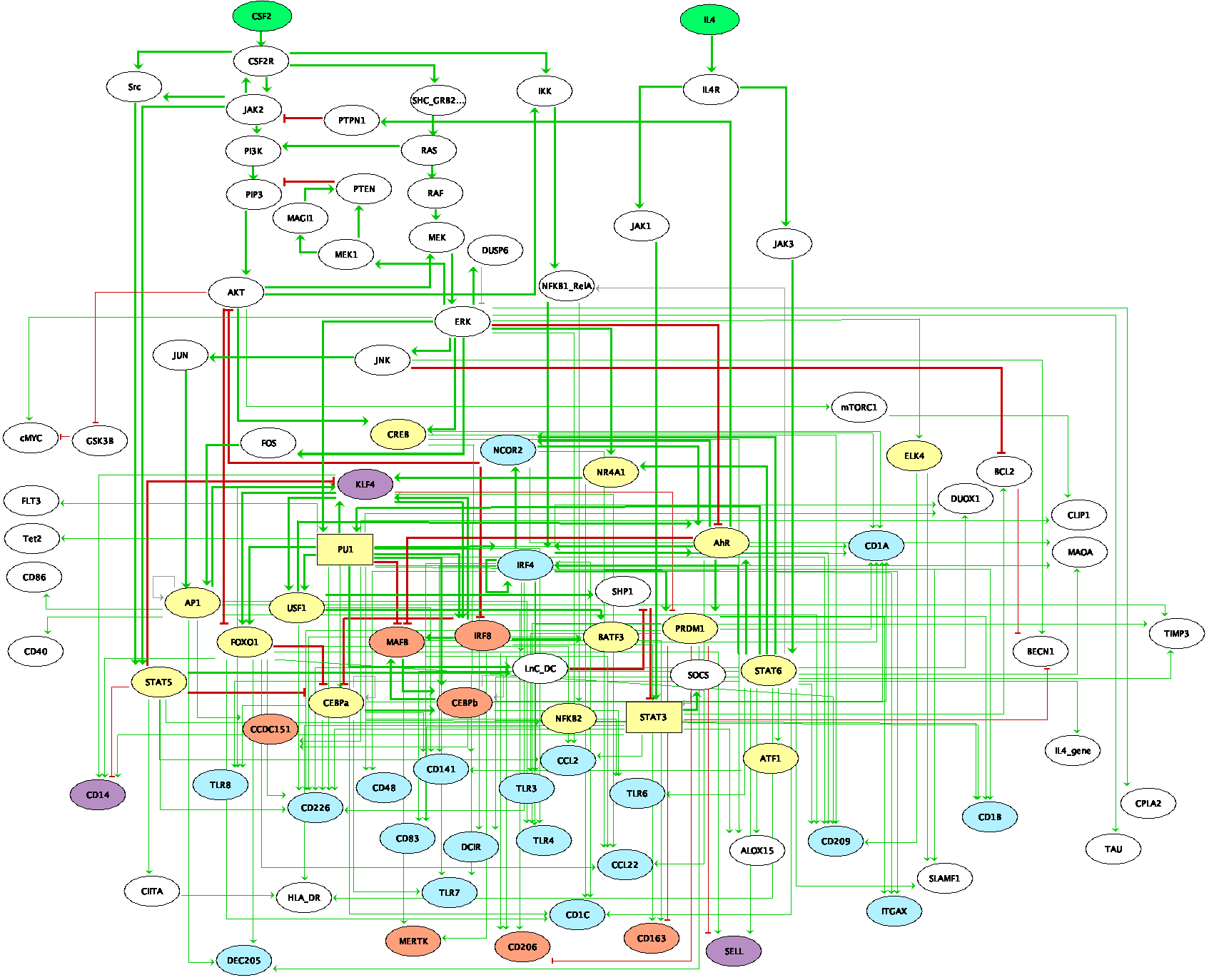
Description of the model "Karen\_MoDC\_16april2020"

Annotation

Sallusto and Lazavecchia in 1994 describe for the first time the in vitro protocol for human monocyte to dendritic cell (moDC) differentiation using granulocyte macrophage colony stimulating factor (CSF2) and interleukin 4 (IL4).  
