

Liposomal Hemin for Anticancer Treatment (Tel Hashomer)

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Prof. Jonathan Leor, Head of the Cardiovascular Research Institute at Tel-Aviv University and Sheba Medical Center and Prof. Margalit Rimona, The Department of Biochemistry and Molecular Biology,

THE NEED

Myocardial infarction (MI) (ie, heart attack) is the irreversible necrosis of heart muscle secondary to prolonged ischemia. Approximately 1.5 million cases of MI occur annually in the United States.

One of the major challenges in modern cardiology is to optimize myocardial healing and repair. After MI, the heart tries to compensate itself by left ventricular remodeling. One of the earliest phases after MI involves acute inflammation leading to fibrosis and scar formation. Neutrophils and monocytes are the first to infiltrate the infarct. Monocytes become macrophages, which then take part in the acute inflammation as well as in the following phases.

Uncontrolled activation of pro-inflammatory macrophages after myocardial infarction (MI) accelerates adverse left ventricular (LV) remodeling and dysfunction.

The TECHNOLOGY

The technology offered here is a method to direct macrophages into healing and reparative activity which could improve myocardial protection, infarct healing and repair. This technology is based on targeting macrophages with liposomes (HA-LP) loaded with hemin.

Hemin, an iron-containing porphyrin, activates heme oxygenase-1 (HO-1), an enzyme with anti-inflammatory and cytoprotective properties, and suppress HIF-alfa with pro-inflammatory properties.

Hyaluronan-liposomes (HA-LP) have hyaluronan bound covalently to their surface. The Hyaluronan polysaccharide is the natural ligand of the CD44 receptor family that are present on the macrophage membrane.

Preliminary experiments of this technology in mouse model of MI, shows that injection of hemin/HA-LP promotes the production of an alternative reparative macrophages that produce therapeutic cytokines. The liposomes can be delivered by intravenous (IV), intracoronary (IC) or intramuscular (IM) injection. The experiments readout shows that during acute MI in mouse, IV injection hemin/HA-L switches the phenotype of macrophages from a pro-inflammatory to a reparative phenotype. Therefore hemin could provide a beneficial therapeutic effect for improving infarct healing or reducing macrophage-mediated inflammation in other diseases such as the vessel wall during

atherosclerosis.Hemin/HA-**liposomes enhance myocardial healing and repair after myocardial infarction.**