Micro-RNAs as Biomarkers for Myocardial Damage after Cardiac Surgery in Children

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- **Successful treatment of disease depends on <u>early detection</u> and <u>appropriate therapy</u>**

- **The presence of certain disease states can be identified by monitoring the expression levels of biomarkers (DNA, RNA, proteins)**

- **Biomarkers are an extremely important tool in areas like oncology, virology inflammation and heart disease**

Congenital Heart Disease (CHD) – some facts:

- **Incidence of congenital heart disease: 8/1000 births**
- **50% of children with CHD will be operated for the repair of the defect during their first years of life**
- **Post-operative myocardial complications are a major cause for morbidity and mortality**

Can we predict which of the children will suffer from post-operative complications?

The Need

Serum biomarkers for early and accurate detection of heart damage following pediatric cardiac surgery

The present biomarkers for detecting heart failure are insufficient as they suffer from lack of specificity (Troponin, CPK)

Additional biomarkers with increased predictive performances are needed for more precise and earlier prediction of complications after pediatric cardiac surgery

Objective

Development of a diagnostic tool that will improve medical management and outcome following cardiac injury

<u>Adequate Biomarker should be:</u>

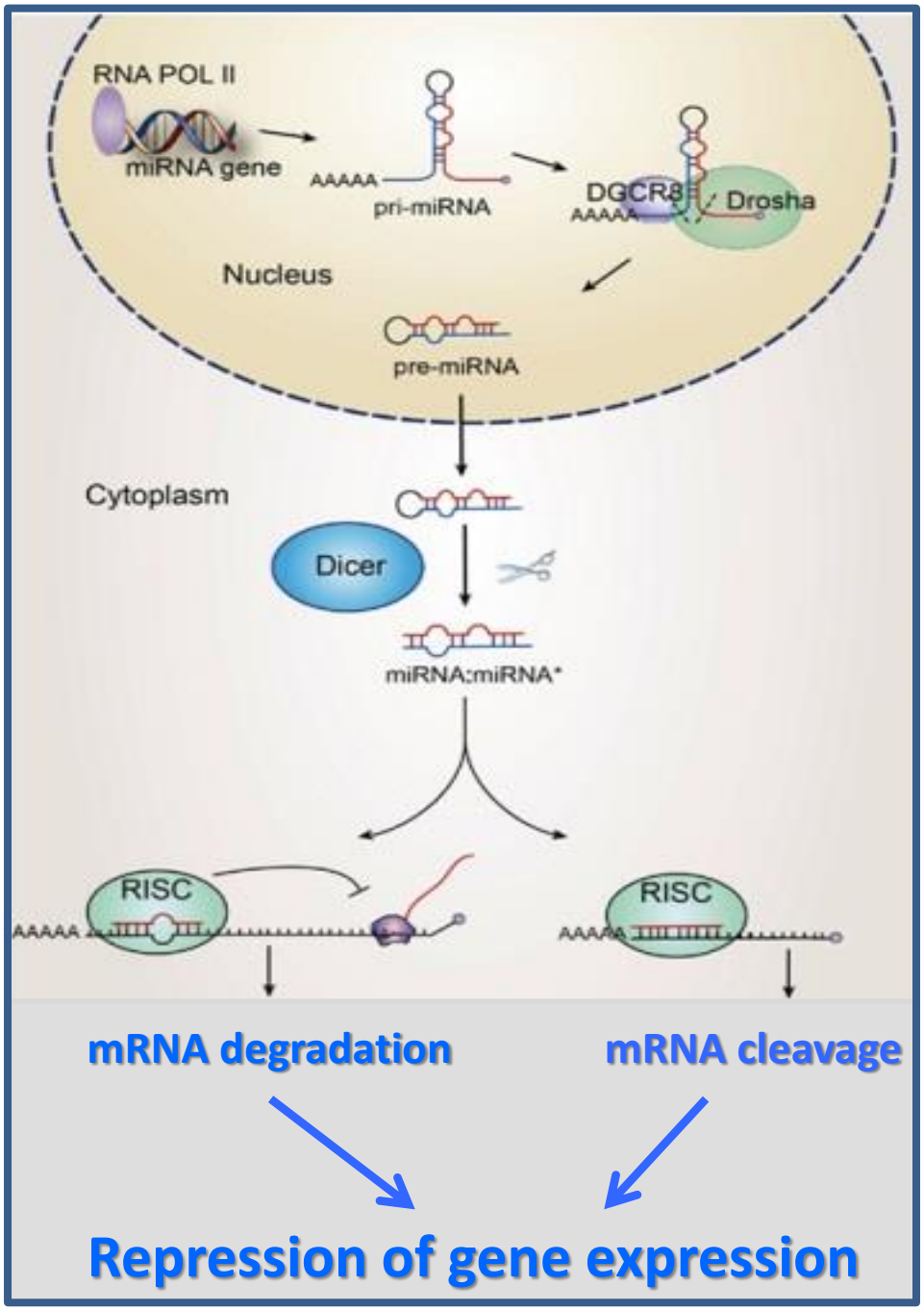
- **Stable**
  - **Rapid release kinetics**
    - **Specific to the organ we would like to monitor**
      - **Detectable in a small sample of serum**

