

From the sponsors

AstraZeneca LP is a proud sponsor of *Nature Medicine's* new innovative feature, 'Special Focus on Atherosclerosis'.

Atherosclerotic coronary artery disease remains the leading cause of death despite many advances in our scientific understanding of this disease process and its pharmacological management. Atherosclerosis may be viewed as a more intricate process than merely the passive deposition of fat in arteries. Indeed, complex interactions between the endothelial cells that line vessels, inflammatory cells and cholesterol-transporting proteins with numerous cardiovascular risk factors lie at the root of this disease. Biological remodeling processes, in combination with metabolic dysfunction (such as insulin resistance and dyslipidemia), promote plaque within the arterial wall. These plaques range from fibrotic, stable lesions to those with a lipid-rich, necrotic core and a thin rupture-prone fibrous cap. Plaque rupture and thrombosis may lead to the most dramatic consequences of atherosclerosis: acute coronary syndromes, stroke and ischemia. New understanding of the biology of atherogenesis has yielded insight into novel mechanisms that can modify plaques and improve patient outcomes.

Lipoprotein retention and modification, reverse cholesterol transport, matrix deposition and vascular-wall inflammation are all examples of local processes in the atherosclerotic plaque that could be targeted for pharmacological intervention.

Recently, it has been elegantly demonstrated with magnetic resonance imaging techniques that lipoprotein modification by statin therapy decreases the amount of lipid present in atherosclerotic plaque. Technical advancements in non-invasive imaging will enable monitoring of local atherosclerotic events in the arterial wall, which will permit the actual assessment of the anti-atherosclerotic potential of emerging pharmacological modalities as opposed to merely observing their surrogate effects on plasma lipoprotein content.

Impressive advances in the basic science of atherosclerotic disease and drug discovery over the next decade will continue to be translated into significant impacts on atherosclerotic disease modification and reduction in overall atherogenic burden.

The content of this web site has focused on capturing the essence of the vast amount of scientific knowledge that has accumulated over the past century in the areas of atherosclerosis and dyslipidemia research. Moreover, video clips from the AstraZeneca-sponsored animation, 'Statins: Therapeutic Benefits in Vascular Disease', have been included on the site as well. Developed by Peter Libby, this animation details the pharmacology of HMG CoA reductase inhibitors (statins), including their mechanism of action and multiple positive pharmacological benefits for the treatment of atherosclerotic disease.

AstraZeneca and *Nature Medicine* hope that the content of this web site will become a valuable scientific and educational resource for you.

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AstraZeneca is a major international healthcare business backed by a strong research base and extensive manufacturing and commercial skills. Its worldwide operations include over 54,000 employees, corporate headquarters in London UK, research and development headquarters in Södertälje, Sweden, and a strong and growing presence in the US market. The company is engaged in the research, development, manufacture and marketing of ethical (prescription) pharmaceuticals and the supply of healthcare services. Global sales in 2001 were \$16.5 billion (£11.4 billion), and total R&D spending in 2001 topped at \$2.7 billion (£1.9 billion).

AstraZeneca is notable for having a long and established presence in the hypertension and heart-failure therapeutic areas, with innovative products such as the β -adrenergic receptor blockers propranolol, metoprolol and atenolol, the angiotensin-converting enzyme inhibitor lisinopril, and the calcium-channel blocker felodipine, but it continues to expand this strong cardiovascular focus with newer interests in dyslipidemia, anti-arrhythmic therapy and antithrombosis.

AstraZeneca holds leading product positions in the therapeutic areas of the cardiovascular, respiratory and gastrointestinal systems, oncology, anesthesia (including pain management), the central nervous system and antimicrobials. It has a powerful portfolio, including Atacand (candesartan cilexetil) for hypertension, Toprol XL (metoprolol succinate) for heart failure, Nexium (esomeprazole) for gastrointestinal disease, Casodex (bicalutamide) and Arimidex (anastrozole) for oncological indications, Zomig (zolmitriptan) for migraine, Seroquel (quetiapine) for schizophrenia and Symbicort (budesonide/formoterol fumarate dihydrate) for the treatment of asthma.

AstraZeneca aims to use its leading positions in many important areas of healthcare to make a difference in the lives of patients and the healthcare providers who treat them. AstraZeneca is committed to continued innovation, close customer relationships, people development and a responsible approach to business.