Biomarkers for Diabetes Therapies

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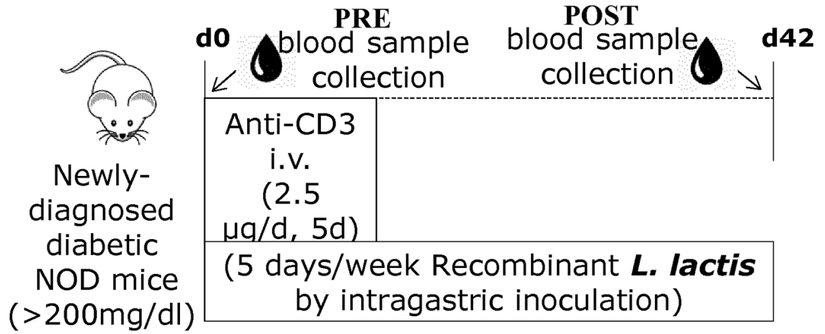
Invention

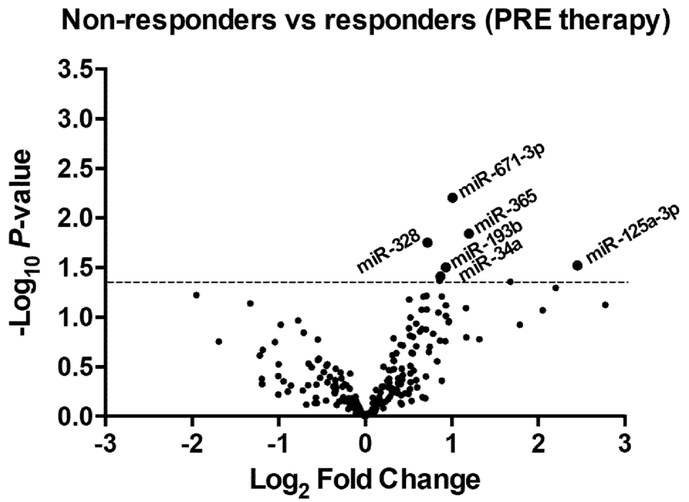
Restoration of immune tolerance in type 1 diabetes is key to reduce or stop beta-cell destruction linked to the resulting insulin deficiency. One proposed solution consists of combinatorial therapy based on anti-CD3 antibodies, administration of genetically modified *Lactobacillus lactis* strains producing pro-insulin and administration of interleukin 10. Nevertheless, such therapy restores normal blood glucose in 60% of cases in a mouse model. Appropriate biomarkers are therefore needed to assess the response to the therapy.

The present invention represents an *in vitro* implementable method and related kit for assessing the response to immune tolerance restoration therapy by evaluating the expression of specific microRNAs (miRNAs) as biomarkers of residual beta-cell function. The method includes oligonucleotide probes specific for prognostic miRNAs and allows for quantification of miR-365 and/or miR-193b levels together with miR-125a and/or miR-34a in plasma samples. The method includes the steps of (i) synthesis of cDNA from miRNAs, and (ii) quantification of the above biomarkers by quantitative PCR, normalised on control miRNAs, in samples taken before and after treatment. Reduced expression of the above biomarkers results in responsiveness to therapy, and vice versa.

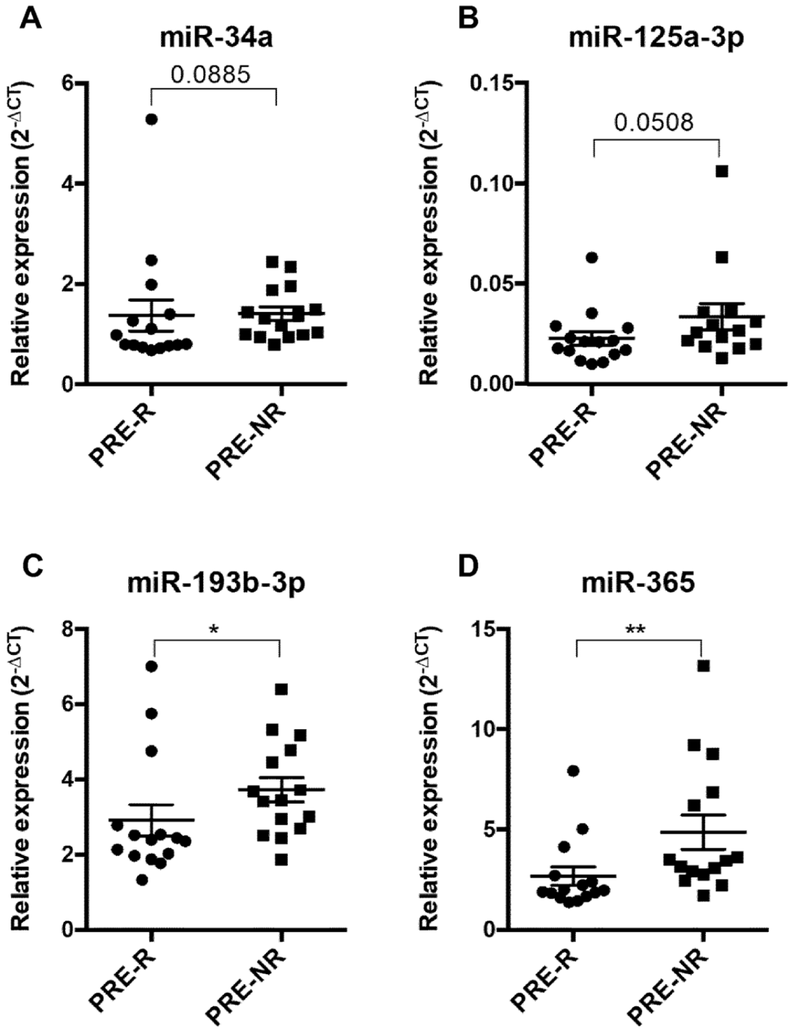
Drawings
& pictures



Strategy for treatment and blood sampling in the diabetic mouse model (NOD mice)



Expression profile of miRNAs in NOD mice in response to therapy (non-responders vs. responders)

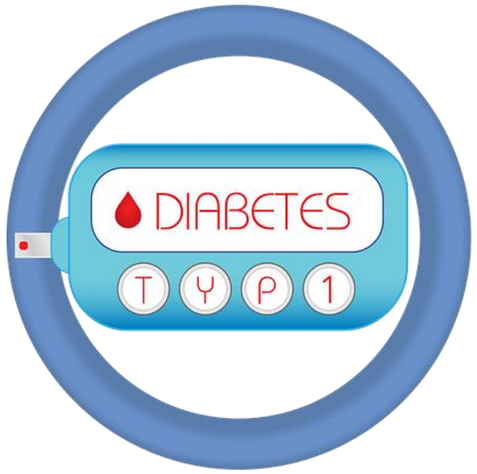


Differential expression of serum miRNAs in response to therapy (non-responders vs. responders);
*p<0.05; **p<0.001

Industrial applications

The technology may be of interest to (bio)pharmaceutical companies having (or wanting to expand to) diagnostic kits for autoimmune diseases including type 1 diabetes in their pipeline.

In particular, the invention will subsequently be used in clinical-hospital settings as a decision-support tool during the follow-up of type 1 diabetes treatments.



Possible developments

Currently evaluated at a TRL of 3, the technology can be further developed within specific technology maturation projects aimed at raising the level and allowing its introduction into the industrial network.

The group is looking for industrial partners operating in the (bio)pharmaceutical sector interested in collaborating on the aforementioned technological maturation of the invention.

The University of Siena is open to specific agreements for the exploitation, licensing or option of the patented invention.

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