microRNAs in acute graft rejection in rat orthotopic liver transplantation
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Introduction

- microRNAs (miRNAs) are short noncoding 21–24 nucleotide sequences that inhibits protein synthesis by targeting messenger RNAs in a sequence specific manner.
- It has been known that gene specific translational silencing by miRNAs regulates various inflammatory responses.

Objectives

- In the present study, we clarified the involvement of miRNAs in the acute liver graft rejection in DA to Lewis rat orthotopic liver transplantation.

Methods

- Orthotopic liver transplantation was performed from DA (RT1a) to Lewis (RT1l) rats without immunospression.
- We studied liver grafts on day 0, day 5, day 7, and day 11, focusing on the degree of acute liver graft rejection, and alteration of miRNA profile during the development of rejection in rat liver grafts. miRNAs in the liver grafts were examined by microRNA array, and analyzed by GeneSpring (Agilent Technologies).

Results

Acute cellular and antibody-mediated rejection in DA to LEW rat orthotopic liver transplantation

The cellular and antibody-mediated rejection developed by day 11 with infiltration of CD3+ T cells and ED1+ macrophages, deposition of IgG, and liver graft dysfunction.

The alterations of miRNAs were evident in rejecting grafts. These miRNAs are known as the function and processes regulated the pathways for various inflammatory responses, immune cells differentiation and signaling, development of immunity and molecular pathways for allograft rejection.

Conclusions

- miRNAs may be involved in various immunological processes including development of innate and acquired immunity, inflammation, T-cell and B-cell mediated immune responses in transplant liver graft rejection.
- miRNAs in transplant immunobiology will provide an exciting framework for developing new biomarkers as well as new therapeutic interventions in transplantation.

References

Intra-Graft Events associated with Graft Acceptance “Acceptance Reaction” in DA to PVG Rat Liver Transplantation
Ishii E, Kuwahara N, Arai T, Kataoka M, Wakamatsu K, Masuda Y, Shimizu A
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Introduction

- In the present study, we examined the characterization of infiltrating cells in accepting liver grafts, in order to clarify the intra-graft events associated with graft tolerance in liver grafts.

Methods

- Orthotopic liver transplantation was performed from DA (RT1a) to PVG (RT1c) rats without immunospression (survival >100 days).

Objective

- In the present study, we examined the characterization of graft infiltrating cells that associated with graft tolerance.

Results

Progressively diminished infiltrating cells

- Day 7
- Day 14
- Day 21
- Day 100

DA donor specific tolerance

- DA skin graft at day 10 on PVG rat after day 100 DA liver transplantation
- Infiltration of CD3+ T cells and ED-1+ macrophages resembled acute cellular rejection, but many Fox P3+Treg cells were evident in accepting grafts.

Conclusions

- The cellular infiltration of tolerance of liver graft is characterized pathologically by the progressively diminished infiltrating cells, as well as persistence of infiltration of Treg cells.

References