

TABLE

Univariate correlation analysis and Glycaemia corrected partial correlation analysis of age with all analysed variables

	Uncorrected correlation Age vs any variable in column 1		Glycaemia corrected partial correlations Age vs any variable in column 1	
	Rho value	p value	Rho value	p value
Glucose (mg/dL)	0.596**	0.007	NA	NA
Hemoglobin (percent)	0.548*	0.023	0.565	0.618
DM2 Years of evolution	0.488	0.153	0.948	0.206
Weight (Kg)	-0.005	0.985	0.935	0.231
Height (m)	-0.305	0.269	0.431	0.717
Body Mass Index	0.055	0.852	0.777	0.433
Total Cholesterol (mg/dl)	0.145	0.567	-0.943	0.216
Triglycerides (mg/dl)	0.157	0.533	-0.811	0.398
HDL(mg/dl)	0.062	0.807	0.174	0.889
LDL(mg/dl)	0.012	0.961	-0.901	0.286
HLA_DR_NIC	-0.409	0.092	-0.996	0.058
HLA_DR_H37Rv	-0.610**	0.007	0.996	0.058
HLA_DR_PHE4	-0.412	0.090	0.842	0.363
HLA_DR_PHE2	-0.488*	0.040	0.984	0.113
HLA_DR_PHE1	-0.186	0.459	0.696	0.510
CD80_NIC	-0.251	0.315	-0.969	0.158
CD80_H37Rv	-0.317	0.200	0.099	0.937
CD80_Phe4	-0.309	0.212	0.308	0.800
CD80_Phe2	-0.065	0.797	0.226	0.855
CD80_Phe1	0.331	0.180	0.513	0.657
CD86_NIC	-0.741**	0.000	-0.865	0.334
CD86_H37Rv	-0.390	0.099	-0.274	0.823
CD86_Phe4	-0.233	0.337	0.999	0.029
CD86_Phe2	-0.290	0.228	0.546	0.633
CD86_Phe1	0.049	0.841	-0.054	0.966
PD-L1_NIC	0.540*	0.017	-0.983	0.119
PD-L1_H37Rv	0.327	0.172	-1.000	0.017
PD-L1_Phe4	-0.106	0.665	0.505	0.663
PD-L1_Phe2	0.131	0.593	-0.475	0.685
PD-L1_Phe1	0.515*	0.024	-0.999	0.032
IL-1B_NIC	0.512	0.130	-0.917	0.262
IL-1B_H37Rv	0.310	0.384	-0.754	0.456
IL-1B_Phe4	0.560	0.093	-0.982	0.120
IL-1B_Phe2	0.719*	0.019	-0.343	0.777
IL-1B_Phe1	0.452	0.189	-0.769	0.442
IL_6_NIC	0.659*	0.038	-0.428	0.675
IL_6_H37Rv	0.280	0.432	-0.901	0.286
IL_6_Phe4	0.498	0.143	-0.488	0.675
IL_6_Phe2	0.471	0.169	-0.901	0.286
IL_6_Phe1	0.055	0.880	-0.923	0.251
IL-8_NIC	0.613	0.059	-0.383	0.750
IL-8_H37Rv	-0.710*	0.021	-0.623	0.572
IL-8_Phe4	-0.722*	0.018	0.407	0.733
IL-8_Phe2	-0.584	0.076	-0.946	0.210
IL-8_Phe1	-0.753*	0.012	-0.996	0.057
IL-12p70_NIC	0.805**	0.005	-0.027	0.983
IL-12p70_H37Rv	-0.476	0.165	-0.994	0.072
IL-12p70_Phe4	-0.254	0.479	0.644	0.555
IL-12p70_Phe2	-0.709*	0.022	-0.831	0.376

