Target-specific Delivery of Therapeutic Agents for Cardiac Infarction Treatment

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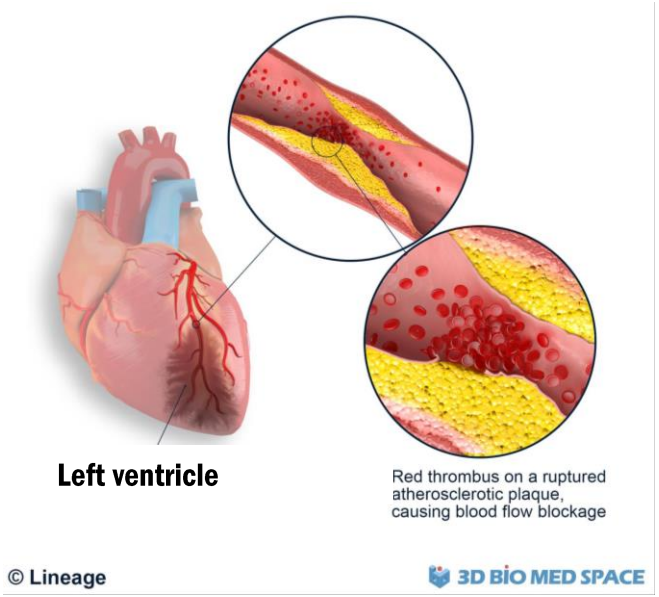
Myocardial Infarction

- A myocardial infarction (MI), most commonly known as heart attack, occurs when blood flow decreases or stops to parts of the heart, leading to damage of the heart muscle
  - Left ventricle undergoes progressive physiological and anatomical transformations, which is the major cause of heart failure
- 34% of patients die acutely from MI and 25% succumb due to downstream heart failure

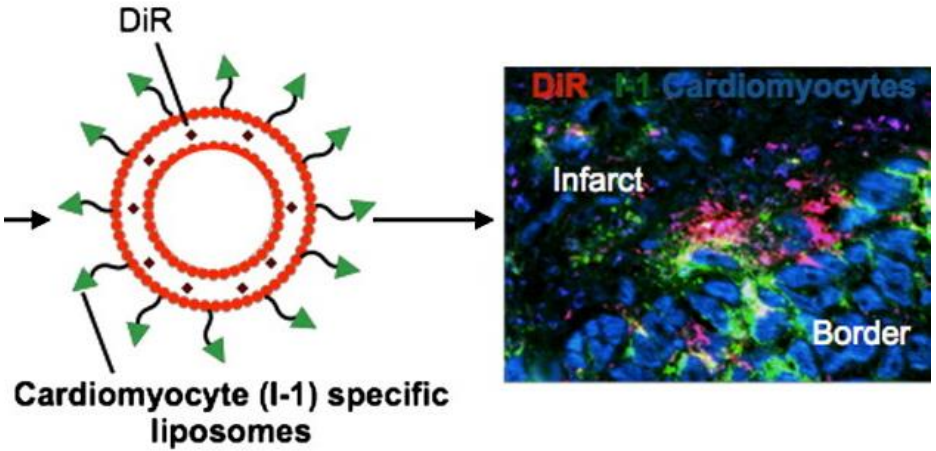
- <u>Clinical Problem</u>:
  - Currently no effective treatments for preventing or reversing the process of left ventricle remodeling initiated by MI
  - Current drugs in use have a short half-life and off-target effects at higher doses



PARP-1 Inhibitor AZ7379

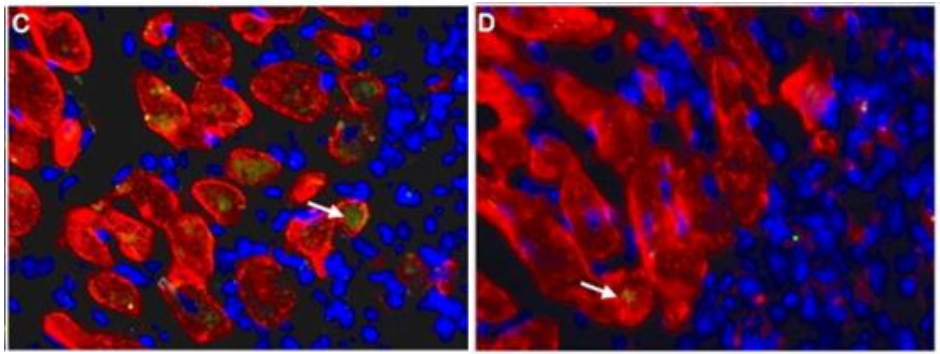
Solution: Researchers at the University of Virginia have developed a liposomal formulation of a poly(ADP-ribose) polymerase-1 inhibitor (AZ7379) that targets damaged tissue

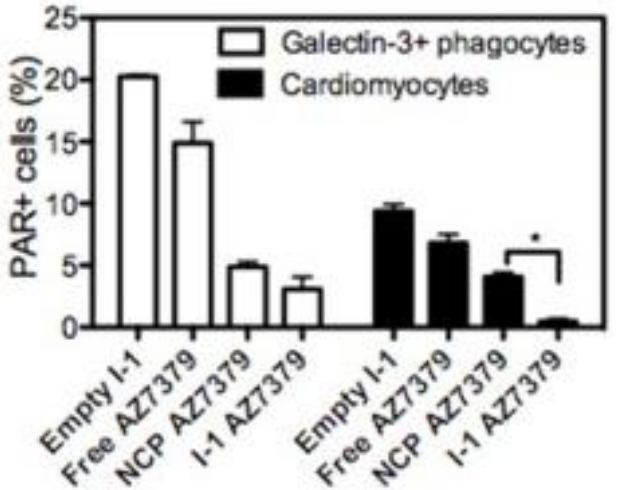
- Liposomes bear peptides specific for cells present in the infarct/border zone -- Increased drug efficacy
  --Minimized off-target effects
- Allows for effective and specific delivery of small molecules
- Liposome-based therapeutics might help improve cardiac function or reverse LV remodeling



AZ7379 I-1 liposome increases efficiency of PARP-1 inhibition in cardiomyocytes and phagocytes

NCP AZ7379 **I-1 AZ7379**





Measurement of the PAR production in cardiomyocytes and phagocytes after targeted delivery of liposomal formulation of AZ7379 (I-1 AZ7379) compared with negative controls: NCP-negative control peptide AZ7379, free AZ7379 and Empty I-1. White arrows point to cardiomyocytes/phagocytes, green indicates PAR expression.

Relevant Publications

- J Controlled Release. 2015. 220: 556-567. **Kelly KA**, et. al.

Intellectual Property

- UVA Tech ID: KELLYK-CARDIAC
  - Title: Target-specific delivery of therapeutic agents
  - PCT Patent Application PCT/US2016/037668 filed Jun 15, 2016