  
In this work we integrated scientific report knowledge of the signaling cascades that initiated the differentiation process, we also integrated new possible transcriptional regulation result from the analysis of regulatory regions from monocyte, dendritic cells and macrophages as negative control of monocyte to moDC, macrophages results after the stimulation of monocytes with CSF2.

<https://www.ncbi.nlm.nih.gov/pubmed/8145033>

Nodes

|  |  |  |  |
| --- | --- | --- | --- |
| ID | Val | Logical function | |
| CSF2 | Input node | |
| Sallusto and Lazavecchia in 1994 describe for the first time the in vitro protocol for human monocyte to dendritic cell (moDC) differentiation using granulocyte macrophage colony stimulating factor (CSF2) and interleukin 4 (IL4).   1. <https://www.ncbi.nlm.nih.gov/pubmed/8145033> |
| IL4 | Input node | |
| Sallusto and Lazavecchia in 1994 describe for the first time the in vitro protocol for human monocyte to dendritic cell (moDC) differentiation using granulocyte macrophage colony stimulating factor (CSF2) and interleukin 4 (IL4).   1. <https://www.ncbi.nlm.nih.gov/pubmed/8145033> |
| CSF2R | 1 | * CSF2 | |
| PMID:22323450. The GM-CSFR contains 2 distinct subunits, the GM CSF specific-chain (GM CSFR; CD116) and the common receptor, which is shared between the GM CSFR, the IL3 receptor,and the IL5 receptor. Downstream signaling cascades areprimarily induced through interaction of effector proteins with the BetaC subunit. Signaling is initiated by the cytoplasmic tyrosine kinasejanus kinase 2 (JAK2), which then acts on various downstreamproteins.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| IL4R | 1 | * IL4 | |
| PMID: 25159217. The IL4 receptor (IL4R) signals the activation of the Janus kinase 3 (JAK3) STAT6 pathway through its common gamma chain, which leads to the development of immature DCs.   1. <https://www.ncbi.nlm.nih.gov/pubmed/25159217> |
| AhR | 1 | * (NCOR2 & USF1 & STAT6) | (IRF4 & STAT6 & !ERK) | |
| PMID: 23430108. Whereas ERK inhibition upregulated AhR dependent transcriptionin in vitro generated monocyte derived cells (moDCs and Macrophages).  FOXO and AhR autoregulation came from putative TFBS perform with matrix-scan with all the matrixes of every TF in the model.   1. <https://www.ncbi.nlm.nih.gov/pubmed/23430108> |
| AP1 | 1 | * JUN & FOS | |
| Macrophage specific H3K4me1 regions were characterized by a distinct motif composition, including GT box, an AP1 like motif, an E box element, the consensus PU.1 motif, a composite CEBP\_bZIP element, and a NFKB motif.   1. <https://pubmed.ncbi.nlm.nih.gov/22550342> |
| ATF1 | 1 | * STAT6 | |
| STAT6  is a putative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study. |
| BATF3 | 1 | * USF1 | IRF8 | |
| PMID: 28781277. KLF4 and BATF3 serve as critical transcription factors downstream of IRF8 to induce the differentiation of monocytes and DCs, respectively.  USF1 is a putative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.   1. <https://www.ncbi.nlm.nih.gov/pubmed/28781277> |
| CEBPa | 1 | * PU1 & !FOXO1 & !IRF8 & !STAT5 | |
| PMID: 28781277. Conversely, IRF8 blocks the activity of the transcription factor CEBPalfa to suppress the neutrophil differentiation program.   CEBP transcription factors, and CEBPb in particular, have long been implicated in the regulation of monocyte macrophage differentiation, whereas CEBPa appears to be more important for the maturation of granulocytes   1. <https://www.ncbi.nlm.nih.gov/pubmed/28781277>   <https://pubmed.ncbi.nlm.nih.gov/21558273/> |
| CEBPb | 1 | * PU1 & (CEBPa | MAFB) | |
