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## Antisense inhibition of HERNA1 reverses cardiac pathology and progression to heart failure

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Recent efforts have identified a subclass of non-coding RNAs templated at genomic enhancers (eRNAs) with gene regulatory function. Due to their genomic position we postulated their function in modulating signal-dependent tissue-specific transcriptional responses. Here we identify HERNA1, a conserved hypoxia-inducible factor (HIF) activated, cardiac-specific eRNA that integrates myocardial hypoxia signaling to regulate expression of a nearby pro-hypertrophic gene cluster in humans and mice. Elevated HERNA1 expression correlates with hypertrophic cardiomyopathy, but inversely correlates with dilated cardiomyopathy in humans. Through gain- and loss-of-function studies, we observe a requirement for HERNA1 in the development of stress-dependent hypertrophic cardiomyopathy and mechanistically, identify direct HERNA1 interaction at the promoters of its downstream targets. In vivo delivery of antisense oligonucleotides targeting HERNA1 reverses cardiac pathogenesis, inhibits heart failure progression and increases overall survival in animals. Taken together, these data unveil a novel heart-specific stress-dependent eRNA pathway and reveals a new strategy for tissue/cell type-specific therapeutics.

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## Fibrinolytic activity in bovine bile lipid: Application of chromatography, mass spectrometry and *in vivo* wound healing assay

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An ether extract of nine different bacterial metabolites combined with two step (ether followed by ethanol) extract of bovine bile lipid is used as an immune stimulatory drug. While characterizing the drug, we observed fibrinolytic activity in the extract through fibrinogen plate assay and fibrin zymography. Background literature emphasized major role of fibrinolytic enzymes in activating immune systems. This increased our curiosity to understand the role of these enzymes in this drug in human physiology. This fibrinolytic enzyme/s has no similarity with plasmin in terms of cross reactivity in *immunoblots* assay and hydrolysis of the specific substrate S-2251. In RP-HPLC analysis, the lipid extract was fractionated into several components. Interestingly, fibrinolytic activity was confined to all the fractions. To purify the enzyme, it was extracted from the lipid by aqueous buffer extraction and applied to CNBr activated fibrinogen substrate affinity column. Purified enzyme was tested for activation of complement system and wound healing through C3 binding and in-vivo wound healing assay respectively. The enzyme will be identified by mass-spectrometric analysis. Also, we propose to finger-print protein components present in bile lipid by MS analysis to have a better insight of the functionality of the lipid component of the drug.

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