**Supplementary Tables and Figures**

|  |  |
| --- | --- |
| Pathway  | miRNAs contributing to the enrichment of pathways  |
| Pathways in cancer  | hsa-miR-16-5p;hsa-miR-181c-5p;hsa-miR-374a-5p;hsa-let-7e-5p;hsa-miR-27b-3p;hsa-miR-26a-5p;hsa-miR-665;hsa-miR-222-3p;hsa-miR-31-3p;hsa-miR-30b-5p;hsa-miR-30c-5p;hsa-miR-28-5p;hsa-miR-155-5p;hsa-miR-378a-3p;hsa-miR-486-5p;hsa-miR-140-3p;hsa-miR-296-5p;hsa-miR-18a-3p;hsa-miR-425-3p |
| PI3K-Akt signaling pathway  | hsa-miR-26a-5p;hsa-miR-374a-5p;hsa-miR-27b-3p;hsa-let-7e-5p;hsa-miR-30b-5p;hsa-miR-30c-5p;hsa-miR-28-5p;hsa-miR-16-5p;hsa-miR-155-5p;hsa-miR-486-5; hsa-miR-140-3p;hsa-miR-31-3p;hsa-miR-222-3p;hsa-miR-665;hsa-miR-181c-5p;hsa-miR-18a-3p;hsa-miR-296-5p;hsa-miR-425-3p;hsa-miR-378a-3p |
| TGF-beta signaling pathway | hsa-miR-374a-5p;hsa-miR-27b-3p;hsa-miR-16-5p;hsa-miR-30b-5p;hsa-miR-30c-5p;hsa-let-7e-5p;hsa-miR-486-5p;hsa-miR-665;hsa-miR-181c-5p;hsa-miR-155-5p;hsa-miR-140-3p;hsa-miR-222-3p;hsa-miR-378a-3p;hsa-miR-26a-5p |

**Supplementary Table 1.** MiRNA contributing to the top canonical pathways influenced by differentially expressed miRNAs in T cells.

|  |  |
| --- | --- |
| Pathway  | miRNAs contributing to the enrichment of pathways |
| Wnt signaling pathway | hsa-miR-222-3p;hsa-miR-26a-5p;hsa-miR-141-3p;hsa-miR-582-5p;hsa-miR-20a-5p;hsa-miR-29b-2-5p;hsa-miR-378a-3p;hsa-miR-19b-3p;hsa-miR-148b-3p;hsa-miR-193a-3p;hsa-miR-30b-5p;hsa-miR-505-3p;hsa-miR-107;hsa-miR-195-5p;hsa-miR-32-5p;hsa-miR-484;hsa-miR-374a-5p;hsa-miR-324-3p;hsa-miR-491-5p;hsa-miR-502-5p;hsa-miR-324-5p |
| Pathways in cancer  | hsa-miR-26a-5p;hsa-miR-374a-5p;hsa-miR-502-5p;hsa-miR-582-5p;hsa-miR-107;hsa-miR-195-5p;hsa-miR-20a-5p;hsa-miR-30b-5p;hsa-miR-141-3p;hsa-miR-222-3p;hsa-miR-148b-3p;hsa-miR-151a-3p;hsa-miR-29b-2-5p;hsa-miR-324-3p;hsa-miR-32-5p;hsa-miR-484;hsa-miR-19b-3p;hsa-miR-491-5p;hsa-miR-193a-3p;hsa-miR-378a-3p;hsa-miR-18a-3p;hsa-miR-324-5p |
| PI3K-Akt signaling pathway  | hsa-miR-222-3p;hsa-miR-29b-2-5p;hsa-miR-20a-5p;hsa-miR-19b-3p;hsa-miR-491-5p;hsa-miR-374a-5p;hsa-miR-141-3p;hsa-miR-32-5p;hsa-miR-195-5p;hsa-miR-148b-3p;hsa-miR-502-5p;hsa-miR-107;hsa-miR-30b-5p;hsa-miR-193a-3p;hsa-miR-26a-5p;hsa-miR-484;hsa-miR-582-5p;hsa-miR-378a-3p;hsa-miR-324-5p;hsa-miR-18a-3p;hsa-miR-151a-3p |