| Macrophage specific H3K4me1 regions were characterized by a distinct motif composition, including GT box, an AP1 like motif, an E box element, the consensus PU.1 motif, a composite CEBP\_bZIP element, and a NFKB motif.  CEBP transcription factors, and CEBPb in particular, have long been implicated in the regulation of monocyte macrophage differentiation, whereas CEBPa appears to be more important for the maturation of granulocytes   1. <https://pubmed.ncbi.nlm.nih.gov/22550342>   <https://pubmed.ncbi.nlm.nih.gov/21558273/> |
| FOS | 1 | * ERK | |
| PMID: 23430108. U0126 treatment significantly reduced the expression of wellknown targets of ERK (FOS, MYC, DUSP6).   1. <https://www.ncbi.nlm.nih.gov/pubmed/23430108> |
| cMYC | 1 | * ERK & !GSK3B | |
| PMID:22323450. PMID: 23430108. U0126 treatment significantly reduced the expression of wellknown targets of ERK (FOS, MYC, DUSP6).   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450>   <https://www.ncbi.nlm.nih.gov/pubmed/23430108> |
| CREB | 1 | * AKT | ERK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| ELK4 | 1 | * ERK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| FOXO1 | 1 | * (PU1 | KLF4) & !AKT | |
| PMID:22323450. Activated PKB regulates many targets, including the FOXO transcription factors, the TSC1 TSC2 complex, and the mTOR complex 1 (mTORC1).  KLF4 is a putative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| IRF4 | 1 | * AhR | (PU1 & STAT6 & NFKB1\_RelA & IRF4) | |
| DCs were found to express IRF4 mRNA and protein constitutively, and STAT and NFkB transcription factors play an important role inregulating IRF4 expression in DCs. IRF4 protein bound to a regulatory element in its own promoter, suggesting an autoregulatory loop controlling IRF4 mRNA expression in DCs.  AhR is a putative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.  Monocytes stimulated with IL4 activates IRF4.   1. <https://pubmed.ncbi.nlm.nih.gov/10453013>   <https://pubmed.ncbi.nlm.nih.gov/29871928/> |
| IRF8 | 1 | * (PU1 | KLF4) & !NCOR2 | |
| PMID: 29262348. We found a statistically significant enrichment of genes upregulated in the IL4 signature in MOs GMCSF IL4(0-72h) treated with scrambled siRNAs (Figure6I) whereas genes downregulated in the IL4 signature were enriched in MOs GMCSF IL4(0-72h) treated with antiNCOR2 siRNAs (Figure 6J), establishing NCOR2 as a key regulator for IL4 induced MO differentiation.  NCOR2 is a putative negative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| KLF4 | 1 | * (NR4A1 & IRF8 & AP1) | (PU1:1 & !STAT5) | |
| PMID: 17762869. PU.1 induced the KLF4 promoter 15 fold.   1. <https://www.ncbi.nlm.nih.gov/pubmed/17762869> |
| MAFB | 1 | * (CEBPb | IRF8) & !AhR & !PU1:2 | |
| PMID: 24070385. Pu.1 in monocytes favors DC development at the expense of a macrophage fate by directly inhibiting expression of the macrophage factor, MafB, suggesting that Pu.1 could be an important decision factor between DC and macrophage commitment.  PMID: 22868453. MafB gene silencing improved the differentiation potential of CD14+ cells into mDCs, increasing the percentage of mDCs by >75%. Furthermore, GATA-1+ and HLA-DR+ mDCs were increased following MafB silencing.   We have shown that the transcription factors MafB and PU.1 induce alternative macrophage or DC fates respectively in myeloblasts.   1. <https://www.ncbi.nlm.nih.gov/pubmed/24070385>   <https://www.ncbi.nlm.nih.gov/pubmed/22868453>  <https://pubmed.ncbi.nlm.nih.gov/28338898/> |
| NFKB1\_RelA | 1 | * IKK | |
| PMID:22323450. Activation is achieved through the IKK complex, which phosphorylates IkB proteins. These are subsequently ubiquitinated and finally degraded, enablingnuclear translocation of canonical NFkB dimers.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| NFKB2 | 1 | * NFKB1\_RelA | STAT5 | |