	Uncorrected correlation Age vs any variable in column 1		Glycaemia corrected partial correlations Age vs any variable in column 1	
	Rho value	p value	Rho value	p value
IL-12p70_Phe1	-0.061	0.867	0.343	0.777
IL-10_NIC	-0.774*	0.009	0.990	0.089
IL-10_H37Rv	-0.854**	0.002	0.620	0.574
IL-10_Phe4	-0.343	0.333	-0.312	0.798
IL-10_Phe2	-0.848**	0.002	-0.548	0.631
IL-10_Phe1	-0.482	0.159	-0.973	0.149
MCP-1_NIC	0.756*	0.011	-1.000	0.003
MCP-1_H37Rv	0.451	0.191	0.156	0.900
MCP-1_Phe4	0.787**	0.007	0.209	0.866
MCP-1_Phe2	-0.323	0.362	-0.995	0.066
MCP-1_Phe1	0.329	0.353	0.664	0.538
MIG_NIC	0.694*	0.026	0.388	0.746
MIG_H37Rv	-0.346	0.328	0.652	0.548
MIG_Phe4	-0.313	0.379	0.941	0.219
MIG_Phe2	0.722*	0.018	-0.846	0.358
MIG_Phe1	0.731*	0.016	0.995	0.061
IP-10_NIC	-0.349	0.324	-0.958	0.184
IP-10_H37Rv	-0.313	0.379	0.031	0.981
IP-10_Phe4	-0.835	0.003	-0.998	0.045
IP-10_Phe2	0.560	0.093	-1.000	0.010
IP-10_Phe1	-0.299	0.402	0.353	0.771
RANTES_NIC	0.049	0.894	-0.614	0.579
RANTES_H37Rv	-0.738*	0.015	0.108	0.931
RANTES_Phe4	0.547	0.101	0.236	0.848
RANTES_Phe2	0.640*	0.046	-0.576	0.609
RANTES_Phe1	0.439	0.204	0.336	0.782
Perc_FAGOCITOSIS_H37Rv	-0.455	0.058	-0.070	0.955
Perc_FAGOCITOSIS_Phe4	-0.244	0.328	-0.637	0.560
Perc_FAGOCITOSIS_Phe2	-0.348	0.157	-0.973	0.147
Perc_FAGOCITOSIS_Phe1	-0.607**	0.008	-0.924	0.249

*: $p < 0.05$; **: $p < 0.01$.

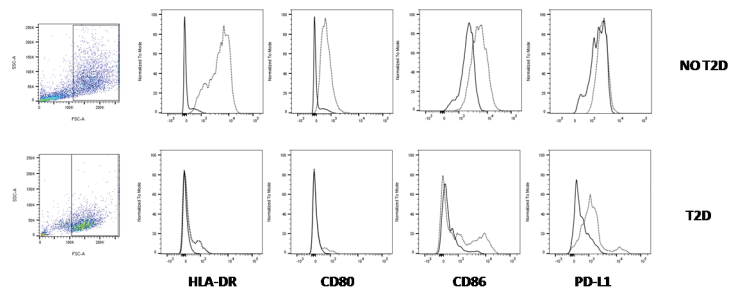


Fig. 1: flow cytometry gating strategy of a representative sample of monocyte-derived macrophages (MDM) in control healthy subjects (NO T2D) and T2D groups. Expression of the activation molecules HLA-DR, CD80, CD86, and PD-L1 in uninfected MDMs from the NO T2D and T2D groups. The solid line represents the negative control (without fluorescence mark) and the dotted line shows the study groups. To define the gate for MDM, we first established the gate for monocytes: CD14 cells were purified by negative selection of peripheral blood mononuclear cells (PBMCs), and cell dispersion was observed based on side and forward scatter parameters, following this CD14⁺/CD3⁻ cells were identified (using anti-CD3-PE and anti-CD14-FITC labelled antibodies) and back gated to the side and forward scatter plot. Based on the back gating parameters, a gate for monocytes was then established and later used to identify MDMs, as shown here.

