory strategies based on vaccination.

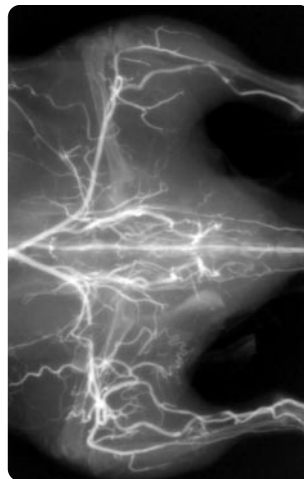


Therapeutic Angiogenesis

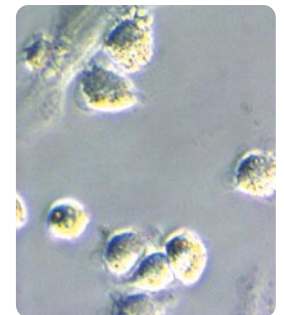
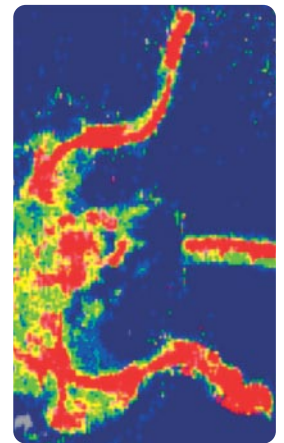
Angiogenesis is the biological phenomenon linked to the formation of new vessels. Therapeutic angiogenesis opens avenues for novel treatment of heart disease, meant to improve cardiac oxygenation and reduce heart failure.

The ability of organisms to spontaneously develop collateral vessels represents an important response to vascular occlusions and operates to improve perfusion of ischemic tissues. In most clinical settings, however, these natural adaptive responses to a compromised perfusion are insufficient to block the progression of ischemic disease in the myocardium or in peripheral vessels.

Therapeutic angiogenesis, by promoting the growth of new vessels from existing vessel wall cells, in conjunction with the recruitment of circulating endothelial progenitor cells (EPCs), is a highly promising strategy to revascularise ischaemic tissues, and thereby to improve functional recovery of injured organs.



Mouse hindlimb circulation



Stem cells



A major goal of the EVGN is to identify genes involved in differentiation, homing and expansion of EPCs, and to assess the effects of cell and non-cell based therapy on function recovery in mouse models of myocardial infarction and hindlimb ischemia.

Clinical programmes to evaluate the therapeutic potential of bone marrow-derived stem cells/EPCs, and measurement of EPC markers in patients with coronary artery disease are being developed.

Training/Education and dissemination

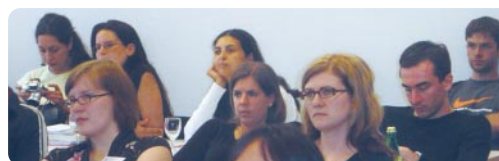
Exchange/Training programmes



The EVGN maximizes the scientific and commercial potential of European Vascular Biology by electronic data-sharing and communication networks, shared research tools, exchange and training programmes, with emphasis on reducing gender inequalities.

The EVGN is actively involved in training the future leading investigators through a European Exchange Programme for junior basic and clinician scientists.

The EVGN provides enriched and continued education by creating an annual Summer School in Vascular Biology for PhD students.



First Summer School in Vascular Biology

- ▶ 4-7 July 2005, Maastricht, The Netherlands
- ▶ 65 participants - 59 EVGN, 6 non EVGN; 19 speakers