| PMID:22323450. In the previous section, GM CSF induced activation of STAT5 and canonical NFkB transcription factors increases the intrinsic immunogenicity of the DCs generated   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| NR4A1 | 1 | * ERK & STAT6 | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| PRDM1 | 1 | * IRF4 & AhR & !KLF4 | |
| PMID: 28930664. PRDM1 silencingsignificantly decreased moDC differentiation, while increasingthe proportion of moMacs (Figure 5D).  IRF4 & KLF4 regulation is due a putative TFBS found with matrix-scan   1. <https://www.ncbi.nlm.nih.gov/pubmed/28930664> |
| PU1 | 1 | * (ERK | STAT6) & !(ERK & STAT6) | |
| 2 | * ERK & STAT6 |
| PMID: 20510871. One study concluded that PU.1 is necessary for all DC development because Sfpi1 homozygotic mutant neonates lacked thymic DCs and were unable to generate DCs in vitro in response to GMCSF.  We have shown that the transcription factors MafB and PU.1 induce alternative macrophage or DC fates respectively in myeloblasts.  IL4 induced threonine phosphorylation of PU.1, which was susceptible to these inhibitors. Because it is known that phosphorylation of PU.1 at serine 148, located within a casein kinase II consensus motif.   1. <https://www.ncbi.nlm.nih.gov/pubmed/20510871>   <https://pubmed.ncbi.nlm.nih.gov/28338898/>  <https://pubmed.ncbi.nlm.nih.gov/11594748/> |
| STAT3 | 1 | * JAK1 & SHP1 | |
| 2 | * JAK1 & !SHP1 |
| However, by far the most important negative regulation occurs at the level of receptor mediated STAT3 activation and is conferred by suppressor of cytokine signalling (SOCS) E3 ubiquitin ligases that enable the degradation of cytokine receptor complexes. SOCS proteins are themselves encoded by STAT target genes and thus provide a transcription dependent negative feedback mechanism.  lncDC bound directly to STAT3 in the cytoplasm, which promoted STAT3 phosphorylation on tyrosine705 by preventing STAT3 binding to and dephosphorylation by SHP1.   1. <https://www.ncbi.nlm.nih.gov/pubmed/30578415>   <https://www.ncbi.nlm.nih.gov/pubmed/27165851>  <https://www.ncbi.nlm.nih.gov/pubmed/28465674>  <https://www.ncbi.nlm.nih.gov/pubmed/24744378> |
| STAT5 | 1 | * Src | JAK2 | |
| PMID:22323450. Of the signaling proteins contributing to GM CSF driven DC development, JAK2 activated STAT5 is the clearest regulator of differentiation.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| STAT6 | 1 | * JAK3 | |
| The IL4 receptor (IL4R) signals the activation of the Janus kinase 3 (JAK3) STAT6 pathway through its common gamma chain, which leads to the development of immature DCs.   1. <https://www.ncbi.nlm.nih.gov/pubmed/25159217>   <https://www.ncbi.nlm.nih.gov/pubmed/10485906>  <https://www.ncbi.nlm.nih.gov/pubmed/16540365> |
| USF1 | 1 | * PU1 | KLF4 | |
| Involvement of USF in myeloid cell differentiation was suggested by Kreider et al  KLF4 is a putative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.   1. <https://pubmed.ncbi.nlm.nih.gov/10085160> |
| NCOR2 | 1 | * IRF4 | AhR | STAT6 | |
| AhR and IRF4 regulation is result from the matrix-scan analysis  We identified NCOR2 as a key transcriptional hub linked to IL4 dependent differentiation of MOs.   1. <https://pubmed.ncbi.nlm.nih.gov/29262348> |
| JAK2 | 1 | * CSF2R & !PTPN1 | |
| PMID:22323450. Src kinases are recruited to BetaC by their SH2 domains that interact with phosphorylated Y612, Y695, and Y750. The STATs are primarily phosphorylated by JAK2, but kinase activity of the Src kinases has also been reported.  PMID: 11694501. In this study, we have shown that PTP1B recognizes TYK2 and JAK2, but not JAK1, and can modulate signaling responses to IFNgamma and IFNalfa   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| Src | 1 | * CSF2R:1 | JAK2 | |
