

Epicardial FSTL1 reconstitution regenerates the adult mammalian heart.

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Public Summary:

The human heart does not effectively regenerate after injury such as after myocardial infarction. Consequently, myocardial infarction is a major cause of human mortality worldwide. Thus, identifying possible therapeutics that can stimulate regeneration would be of enormous importance. We found that a variant of a natural protein known as Fstl1 protein (FSTL1) can improve heart function and decrease mortality in both mouse and pig models of myocardial infarction. Thus, we propose that FSTL1 therapy could be an effective way to reverse myocardial death and remodelling following myocardial infarction in humans.

Scientific Abstract:

The elucidation of factors that activate the regeneration of the adult mammalian heart is of major scientific and therapeutic importance. Here we found that epicardial cells contain a potent cardiogenic activity identified as follistatin-like 1 (Fstl1). Epicardial Fstl1 declines following myocardial infarction and is replaced by myocardial expression. Myocardial Fstl1 does not promote regeneration, either basally or upon transgenic overexpression. Application of the human Fstl1 protein (FSTL1) via an epicardial patch stimulates cell cycle entry and division of pre-existing cardiomyocytes, improving cardiac function and survival in mouse and swine models of myocardial infarction. The data suggest that the loss of epicardial FSTL1 is a maladaptive response to injury, and that its restoration would be an effective way to reverse myocardial death and remodelling following myocardial infarction in humans.

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