

**ESM Table 3** DNA methylation levels at gene promoter regions in rat islets measured by bisulfite MassArray analysis

Gene	3M (%)	15M (%)	p value
Gene expression down-regulated with age			
<i>Aurkb</i>	2.2 (± 0.1)	3.1 (± 0.2)	<b>0.0087</b>
<i>Gjb6</i>	75.9 (± 2.9)	76.3 (± 1.9)	0.7879
<i>Fam183b</i>	9.5 (± 1.2)	10.9 (± 0.7)	0.5844
<i>Cartpt</i>	6.1 (± 0.3)	8.53 (± 0.27)	<b>0.0022</b>
<i>Npy</i>	2.1 (± 0.3)	3.3 (± 0.2)	<b>0.0152</b>
<b><i>Cd79b</i></b>	91.7 (± 2.1)	86.1 (± 1.1)	<b>0.0455</b>
<i>Abcc8</i>	4.3 (± 0.2)	5.6 (± 0.2)	<b>0.0043</b>
<i>Gipr</i>	12.4 (± 1.2)	16.1 (± 0.8)	<b>0.026</b>
<b><i>Pyy</i></b>	48.4 (± 2.6)	32.9 (± 0.8)	<b>0.0022</b>
<b><i>Gpr119</i></b>	12.0 (± 4.5)	40.3 (± 3.6)	<b>0.0087</b>
Gene expression up-regulated with age			
<b><i>Cxcl9</i></b>	72.0 (± 1.5)	59.8 (± 0.6)	<b>0.0022</b>
<b><i>Spp1</i></b>	71.8 (± 0.6)	62.2 (± 0.6)	<b>0.0022</b>
<i>Reg3a</i>	93.8 (± 0.7)	91.9 (± 0.5)	<b>0.0455</b>
<b><i>Reg3b</i></b>	2.4 (± 0.6)	14.6 (± 1.9)	<b>0.0022</b>
<b><i>Tf</i></b>	30.2 (± 0.9)	21.8 (± 1.1)	<b>0.0043</b>
<b><i>Prss35</i></b>	29.7 (± 1.9)	23.3 (± 0.6)	<b>0.0087</b>
<i>Serpina1a</i>	60.3 (± 3.6)	50.2 (± 2.9)	0.1212
<b><i>Col3a1</i></b>	67.4 (± 3.2)	49.3 (± 2.3)	<b>0.0087</b>
<b><i>C4b</i></b>	68.1 (± 2.6)	41.9 (± 2.8)	<b>0.0022</b>
<b><i>Dpt</i></b>	78.4 (± 2.1)	61.1 (± 2.3)	<b>0.0022</b>
<i>Aldob</i>	16.7 (± 3.4)	18.5 (± 1.6)	0.5714
<i>Ptfla</i>	10.2 (± 0.5)	9.4 (± 0.2)	0.303
<b><i>Cldn10</i></b>	63.5 (± 5.0)	77.7 (± 2.1)	<b>0.026</b>
<i>Colla1</i>	37.4 (± 1.5)	33.4 (± 3.4)	0.1797
<i>Gatm</i>	4.8 (± 0.1)	5.0 (± 0.2)	0.329
<i>Lgals3</i>	2.9 (± 0.2)	2.9 (± 0.3)	0.7273

<b>Mgst1</b>	16.9 (± 1.8)	11.5 (± 0.2)	<b>0.0043</b>
<i>Kcnq1</i>	3.5 (± 0.6)	3.3 (± 0.5)	0.8983
<b>Lgals1</b>	35.6 (± 2.1)	26.9 (± 0.3)	<b>0.026</b>
<b>Pah</b>	86.8 (± 0.7)	56.5 (± 1.7)	<b>0.0022</b>
<i>Fmo1</i>	65.3 (± 1.9)	62.2 (± 2.5)	0.474
<b>Il33</b>	92.1 (± 0.8)	77.3 (± 3.3)	<b>0.0043</b>
<i>Tspan8</i>	20.2 (± 1.4)	18.2 (± 3.0)	0.974
<i>Ptger3</i>	8.2 (± 0.9)	9.3 (± 0.5)	0.5714
<i>S100a6</i>	23.5 (± 1.4)	21.8 (± 0.8)	0.3052
<i>Ccdc80</i>	1.6 (± 0.1)	2.8 (± 0.7)	0.3203
<i>Ddah1</i>	6.2 (± 0.4)	6.2 (± 0.4)	0.8939
<b>S100a4</b>	81.2 (± 1.6)	75.0 (± 1.0)	<b>0.0087</b>
<i>Gbp2</i>	55.2 (± 2.5)	53.1 (± 2.3)	0.5628
<i>Lgals2</i>	41.2 (± 2.9)	43.3 (± 9.1)	0.8745
<i>Ctss</i>	84.7 (± 1.5)	84.8 (± 0.3)	> 0.9999
<i>Itgb6</i>	19.4 (± 3.1)	25.4 (± 1.8)	0.0931
<b>Fbp2</b>	59.4 (± 5.0)	34.9 (± 2.6)	<b>0.0022</b>
<i>Serping1</i>	9.6 (± 0.9)	13.3 (± 0.3)	<b>0.026</b>
<i>Tspan4</i>	6.1 (± 0.2)	5.9 (± 0.6)	0.0931
<b>Dmbt1</b>	66.2 (± 3.2)	74.1 (± 1.1)	<b>0.026</b>
<b>LINE-1</b>	84.2 (± 0.5)	78.7 (± 0.5)	<b>0.0022</b>

Data represent mean values ± SEM (n=5-6 samples per group). P values were obtained by Mann-Whitney tests and significant differences are written in bold. Gene symbols written in bold and color are those that associate an absolute difference in methylation above 5% and p value <0.05 (red – loss of methylation with age; blue – gain of methylation with age).