| PMID:22323450. Src kinases are recruited to BetaC by their SH2 domains that interact with phosphorylated Y612, Y695, and Y750. The STATs are primarily phosphorylated by JAK2, but kinase activity of the Src kinases has also been reported.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| PI3K | 1 | * RAS | JAK2 | |
| PMID:22323450. Activity of PI3K is promoted by JAK2 mediated phosphorylation of p85   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| PIP3 | 1 | * PI3K & !PTEN | |
| PI3K functions mainly through the generation of PIP3, an activity counteracted by phosphatases PTEN and SHIP.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| AKT | 1 | * PIP3 & !NCOR2 | |
| PMID:22323450. PIP3 acts as a second messenger, regulating a large variety of downstream targets, including protein kinase B (PKB; also called AKT).  Promotes activation of phosphatidylinositol 3 kinase and of the AKT1 signaling cascade   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450>   <https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTK2B&keywords=PTK2B> |
| PTEN | 1 | * MAGI1 & MEK1 | |
| MAGI1 contains six PDZ domains, a guanylate kinase, GUK, domain, and two WW domains flanked by two PDZ domains. PTEN binds selectively to the second PDZ domain of MAGI1. PTEN interacted indirectly with beta\_catenin by binding the scaffolding protein MAGI1b. scaffolding molecules such as MAGI1b, which was reported to interact with beta catenin  We report the existence of a ternary complex between MEK1, MAGI1, and PTEN, mediating the translocation of PTEN to the membrane and therefore regulating the concentration of PIP3 and AKT activation. Both MEK1 and MAGI1 are necessary for complex formation, and PTEN will not bind to one component if the other is missing.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450>   <https://www.ncbi.nlm.nih.gov/pubmed/23453810> |
| MEK1 | 1 | * ERK | |
| PMID: 23453810. Thus, phosphorylation of MEK1 T292 relays a negative feedback within the ERK pathwayand initiates the deactivation of the PIP3 AKT pathway through the membrane localization of MAGI PTEN, acting as a temporal switch for both cascades. Thus, ERK differentially regulates binding of MEK1 to WW domain containing proteins and may negatively affect survival by promoting the translocation of WOX1 to the mitochondria (Lin et al., 2011) and the membrane recruitment of PTEN in the context of the MEK1/ MAGI1/PTEN complex.   1. <https://www.ncbi.nlm.nih.gov/pubmed/23453810> |
| MAGI1 | 1 | * MEK1 | |
| PMID: 23453810. Thus, MEK1 is essential for the formation of a complex containing MAGI1 and PTEN and for their membrane translocation upon growth factor stimulation. Mutation of the WW domains of MAGI1, in particular of WW2, strongly reduced MEK1 binding by a WW MAGI1 fragment or by full length MAGI1. We report the existence of a ternary complex between MEK1, MAGI1, and PTEN, mediating the translocation of PTEN to the membrane and therefore regulating the concentration of PIP3 and AKT activation. Both MEK1 and MAGI1 are necessary for complex formation, and PTEN will not bind to one component if the other is missing. MEK1 ablation prevented MAGI1 membrane translocation   1. <https://www.ncbi.nlm.nih.gov/pubmed/23453810> |
| CLIP1 | 1 | * mTORC1 | PU1 | |
| mTOR signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04150> |
| mTORC1 | 1 | * AKT | |
| PMID: 22323450. Activated PKB regulates many targets, including the FOXO transcription factors, the TSC1 TSC2 complex, and the mTOR complex 1 (mTORC1). PMID: 27614799   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| SHC\_GRB2\_mSOS | 1 | * CSF2R | |