Dissemination



The EVGN organizes an annual European Vascular Biology Research Conference

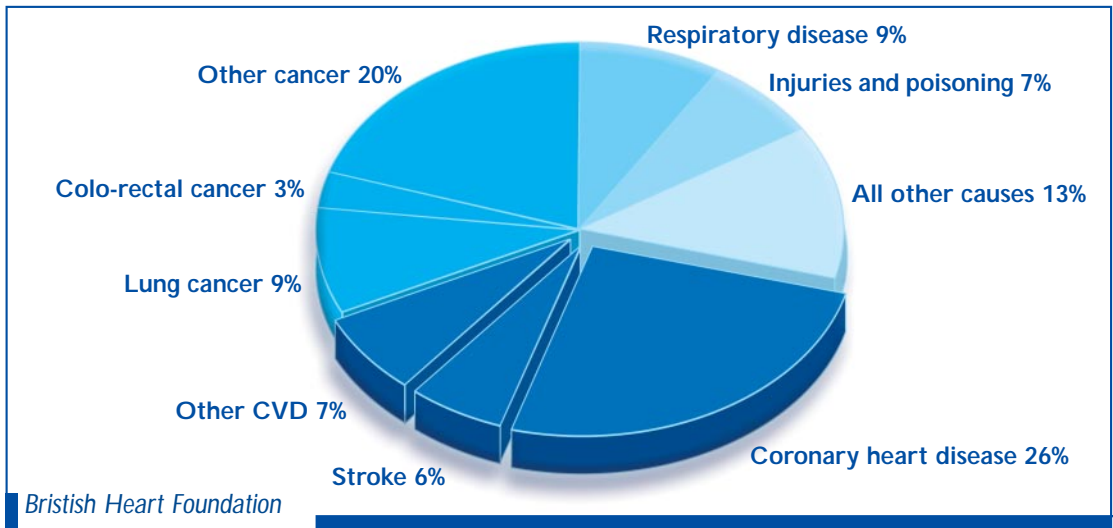
First EVBRC

Supported by an unrestricted grant from Servier



- ▶ 13-16 December 2004, Cambridge, United Kingdom
- ▶ 142 participants - 120 EVGN, 22 non EVGN; 17 plenary lectures; 23 parallel sessions; 18 poster presentations





Cardiovascular diseases (CVD) cause about 50% of deaths in Europe. The indirect and direct costs of CVD for European countries is 3 billions euros*. Coronary heart disease and stroke, which result from atherosclerosis, constitute 80% of CVD.

**The European Commission Conference: The Future of Cardiovascular Research in Europe, Brussels, 19 March 2004*

Age-specific incidence rates for cardiovascular disease have fallen by half over the past 30 years in the economically advanced European nations, as the result of better prevention and treatments based on growing knowledge of vascular biology, but the ageing population and adverse trends in obesity and diabetes threaten these improvements. There is also an alarming increase in heart failure, the end stage of coronary heart disease.

Future advances to diminish cardiovascular disease incidence and mortality depend on developing entirely new strategies. Genomics and proteomics together with the complete human genome sequence open up fresh horizons for molecular understanding of cardiovascular disease, for identifying new diagnostic measurements and developing new pharmacological, gene and cell-based therapies.

 **EVGN: linking Europe in the Fight against Heart Disease**

The European Vascular Genomics Network (EVGN), the first Network of Excellence created in the cardiovascular field, is a timely initiative aimed to maximise the impact of the post-genome era on Vascular Biology so as to optimise the conversion of research results into concrete health, social and economic benefits.

EVGN Executive Committee

- Alain Tedgui, *Scientific Coordinator*
- Andrew C. Newby, *Co Director*
- Ingrid Fleming, *Endothelial Dysfunction Team Leader*
- Thomas Lüscher, *Endothelial Dysfunction Team Leader*
- Martin Bennett, *Plaque Instability Team Leader*
- Mat Daemen, *Plaque Instability Team Leader*
- Elisabetta Dejana, *Therapeutic Angiogenesis Team Leader*
- Stefanie Dimmeler, *Therapeutic Angiogenesis Team Leader*
- Andreas Zeiher, *Clinician Advisor*
- Göran K Hansson, *Chairman of the Communication Sub-Committee*
- Bernard Lévy, *Chairman of the Mobility Sub-Committee*
- John Martin, *Chairman of the Exploitation Sub-Committee*
- Harry Struijker-Boudier, *Chairman of the Education Sub-Committee*
- Carlie De Vries, *Chairman of the Gender & Equality Sub-Committee*



EVGN in numbers

- 10** countries
- 25** institutions
- 2** biotechnology companies
- 1** management company
- 35** academic/clinical groups
- 285** basic/clinician scientists
- 9M€** European Commission grant for integration
- 60M€** total budget
- 5** year duration (2004-2008)

- University of Bristol
- Chancellors Master and Scholars of the University of Cambridge
- St. George's Hospital Medical School
- The University of Birmingham
- University College London
- Ark Therapeutic Ltd

● Karolinska Institute

Finland

● University of Kuopio

- Cardiovascular Research Institute of Maastricht
- Vrije Universiteit Medical Center
- Leiden University
- Academic Medical Center, University of Amsterdam

Sweden

United Kingdom

The Netherlands

Germany

- National Institute for Health and Medical Research
- European Center for Biology and Medical Research
- Inserm-Transfert SA

France

- Johann Wolfgang Goethe University Hospital
- Johannes Gutenberg University Hospital
- University of Bonn

Switzerland

Austria

- University of Vienna
- University of Innsbruck
- Technoclone GmbH

Italy

- University Hospital of Zürich
- University Hospital of Geneva

- The FIRC Institute of Molecular Oncology
- Vita-Salute, San Raffaele University
- University of Torino

The Hebrew University of Jerusalem

Israel

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