**Supplementary Table 2.** MiRNA contributing to the top canonical pathways influenced by differentially expressed miRNAs in B cells.

|  |  |  |
| --- | --- | --- |
| **anti-SSA+ patients vs. controls** |  | **anti-SSA-patients vs. controls** |
| miRNAs | fold change in CD4 cells | p value | miRNAs | fold changein CD4 cells | p value |
| **hsa-let-7d-3p** | -2.20 | 1.2110-5 | **hsa-let-7d-3p** | -3.10 | 2.1410-6 |
| hsa-miR-26a-5p | -1.36 | 1.7910-4 |  |  |  |
| **hsa-miR-378a-3p** | -1.44 | 7.0710-4 | **hsa-miR-378a-3p** | -1.21 | 0.045 |
| **hsa-miR-28-5p** | 1.34 | 7.3410-4 | **hsa-miR-28-5p** | 1.40 | 0.002 |
| hsa-miR-30c-5p | -1.18 | 0.002 | hsa-miR-181c-5p | 1.67 | 0.004 |
| hsa-miR-23b-3p | -1.34 | 0.006 | hsa-miR-874 | -1.22 | 0.016 |
| hsa-let-7e-5p | -1.45 | 0.006 | hsa-miR-140-5p | 1.14 | 0.019 |
| hsa-miR-30b-5p | -1.21 | 0.007 | hsa-miR-155-5p | 1.36 | 0.022 |
| hsa-miR-598 | -1.45 | 0.008 | hsa-miR-665 | -1.61 | 0.039 |
| hsa-miR-140-3p | 1.17 | 0.012 | hsa-let-7g-5p | 1.14 | 0.029 |
| **hsa-miR-425-3p** | -1.30 | 0.013 | **hsa-miR-425-3p** | -1.37 | 0.001 |
| hsa-miR-505-3p | -1.56 | 0.014 | hsa-miR-296-5p | 1.34 | 0.035 |
| hsa-miR-23a-3p | -1.32 | 0.017 | hsa-miR-31-5p | -1.37 | 0.046 |
| **hsa-miR-486-5p** | 1.55 | 0.018 | **hsa-miR-486-5p** | 1.58 | 0.024 |
| hsa-miR-27b-3p | -1.34 | 0.023 | hsa-miR-95 | 1.32 | 0.046 |
| hsa-miR-374a-5p | -1.23 | 0.028 | hsa-miR-22-3p | 1.47 | 0.049 |
| **hsa-miR-31-3p** | -1.37 | 0.031 | **hsa-miR-31-3p** | -1.52 | 0.039 |
| hsa-let-7i-5p | 1.12 | 0.038 |  |  |  |  |
| hsa-miR-107 | 1.21 | 0.042 |  |  |  |  |
| hsa-miR-330-3p | 1.48 | 0.042 |  |  |  |  |
| hsa-miR-146a-5p | 1.33 | 0.044 |  |  |  |  |
| hsa-miR-484 | 1.30 | 0.047 |  |  |  |  |

**Supplementary Table 3.** Differentially expressed miRNAs with a p-value < 0.05 in the discovery cohort in **T lymphocytes (TL)** from anti-SSA+ pSS patients and anti-SSA- pSS patients compared to the controls, respectively. MiRNAs present in both anti-SSA positive and negative patients are highlighted in bold letters. Nominal p-values without correction for multiple comparisons are shown.