| PMID:22323450. The principle MAPK pathway activated by the GM CSF receptor is the MEK ERK pathway. Recruitment of mSOS to the SHC GRB2 complex enables mSOS to catalyze RAS activation.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| RAS | 1 | * SHC\_GRB2\_mSOS | |
| PMID:22323450. The principle MAPK pathway activated by the GM CSF receptor is the MEK ERK pathway. Recruitment of mSOS to the SHC GRB2 complex enables mSOS to catalyze RAS activation. Formation of active GTP bound RAS from inactive GDP bound RAS leads to the successive activation of RAF, MEK, and ERK.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| RAF | 1 | * RAS | |
| PMID:22323450. The principle MAPK pathway activated by the GM CSF receptor is the MEK ERK pathway. Recruitment of mSOS to the SHC GRB2 complex enables mSOS to catalyze RAS activation. Formation of active GTP bound RAS from inactive GDP bound RAS leads to the successive activation of RAF, MEK, and ERK.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| MEK | 1 | * RAF | AKT | |
| PMID:22323450. The principle MAPK pathway activated by the GM CSF receptor is the MEK ERK pathway. Recruitment of mSOS to the SHC GRB2 complex enables mSOS to catalyze RAS activation. Formation of active GTP bound RAS from inactive GDP bound RAS leads to the successive activation of RAF, MEK, and ERK.  PKB (AKT) promotes activation of the MAP kinase signaling cascade, including activation of MAPK1/ERK2, MAPK3/ERK1 and MAPK8/JNK1   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| ERK | 1 | * MEK | |
| DUSPG Inactivates MAP kinases. Has a specificity for the ERK family.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450>   <https://www.ncbi.nlm.nih.gov/pubmed/9858808> |
| JUN | 1 | * JNK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| JNK | 1 | * ERK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| TAU | 1 | * ERK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| CPLA2 | 1 | * ERK | |
| MAPK signaling pathway Homo sapiens   1. <https://www.genome.jp/dbget-bin/www_bget?hsa04010> |
| FLT3 | 1 | * PU1 | |
| PMID: 24070385. Indeed, Pu.1 directly regulated Flt3 expression on DCs and their precursors in a dose-dependent manner.   1. <https://www.ncbi.nlm.nih.gov/pubmed/24070385> |
| GSK3B | 1 | * !AKT | |
| PMID:22323450. Activity of glycogen synthase kinase 3 (GSK3B), which is negatively regulated by AKT dependent phosphorylation,appears required to avoid human monocyte to macrophage differentiationin monocyte derived DC differentiation cultures.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| IKK | 1 | * CSF2R | AKT | |
| PMID:22323450. GM CSF induced canonical NFkB activation thus appearscrucial to ensure differentiation and survival of DC precursors.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| JAK3 | 1 | * IL4R | |
| PMID: 23124025 PMID: 25159217. The IL4 receptor (IL4R) signals the activation of the Janus kinase 3 (JAK3) STAT6 pathway through its common gamma chain, which leads to the development of immature DCs.   1. <https://www.ncbi.nlm.nih.gov/pubmed/25159217>   <https://www.ncbi.nlm.nih.gov/pubmed/23124025> |
| JAK1 | 1 | * IL4R | |
| PMID: 27165851. IL4 receptor complexes are deficient of intrinsic kinase activity. Rather, signal transduction is initiated by receptor-associated kinases i.e. a member of JAK family (JAK1, JAK2, JAK3 and TyK2).   1. <https://www.ncbi.nlm.nih.gov/pubmed/27165851> |
| SHP1 | 1 | * USF1:1 & !LnC\_DC | |
| PMID: 28465674. LncDC expression is essential for differentiation of human monocytes into dendritic cells. LncDC promotes STAT3 phosphorylation via inhibiting the action of Src homology region 2 domain containing phosphatase 1 (SHP1)   1. <https://www.ncbi.nlm.nih.gov/pubmed/28465674> |
| CIITA | 1 | * STAT5 | |
