

Hypermethylated				
Illumina ID	Position	Gene name	Function	Rho
cg24617445	chr8:131156242	ASAP1	The protein encoded by this gene is a GTPase-activating enzyme involved in regulation of membrane trafficking and cytoskeleton remodeling.	0.62
cg08163193	chr9:34692051	CCL19	The cytokine encoded by this gene may play a role in normal lymphocyte recirculation and homing. It also plays an important role in trafficking of T cells in thymus, and in T cell and B cell migration to secondary lymphoid organs.	0.56
cg14481832	chr16:57392534	CCL22	The cytokine encoded by this gene displays chemotactic activity for monocytes, dendritic cells, natural killer cells and for chronically activated T lymphocytes.	0.54
cg24310395	chr3:39309435	CX3CR1	Involved in the recruitment of CD16+ monocytes into synovial tissues in RA patients.	0.51
cg14789529	chr1:206941464	IL10	Cytokine produced primarily by monocytes and to a lesser extent by lymphocytes. This cytokine has pleiotropic effects in immunoregulation and inflammation. It down-regulates the expression of Th1 cytokines, MHC class II Ags, and costimulatory molecules on macrophages	0.57
cg08879111	chr2:102606829	IL1R2	Cytokine receptor that belongs to the interleukin 1 receptor family. This protein binds interleukin alpha (IL1A), interleukin beta (IL1B), and interleukin 1 receptor, type I(IL1R1/IL1RA), and acts as a decoy receptor that inhibits the activity of its ligands.	0.57
cg00294382	chr12:56732721	IL23A	Monocyte derived interleukin (IL)-23 promotes synovial IL-17A expression in RA.	0.56
cg01126481	chr6:45508422	RUNX2	Transcription factor that is essential for osteoblastic differentiation and skeletal morphogenesis.	0.68
cg24312520	chr17:40489785	STAT3	Transcription factor activated in response to various cytokines and growth factors (e.g. IFNs, IL10, IL6), and plays a key role in many cellular processes such as cell growth and apoptosis.	0.57
cg21926290	chr5:118725443	TNFAIP8	TNF-alpha induced Protein 8 is a protein that suppresses the TNF-mediated apoptosis by inhibiting caspase-8 activity.	0.67

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cg08356841	chr1:150793838	ARNT	This gene encodes a protein containing a basic helix-loop-helix domain. The protein is involved in xenobiotic metabolism as well in cellular adaptation to hypoxia.	-0.45
cg26478409	chr15:73994777	CD276	The protein encoded by this gene belongs to the immunoglobulin superfamily, and thought to participate in the regulation of T-cell-mediated immune response.	-0.55
cg10507445	chr19:52264303	FPR2	This gene encodes for a neutrophil chemotactic factor. Its activation could also result in anti-inflammatory outcomes counteracting the actions of proinflammatory signals such as LTB4	-0.52
cg18388786	chr10:134924050	GPR123	It belongs to the adhesion family of G-protein-coupled receptors. Members of this family regulate blood pressure, immune responses, food intake and development.	-0.52
cg21027759	chr1:206970717	IL19	Cytokine that belongs to the IL10 cytokine subfamily. It is preferentially expressed in monocytes. It can bind the IL20 receptor complex and lead to the activation of STAT3. A similar cytokine in mouse is reported to up-regulate the expression of IL6 and TNF α and induce apoptosis, which suggests a role of this cytokine in inflammatory responses.	-0.51
cg06383401	chr2:113825234	IL1F10	Member of the interleukin 1 cytokine family. This cytokine is thought to participate in a network of interleukin 1 family members to regulate adapted and innate immune responses.	-0.52
cg27656400	chr16:3114056	IL32	It induces TNF α , IL1 β , IL6 and chemokines, being a pivotal proinflammatory mediator in RA.	-0.53
cg08090769	chr12:66582568	IRAK3	This gene encodes a member of the interleukin-1 receptor-associated kinase protein family. Members of this family are essential components of the Toll/IL-R immune signal transduction pathways. This protein is primarily expressed in monocytes and macrophages and functions as a negative regulator of Toll-like receptor signaling.	-0.59
cg04988978	chr17:56359578	MPO	Myeloperoxidase is a heme protein synthesized during myeloid differentiation. The MPO serum concentration increase in RA patients with chronic inflammation.	-0.53
cg01680062	chr21:36185960	RUNX1	RUNX1 is a transcription factor that forms a complex with the cofactor CBF β . This complex provides stability to the RUNX1 protein which is involved in the generation of hematopoietic stem cells and for their differentiation into myeloid and lymphoid lines.	-0.51

Supplementary Table 6. Selected CpG sites which DNA methylation displays an absolute Spearman coefficient correlation > 0.45.