Micro-RNAs (miRNAs)

- Short non-coding RNAs (~22 nt)
- Encoded by the DNA
- Transcribed by RNA Pol II
- Processed in the nucleus
- Exported to the cytoplasm
- Processed by Dicer
- Repress gene expression by:

  mRNA degradation

  mRNA cleavage



miRNAs

- Involved in all biological processes
- Tissue-specific expression pattern
- High biostability when excreted into plasma

Emerged as plasma biomarkers

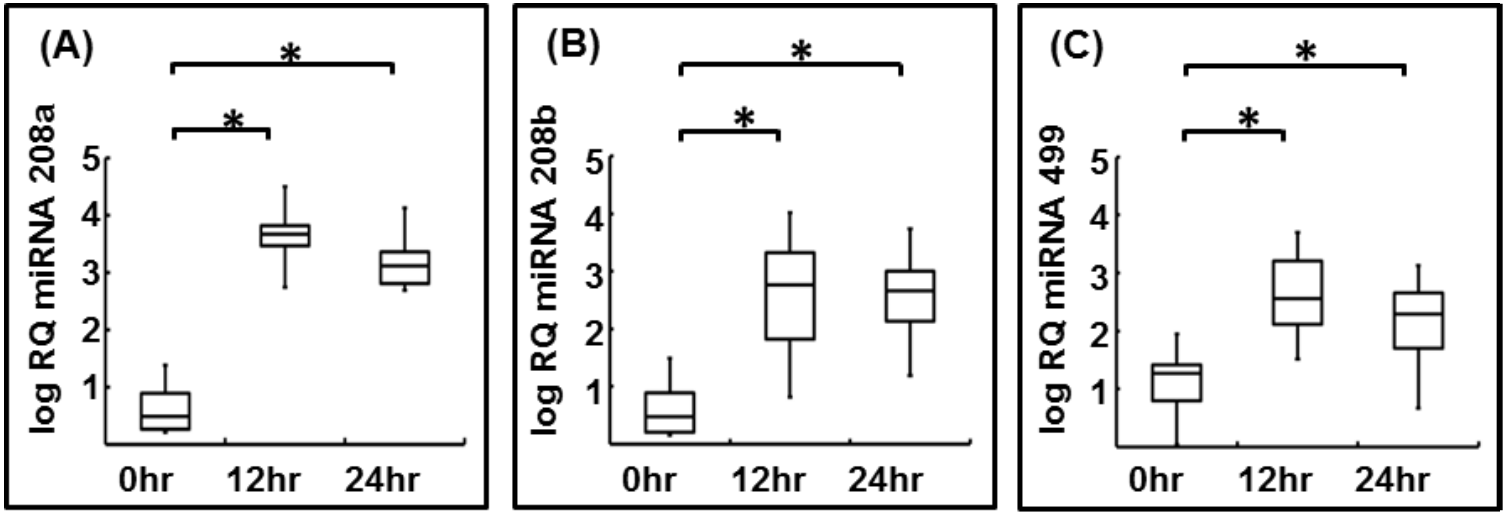
for many pathological states

(cancer, diabetes, viral infections)