| PMID:22323450. STAT5 promotes expression of MHC class II transactivatorprotein (CIITA), which is essential for transcriptionalactivity of the MHC class II promoter.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| ITGAX | 1 | * IRF4 & PU1 & PRDM1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  PMID: 28338898. PU.1 transactivates the Itgax promoter via direct binding to the cis element on the gene in DCs and through gene regulation of a partner molecule, IRF4, which transactivates the Itgax gene in a synergistic manner with PU.1.  All 11 subpopulations expressed the moDC markers CD1c, CD226, CD48, and CD11c.  moDC marker accoding with Radford et al 2014   1. <https://www.ncbi.nlm.nih.gov/pubmed/28338898>   <https://www.ncbi.nlm.nih.gov/pubmed/29262348>  <https://pubmed.ncbi.nlm.nih.gov/24513968>  <https://pubmed.ncbi.nlm.nih.gov/27401672>  <https://pubmed.ncbi.nlm.nih.gov/29448070> |
| LnC\_DC | 1 | * PU1 & IRF4 & STAT5 | |
| PMID: 28465674 PMID: 24744378 lncDC bound directly to STAT3 in the cytoplasm, which promoted STAT3 phosphorylation on tyrosine705 by preventing STAT3 binding to and dephosphorylation by SHP1. PU.1 directs lncDC expression in human cDCs   1. <https://www.ncbi.nlm.nih.gov/pubmed/28465674>   <https://www.ncbi.nlm.nih.gov/pubmed/24744378> |
| IL4\_gene | 1 | * STAT6 | |
|  |
| DUOX1 | 1 | * STAT6 & IRF4 & PU1 | |
| We observed very specific demethylationin DC differentiation at a CpG site in thegene bodies of DUOX1, an oxidase involved in the antimicrobial mediated response, and the signallingreceptor SLAMF1   1. <https://www.ncbi.nlm.nih.gov/pubmed/23124025>   <https://pubmed.ncbi.nlm.nih.gov/26758199> |
| SLAMF1 | 1 | * STAT6 & IRF4 & ELK4 | |
| We observed very specific demethylationin DC differentiation at a CpG site in thegene bodies of DUOX1, an oxidase involved in the antimicrobial mediated response, and the signallingreceptor SLAMF1   1. <https://www.ncbi.nlm.nih.gov/pubmed/23124025>   <https://pubmed.ncbi.nlm.nih.gov/26758199> |
| MAOA | 1 | * STAT6 & NCOR2 & PU1 | |
| PMID: 23124025. IL4 can use only the IL4Ralpha,Jak1,Stat3,Stat6 cascade to regulate the expression of some critical inflammatory genes, including ALOX15, monoamine oxidase A (MAOA), and the scavenger receptor CD36.  PMID: 29262348. We found a statistically significant enrichment of genes upregulated in the IL4 signature in MOs GMCSF IL4(0-72h) treated with scrambled siRNAs (Figure6I) whereas genes downregulated in the IL4 signature were enriched in MOs GMCSF IL4(0-72h) treated with antiNCOR2 siRNAs (Figure 6J), establishing NCOR2 as a key regulator for IL4 induced MO differentiation.   1. <https://www.ncbi.nlm.nih.gov/pubmed/23124025>   <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| HLA\_DR | 1 | * STAT3 | (STAT6 & CIITA) | |
| PMID: 22323450. STAT5 promotes expression of MHC class II transactivatorprotein (CIITA), which is essential for transcriptionalactivity of the MHC class II promoter. PMID: 28465674   1. <https://www.ncbi.nlm.nih.gov/pubmed/22323450>   <https://www.ncbi.nlm.nih.gov/pubmed/28465674>  <https://pubmed.ncbi.nlm.nih.gov/29262348>  <https://pubmed.ncbi.nlm.nih.gov/29448070> |
| ALOX15 | 1 | * CREB & STAT6 & STAT3 | |
| PMID: 16540365. IL4 can use only the IL4Ralpha,Jak1,Stat3,Stat6 cascade to regulate the expression of some critical inflammatory genes, including ALOX15, monoamine oxidase A (MAOA), and the scavenger receptor CD36.   1. pubmed.ncbi.nlm.nih.gov/16540365 |
| TIMP3 | 1 | * STAT6 & AP1 & IRF4 | |
| TIMP3 are used to demonstrate the unique regulation of these gene by IL4   1. <https://pubmed.ncbi.nlm.nih.gov/23124025> |
| DUSP6 | 1 | * ERK | |
| PMID: 23430108. U0126 treatment significantly reduced the expression of wellknown targets of ERK (FOS, MYC, DUSP6).   1. <https://www.ncbi.nlm.nih.gov/pubmed/23430108> |