|  |  |
| --- | --- |
| **anti-SSA+ patients vs. controls** | **anti-SSA- patients vs. controls** |
| miRNAs | fold change in CD19 cells | p value | miRNAs | fold change in CD19 cells | p value | miRNAs | fold change in CD19 cells | p value |
| hsa-miR-324-5p | 2.06 | 2.4010-4 | hsa-miR-32-5p | -1.77 | 0.013 | hsa-let-7d-3p | -1.99 | 0.003 |
| hsa-miR-26a-5p | -1.55 | 3.3010-4 | hsa-miR-29b-2-5p | 1.49 | 0.013 | hsa-miR-210 | 1.52 | 0.006 |
| hsa-miR-20a-5p | -1.25 | 3.8210-4 | hsa-miR-29b-3p | -1.81 | 0.015 |  |  |  |
| **hsa-miR-107** | 1.43 | 6.4410-4 | hsa-miR-199a-5p | 3.23 | 0.016 | **hsa-miR-107** | 1.28 | 0.022 |
| **hsa-miR-222-3p** | 1.60 | 6.7010-4 | hsa-miR-362-5p | 1.61 | 0.017 | **hsa-miR-222-3p** | 1.34 | 0.003 |
| **hsa-miR-30b-5p** | -1.63 | 7.7210-4 | hsa-miR-30c-5p | -1.25 | 0.020 | **hsa-miR-30b-5p** | -1.41 | 0.002 |
| hsa-miR-19b-3p | -1.58 | 8.1010-4 | hsa-miR-505-3p | -1.94 | 0.021 |  |  |  |
| hsa-miR-484 | 1.78 | 9.7510-4 | **hsa-miR-582-5p** | -1.63 | 0.021 | **hsa-miR-582-5p** | -1.72 | 0.041 |
| hsa-miR-141-3p | -2.50 | 0.001 | hsa-miR-19a-3p | -1.32 | 0.026 | hsa-miR-125b-5p | -2.02 | 0.040 |
| hsa-miR-454-3p | 1.25 | 0.003 | hsa-miR-192-5p | -1.44 | 0.026 |  |  |  |
| hsa-miR-15a-5p | -1.39 | 0.003 | hsa-miR-130b-3p | 1.73 | 0.026 | hsa-miR-148b-3p | -1.21 | 0.044 |
| hsa-miR-652-3p | 1.57 | 0.004 | hsa-miR-18a-5p | 1.46 | 0.027 | hsa-miR-27b-3p | -1.53 | 0.048 |
| hsa-miR-195-5p | -1.89 | 0.004 | hsa-miR-106b-5p | -1.19 | 0.028 |  |  |  |
| hsa-miR-378a-3p | -1.55 | 0.004 | hsa-miR-103a-3p | 1.26 | 0.029 |  |  |  |
| **hsa-miR-324-3p** | 1.27 | 0.005 | hsa-miR-365a-3p | 1.55 | 0.031 | **hsa-miR-324-3p** | 1.17 | 0.025 |
| hsa-miR-18b-5p | 1.64 | 0.007 | hsa-miR-26b-5p | -1.39 | 0.032 |  |  |  |
| hsa-miR-128 | 1.69 | 0.007 | hsa-miR-101-3p | -1.62 | 0.033 |  |  |  |
| **hsa-miR-18a-3p** | 2.05 | 0.008 | hsa-miR-139-5p | 2.46 | 0.035 | **hsa-miR-18a-3p** | 1.83 | 0.021 |
| hsa-miR-374a-5p | -1.66 | 0.008 | hsa-miR-142-5p | -1.67 | 0.046 |  |  |  |
| hsa-miR-215 | -1.53 | 0.008 | hsa-miR-486-5p | 1.69 | 0.048 |  |  |  |
| **hsa-miR-151a-3p** | 1.44 | 0.012 |  |  |  | **hsa-miR-151a-3p** | 1.37 | 0.021 |

**Supplementary Table 4**. Differentially expressed miRNAs with a p-value < 0.05 in the discovery cohort in **B lymphocytes (BL)** from anti-SSA+ pSS patients and anti-SSA- pSS patients compared to the controls, respectively. MiRNAs present in both anti-SSA positive and negative patients are highlighted in bold letters. Nominal p-values without correction for multiple comparisons are shown.

