Agonists at the Natriuretic Peptide Receptor-C with Therapeutic Potential for Cardiovascular Disease

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Description:

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Summary

Scientists at UCL have developed small molecule CNP mimetics selective for NPR-C, which they have identified as a druggable target for a group of cardiovascular diseases.

The Technology and its Advantages

C-type natriuretic peptide (CNP) belongs to a family with vasodilator and diuretic properties and with an important role in cardiovascular homeostasis via binding and activation of natriuretic peptide receptor-C (NPR-C). Studies at UCL have indicated that selective, small molecule agonists at NPR-C that pharmacologically mimic the beneficial, vasoprotective actions of CNP could have therapeutic value in cardiovascular diseases (i.e. atherosclerosis, myocardial infarction and stroke). We have developed a family of such compounds and identified a lead compound with good potency and selectivity.

Current drug therapy for acute MI remains dual anti-platelet therapy (aspirin and clopidogrel), anticoagulation (low molecular weight heparin), organic nitrates, and beta-blockers. For ST-segment elevation MI, patients receive thrombolysis or primary angioplasty and stent insertion, during which procedure they receive additional anti-platelet therapy using GpIIb/IIa antagonists. The competitive advantage of NPR-C agonists is that they would target directly multiple aspects of atherogenesis (the cause of MI and other cardiovascular disorders such as stroke): they stimulate regeneration of endothelial cells, reduce smooth muscle hyperplasia, and inhibit leukocyte recruitment. In addition they have anti-platelet effects, reducing adhesion and aggregation, already known to be effective in the treatment of MI. These agonists could slow progression of vascular disease and reduce the frequency of acute events (by slowing the progression of coronary artery disease) and could also reduce the extent of damage should ischaemia ensue (via inhibition of platelet activation and the formation of platelet activation and the formation of platelet-neutrophil complexes).

Market Opportunity

Myocardial Infarction (MI; heart attack) is an ischaemia-based cardiovascular disorder that represents the major cause of death in the western world, accounting for approximately 7.6 million deaths per annum. In the US and UK there are more than 800,000 & 200,000 deaths per annum, respectively, as a result of cardiovascular disease (CVD), of which ~50% are accounted for by MI. CVD accounts for approximately one third of all

respectively, as a result of cardiovascular disease (CVD), of which ~50% are accounted for by MI. CVD accounts for approximately one third of all premature deaths in the UK. For those who survive, late complications of acute MI include heart failure, with 67,000 new cases per year resulting in substantial financial (£625 million per year) and personal (50% 5-year mortality) costs. Healthcare costs for the treatment of CVD are estimated at £160 billion and £16 billion in the US and UK , respectively. The World Health Organisational (WHO) projections of mortality to 2030 predict that ischaemic heart disease will retain its position as the most common cause of death worldwide and the prevalence of disability resulting from this disorder will increase dramatically. Indeed, the current tendency towards increased obesity and smoking worldwide is predicted to halt the decline in deaths from CVD and may even reverse this trend.

Intellectual Property Status

A UK patent application has been filed (priority date 30th July 2010)

Further Information

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