Our Study – Preliminary Results

- Samples were obtained from pediatric patients with CHD, pre-operatively, 12hours and 24hours after the operation
- miRNAs were extracted from serum samples
- The relative amount of the miRNAs in plasma was measured by QRT-PCR
- The miRNAs of interest: miR-208a, -208b, -499

Levels of serum-derived miRNA-208a, -208b, -4[illegible] are highly elevated following cardiac surgery

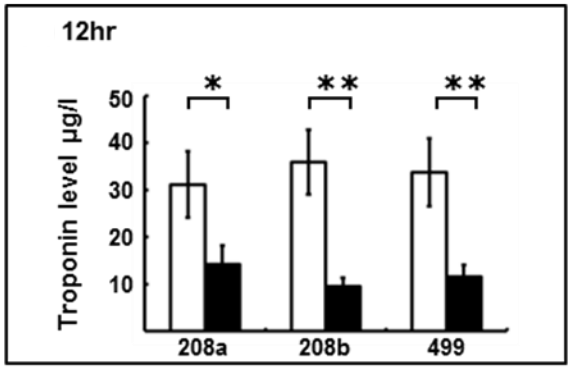


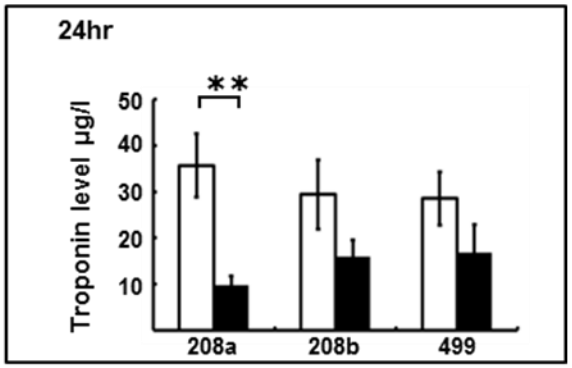
Preliminary correlations

High miRNA group

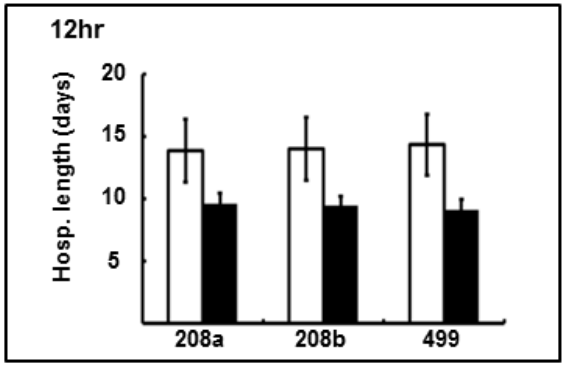
Low miRNA group

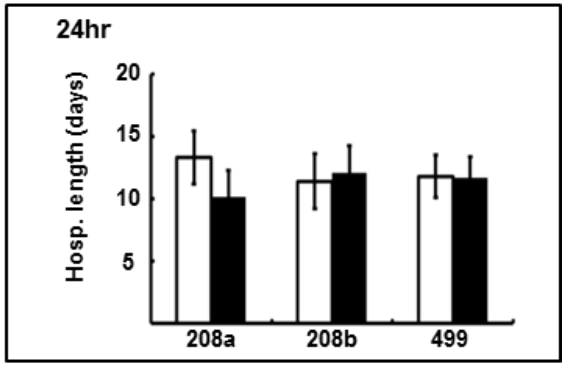
Troponin





Hospitalization length





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Conclusions

- **Circulating miRNAs-208a, -208b, and -499 are detectable in the plasma of children undergoing cardiac surgery**

- **The amount of these miRNAs rises sharply at 12h after the operation and then declines**

- **We suggest that these miRNAs may serve as novel biomarkers for monitoring and forecasting postoperative myocardial injury and recovery**

Keren's project

- **Do we see additional correlations between the relative amount of miRNA and the post operative course in earlier samples?**

- **Do we see additional correlations between the amount of the miRNAs and the post-operative course when we compare between operations performed with cardiac arrest to those that are carried out without cardiac arrest.**

- ❑ **Extract miRNAs from serum samples**
- ❑ **Prepare cDNA from the miRNAs of interest**
- ❑ **Quantify miRNAs using QRT-PCR**
- ❑ **Statistical analysis to search for correlations**

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Thank-you!

Good luck!!!