|  |  |  |
| --- | --- | --- |
| miRNAs | fold change in CD19 cells | p value |
| hsa-miR-210 | -1.48 | 5.9010-4 |
| hsa-miR-26a-5p | -1.47 | 0.001 |
| hsa-miR-362-5p | 2.00 | 0.002 |
| hsa-miR-484 | 1.75 | 0.005 |
| hsa-miR-199a-5p | 3.82 | 0.007 |
| hsa-miR-652-3p | 1.67 | 0.008 |
| hsa-miR-140-5p | -1.37 | 0.009 |
| hsa-miR-15a-5p | -1.36 | 0.011 |
| hsa-miR-20a-5p | -1.20 | 0.013 |
| hsa-miR-454-3p | 1.25 | 0.013 |
| hsa-miR-18b-5p | 1.60 | 0.014 |
| hsa-miR-99b-5p | 3.45 | 0.016 |
| hsa-miR-19b-3p | -1.44 | 0.018 |
| hsa-miR-103a-3p | 1.31 | 0.018 |
| hsa-miR-128 | 1.68 | 0.019 |
| hsa-miR-145-5p | 4.89 | 0.019 |
| hsa-miR-324-5p | 1.56 | 0.021 |
| hsa-miR-215 | -1.70 | 0.022 |
| hsa-miR-199b-5p | 2.04 | 0.028 |
| hsa-miR-125a-5p | 2.77 | 0.032 |
| hsa-miR-30c-5p | -1.17 | 0.038 |
| hsa-miR-29b-3p | -1.77 | 0.039 |
| hsa-miR-126-5p | 3.39 | 0.040 |
| hsa-miR-25-3p | -1.22 | 0.046 |
| hsa-miR-18a-5p | 1.42 | 0.047 |

**Supplementary Table 5.** Differentially expressed miRNAs with a p-value < 0.05 in the discovery cohort in **B Lymphocytes** from anti-SSA+ pSS patients compared to anti-SSA- pSS patients. Nominal p-values without correction for multiple comparisons are shown.

|  |  |
| --- | --- |
| **T cells** | **B cells** |
| miRNAs | in human panel I | Previous association with diseases | miRNAs | in human panel I | Previous association with diseases |
| hsa-let-7d-3p | + | MS [1] | hsa-miR-30b-5p | + | pSS [2] |
| hsa-miR-28-5p | + | RA [3] | hsa-miR-222-3p | + | pSS [2] |
| hsa-miR-378a-3p | + | INF [4] | hsa-miR-18a-3p | + | miR17-92 cluster [5], pSS [6] |
| hsa-miR-26a-5p | + | MS [7], BC[8] | hsa-miR-19b-3p | + | miR17-92 cluster [5], pSS [6] |
| hsa-miR-30b-5p | + | pSS [2] | hsa-miR-26a-5p | + | MS [7] |
| hsa-miR-140-3p | + | T1D [9] | hsa-miR-20a-5p | + | MS [10] |
| hsa-miR-30c-5p | + | T1D [9] | hsa-miR-32-5p | + | MS [11] |
| hsa-miR-155-5p | + | pSS [12, 13] | hsa-let-7d-3p | + | MS [1] |
| hsa-miR-31-3p | + | SLE [14] | hsa-miR-378a-3p | + | INF [4] |
| hsa-miR-222-3p | + | pSS [2] | hsa-miR-146a-5p | - | pSS [12, 13], SLE [15], RA [16, 17] |
| hsa-miR-16-5p | + | SLE [18] |  |  |
| hsa-miR-146a-5p | - | pSS [12, 13], SLE [15], RA [16, 17] |  |  |  |

**Supplementary Table 6.** Significantly differentially expressed miRNAs identified in the discovery cohort that were chosen for validation in the replication cohort. ‘+’ denotes miRNAs that were found significantly differentially expressed in the discovery cohort using the human panel I; ‘-̓ denotes miRNAs that were not found significantly expressed in the discovery cohort human panel I but nonetheless included due to previous reports; INF: Inflammation,;MS: Multiple sclerosis pSS: primary Sjøgren’s syndrome; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; T1D type 1 diabetes.



**Supplementary Figure 1.** Representative boxplots of miRNA expression in both the discovery and the replication cohort in CD4+ T cells. Data from controls is shown in red, data from patients in turquoise.

****

**Supplementary Figure 2.** Representative boxplots of miRNA expression in both the discovery and the replication cohort in CD19+ B cells. Data from controls is shown in red, data from patients in turquoise.



**Supplementary Figure 3.** Complementary binding between hsa-miR-30b-5p and the 3’UTR of *BAFF* mRNA.



**Supplementary Figure 4.** FACS strategy for the isolation of transfected cells. Transfected cells were analyzed by flow cytometry and only highly positive cells were isolated. **A.** Lipofectamine Control ; **B.** Inhibitor hsa-miR-30b-5p at a concentration of 100nM 48 hrs post transfection ; **C.** Overlay of A (red) and B (green).