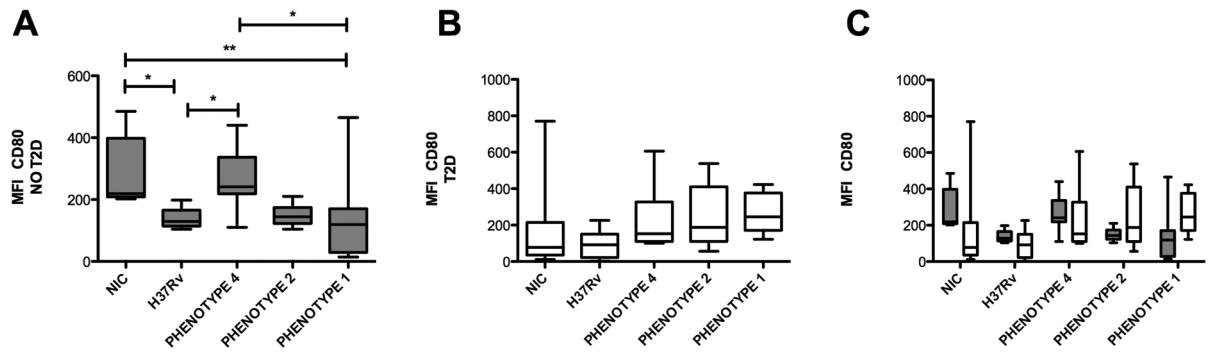


Fig. 2: expression of costimulatory cell-surface markers in monocyte-derived macrophages (MDM) following *Mycobacterium tuberculosis* (Mtb) infection in the context of type 2 diabetes (T2D). Plots showing the median and interquartile range of fluorescent intensity (MFI) for MDM expression of CD80, as measured by flow cytometry in basal cells (NIC = non infected control), or after Mtb infection with the indicated strains for 24 h at an multiplicity of infection (MOI) of 5 in cells derived from healthy subjects (NO T2D, grey bars) or patients with diabetes (T2D, white bars). Intragroup comparisons were performed with a Kruskal-Wallis test followed by Dunn's multiple comparison post-test. Panel A, show the MFI and interquartile range for the comparison in the healthy control group; panel B represent the intragroup comparison for cells derived from patients with diabetes. A two-way ANOVA analysis with Bonferroni's post-hoc test was used to compare patients with diabetes and healthy subjects subjected to different treatments, as shown in panel C. For each group n = 9. *p < 0.05; **p < 0.01; ***p < 0.001.

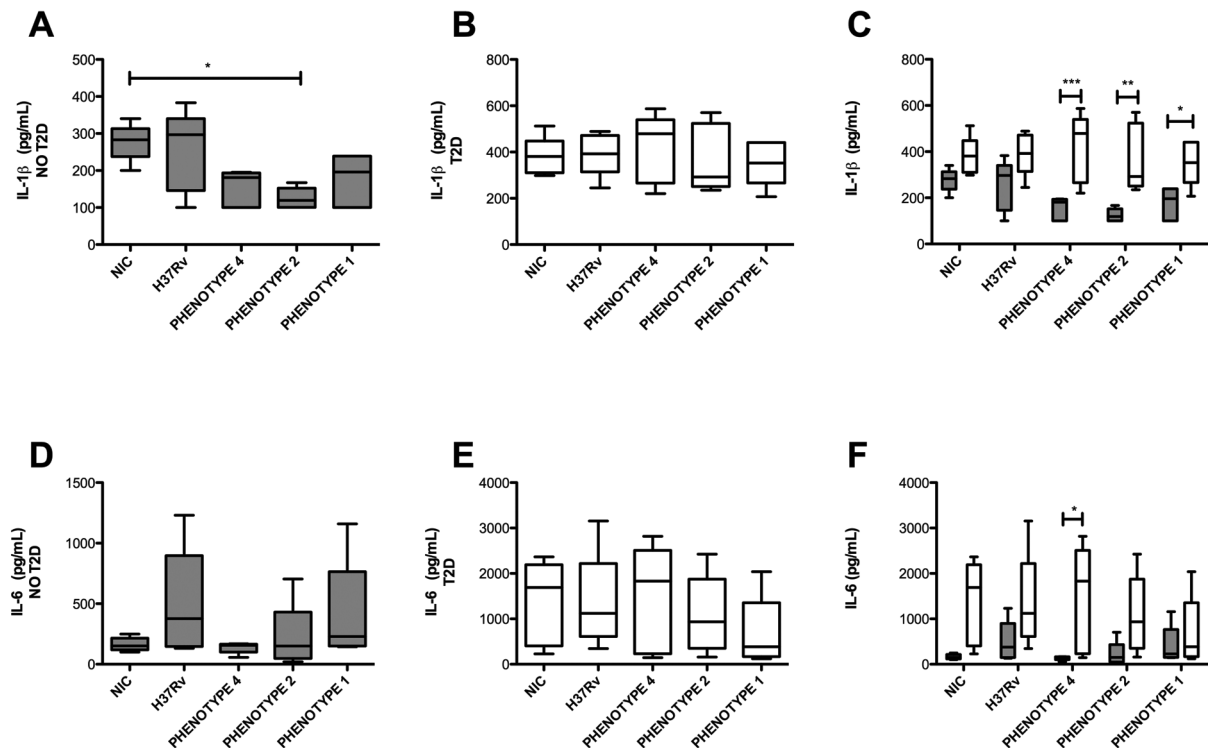


Fig. 3: secretion of IL-1 β and IL-6 by monocyte-derived macrophages (MDM) from patients with diabetes and healthy subjects upon *Mycobacterium tuberculosis* (Mtb) infection. MDMs were infected over a period of 24 h at an multiplicity of infection (MOI) of 5, and the cytokine levels in the culture supernatants were evaluated using a cytometric bead array (CBA) assay. Plots show the median and interquartile range values in basal cells (NIC = non infected control), or after Mtb infection with the indicated strains in cells derived from healthy subjects [NO type 2 diabetes (T2D), grey bars] or patients with diabetes (T2D, white bars). Intragroup comparisons were performed using a Kruskal-Wallis test and Dunn's multiple comparison post-test (panels A-B and D-E, respectively). A two-way ANOVA analysis with Bonferroni's post-hoc test was used to compare patients with diabetes and healthy subject groups subjected to different treatments, as shown in panels C and F. NO T2D group, n = 5; T2D group, n = 5; *p < 0.05; **p < 0.01; ***p < 0.001. For IL-1 β the two-way ANOVA interaction P value was 0.2941, the diabetes status p value was < 0.0001, and the infection status p value was 0.2498; for IL-6, the two-way ANOVA interaction p value was 0.5300, the diabetes status p value < 0.0001, and the infection status p value was 0.8092.

