MicroRNAs 106b and 222 improve hyperglycemia in a mouse model of insulin-deficient diabetes via pancreatic β-cell proliferation

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Major symptoms of diabetes mellitus manifest, once pancreatic β-cell numbers have become inadequate. Although natural regeneration of β-cells after injury is very limited, bone marrow (BM) transplantation (BMT) promotes their regeneration through undetermined mechanism(s) involving inter-cellular (BM cell-to-β-cell) crosstalk. We found that two microRNAs (miRNAs) contribute to BMT-induced β-cell regeneration. Screening murine miRNAs in serum exosomes after BMT revealed 42 miRNAs to be increased. Two of these miRNAs (miR-106b-5p and miR-222-3p) were shown to be secreted by BM cells and increased in pancreatic islet cells after BMT. Treatment with the corresponding anti-miRNAs inhibited BMT-induced β-cell regeneration. Furthermore, intravenous administration of the corresponding miRNA mimics promoted post-injury β-cell proliferation through Cip/Kip family down-regulation, thereby ameliorating hyperglycemia in mice with insulin-deficient diabetes. Thus, these identified miRNAs may lead to the development of therapeutic strategies for diabetes.