**Supplementary References**

1 Sondergaard HB, Hesse D, Krakauer M, Sorensen PS, Sellebjerg F. Differential microRNA expression in blood in multiple sclerosis. *Mult Scler* 2013;**19**(14):1849-57.

2 Alevizos I, Alexander S, Turner RJ, Illei GG. MicroRNA expression profiles as biomarkers of minor salivary gland inflammation and dysfunction in Sjogren's syndrome. *Arthritis Rheum* 2011;**63**(2):535-44.

3 Murata K, Furu M, Yoshitomi H, et al. Comprehensive microRNA analysis identifies miR-24 and miR-125a-5p as plasma biomarkers for rheumatoid arthritis. *PLoS One* 2013;**8**(7):e69118.

4 Ruckerl D, Jenkins SJ, Laqtom NN, et al. Induction of IL-4Ralpha-dependent microRNAs identifies PI3K/Akt signaling as essential for IL-4-driven murine macrophage proliferation in vivo. *Blood* 2012;**120**(11):2307-16.

5 Xiao C, Srinivasan L, Calado DP, et al. Lymphoproliferative disease and autoimmunity in mice with increased miR-17-92 expression in lymphocytes. *Nat Immunol* 2008;**9**(4):405-14.

6 Alevizos I, Illei GG. MicroRNAs in Sjogren's syndrome as a prototypic autoimmune disease. *Autoimmun Rev* 2010;**9**(9):618-21.

7 Zahednasab H, Balood M. The role of miR-326 and miR-26a in MS disease activity. *Gene* 2014;**548**(1):158.

8 Padgett KA, Lan RY, Leung PC, et al. Primary biliary cirrhosis is associated with altered hepatic microRNA expression. *J Autoimmunity* 2009;**32**(3-4):246-53.

9 Collares CV, Evangelista AF, Xavier DJ, et al. Identifying common and specific microRNAs expressed in peripheral blood mononuclear cell of type 1, type 2, and gestational diabetes mellitus patients. *BMC Res Notes* 2013;**6**:491.

10 Keller A, Leidinger P, Steinmeyer F, et al. Comprehensive analysis of microRNA profiles in multiple sclerosis including next-generation sequencing. *Mult Scler* 2014;**20**(3):295-303.

11 Yang D, Wang WZ, Zhang XM, et al. MicroRNA expression aberration in Chinese patients with relapsing remitting multiple sclerosis. *J Mol Neurosci* 2014;**52**(1):131-7.

12 Shi H, Zheng LY, Zhang P, Yu CQ. miR-146a and miR-155 expression in PBMCs from patients with Sjogren's syndrome. *J Oral Pathol Med* 2014;**43**(10):792-7.

13 Pauley KM, Stewart CM, Gauna AE, et al. Altered miR-146a expression in Sjogren's syndrome and its functional role in innate immunity. *Eur J Immunol* 2011;**41**(7):2029-39.

14 Martinez-Ramos R, Garcia-Lozano JR, Lucena JM, et al. Differential expression pattern of microRNAs in CD4+ and CD19+ cells from asymptomatic patients with systemic lupus erythematosus. *Lupus* 2014;**23**(4):353-9.

15 Tang Y, Luo X, Cui H, et al. MicroRNA-146A contributes to abnormal activation of the type I interferon pathway in human lupus by targeting the key signaling proteins. *Arthritis Rheum* 2009;**60**(4):1065-75.

16 Nakasa T, Miyaki S, Okubo A, et al. Expression of microRNA-146 in rheumatoid arthritis synovial tissue. *Arthritis Rheum.* 2008;**58**(5):1284-92.

17 Pauley KM, Satoh M, Chan AL, Bubb MR, Reeves WH, Chan EK. Upregulated miR-146a expression in peripheral blood mononuclear cells from rheumatoid arthritis patients. *Arthritis Res Ther* 2008;**10**(4):R101.

18 Wang H, Peng W, Ouyang X, Li W, Dai Y. Circulating microRNAs as candidate biomarkers in patients with systemic lupus erythematosus. *Transl Res* 2012;**160**(3):198-206.