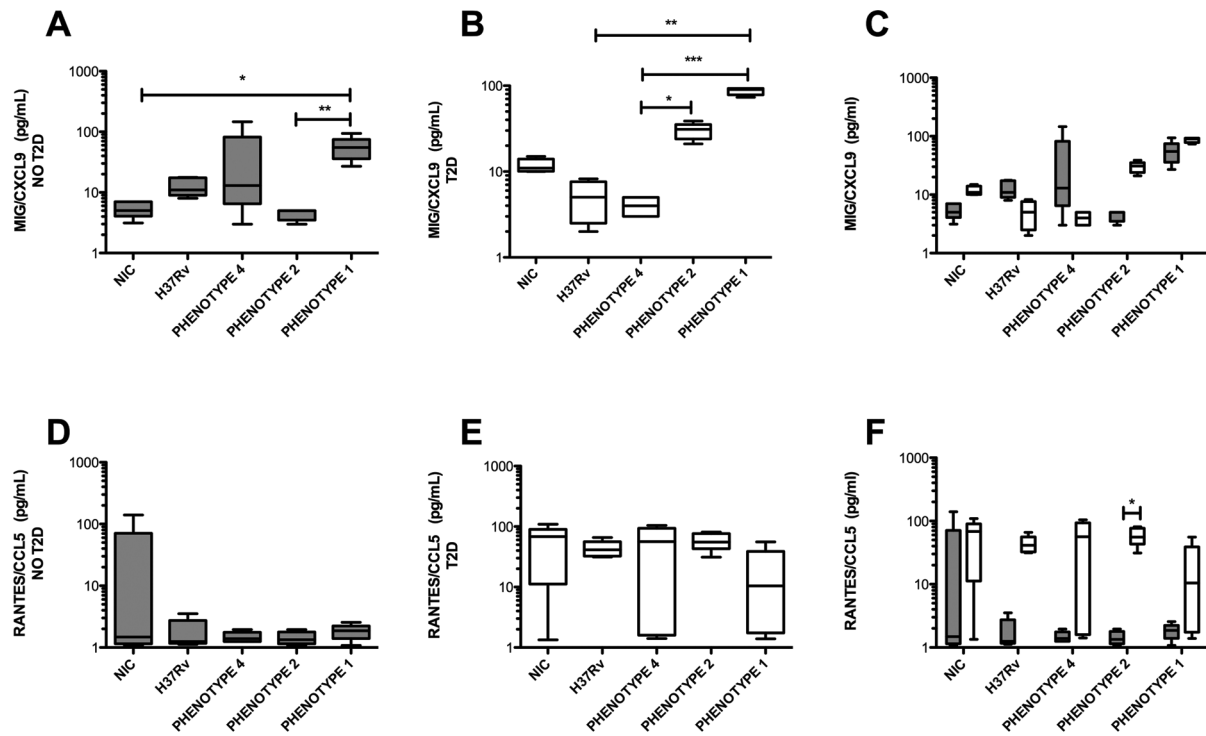


Fig. 4: secretion of MIG and RANTES by monocyte-derived macrophages (MDM) from patients with diabetes and healthy subjects following *Mycobacterium tuberculosis* (Mtb) infection. MDMs from healthy subjects [NO type 2 diabetes (T2D), grey bars] and patients with diabetes (T2D, white bars) were infected over a period of 24 h at an multiplicity of infection (MOI) of 5, culture supernatants were recovered and evaluated using a cytometric bead array (CBA) assay. Graphs show the median and interquartile range values in basal cells (NIC = non infected control), or after Mtb infection with the indicated strains. Intragroup comparisons were performed using a Kruskal-Wallis test and Dunn's multiple comparison post-test (panels A-B and D-E, respectively), while comparison between groups was performed by a two-way ANOVA analysis with Bonferroni's post-hoc test, as shown in panels C and F. In each study group n = 5. *p < 0.05; **p < 0.01; ***p < 0.001. For MIG, the two-way ANOVA interaction p value was 0089, the diabetes status p value was 0.4765, and the infection status p value was < 0.0001; for RANTES, the two-way ANOVA interaction p value was 0.5400, the diabetes status p value was < 0.0001, and the infection status p value was 0.2297.