EGFR antagonist-mediated prevention of post myocardial infarction ruptures

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Technology description

Background:

Cardiovascular disease is a leading cause of death worldwide, claiming the lives of an estimated 17 million people annually. Myocardial infarctions (MI), or heart attacks, are a leading cause of mortality and morbidity. Complications following MI include maladaptive left ventricle (LV) tissue remodeling and cardiac rupture. Cardiac rupture refers to a tear or rupture in the left ventricle of the heart, and it is documented through autopsy to occur in up to 65% of patients following an acute MI. Rupture is usually fatal and is responsible for over 25,000 deaths a year in the United States alone. Maladaptive LV remodeling following an MI predisposes patients to cardiac rupture and chronic heart failure. Importantly, thrombolytic therapy and pharmaceutical interventions aimed at reducing maladaptive LV remodeling (i.e. ACEIs, ARBs, beta blockers, aldosterone antagonists, etc.) also impair the normal heart healing processes that follow a heart attack leading to an increase in the incidence of rupture associated deaths.

Description of the Invention:

Tissue remodeling in the heart is mediated by a delicate balance between matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs). TIMP-3 is expressed at high levels in healthy hearts and is decreased in diseased hearts exhibiting maladaptive remodeling after an MI. Our scientists have shown that the proportion of TIMP-3 knock out (KO) mice that die following an MI is higher than their wild type (WT) counterparts, and this is due to cardiac ruptures which were four times more likely to occur in a TIMP-3 KO than a WT mouse following an MI. TIMP-3’ s ability to inhibit MMPs results in an inhibition of EGF/EGFR signaling, which allows the production of collagen synthesis and normal heart repair. Treating the TIMP-3 KO mice with an EFGR antagonist restored normal heart healing resulting in a significantly decreased incidence of rupture and increased survival. This technology covers the use of a broad range of EGF/EGFR antagonists in the treatment and prevention of cardiovascular disease including maladaptive LV remodeling and cardiac rupture.

Advantages

• Restores normal heart healing to reduce the incidence of cardiac rupture and death in heart attack

patients
• Potential combination therapy with thrombolytics and therapies to prevent maladaptive LV remodeling (i.e. ACEIs, ARBs, beta blockers, aldosterone antagonists, etc...) to reduce the incidence of side effect ruptures
• EGFR antagonists have an existing safety profile in humans.

Institution

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