| CCL2 | 1 | * ERK & STAT5 & STAT3 & FOXO1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  PMID: 22328945. ERK upregulated CCL2 expression while impairing the expression of DC maturation markers (RUNX3, ITGB7, IDO1). CCL2, a chemokine constitutively produced by immature MDDCs.  monocyte chemoattractant protein 1 (CCL2) have been identified as chemokines/receptors that have an important role in the migration and recruitment of monocytes during the pathogenesis of several inflammatory diseases.  PMID: 23430108. The CCL2 chemokine directs monocyte/macrophage recruitmentinto tissues under resting and inflamed conditions.   1. <https://www.ncbi.nlm.nih.gov/pubmed/22328945>   <https://www.ncbi.nlm.nih.gov/pubmed/23430108> |
| CCL22 | 1 | * (AhR & NCOR2 & FOXO1) | (KLF4 & MAFB) | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  PMID: 29262348. We found a statistically significant enrichment of genes upregulated in the IL4 signature in MOs GMCSF IL4(0-72h) treated with scrambled siRNAs (Figure6I) whereas genes downregulated in the IL4 signature were enriched in MOs GMCSF IL4(0-72h) treated with antiNCOR2 siRNAs (Figure 6J), establishing NCOR2 as a key regulator for IL4 induced MO differentiation.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| TLR3 | 1 | * IRF4 | PRDM1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| TLR4 | 1 | * AP1 | IRF4 | PRDM1 | PU1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| TLR6 | 1 | * CEBPa | CEBPb | STAT6 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| TLR7 | 1 | * CEBPa | CEBPb | IRF4 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| TLR8 | 1 | * KLF4 | CEBPa | STAT6 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| CD48 | 1 | * PU1 & IRF4 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  All 11 subpopulations expressed the moDC markers CD1c, CD226, CD48, and CD11c.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| CD1A | 1 | * (BATF3 | CEBPa | CEBPb | CREB) & IRF4 & PU1 & PRDM1 & NCOR2 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  PMID:11306493 IL4 signaling upregulates CD1a on cell surface of DC cells.  PMID: 29262348. We found a statistically significant enrichment of genes upregulated in the IL4 signature in MOs GMCSF IL4(0-72h) treated with scrambled siRNAs (Figure6I) whereas genes downregulated in the IL4 signature were enriched in MOs GMCSF IL4(0-72h) treated with antiNCOR2 siRNAs (Figure 6J), establishing NCOR2 as a key regulator for IL4 induced MO differentiation.   1. <https://www.ncbi.nlm.nih.gov/pubmed/11306493>   <https://www.ncbi.nlm.nih.gov/pubmed/29262348>  <https://pubmed.ncbi.nlm.nih.gov/27401672>  <https://pubmed.ncbi.nlm.nih.gov/29448070>  <https://pubmed.ncbi.nlm.nih.gov/17595377> |
| CD1B | 1 | * (CEBPa | CEBPb | IRF4) & PRDM1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  Human inflammatory moDC are HLADR CD11c cells that express markers found on classical DC such as CD1c, CD1a, CD1b   1. <https://pubmed.ncbi.nlm.nih.gov/29448070> |
| CD1C | 1 | * FOXO1 & IRF4 & NR4A1 & PU1 & STAT6 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  DC associated (CD1C, ZBTB46) genes.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348>   <https://pubmed.ncbi.nlm.nih.gov/29448070> |
| CD40 | 1 | * AP1 | |
| moDC marker accoding with Radford et al 2014   1. <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| CD86 | 1 | * AP1 | |
| MOs (GM CSF IL4 ) we identified subsets that either expressed HLA-DR and CD86 or CD1a and FceR1, the former representing a subpopulationwith elevated antigen presenting capacity.   1. <https://pubmed.ncbi.nlm.nih.gov/29262348>   <https://pubmed.ncbi.nlm.nih.gov/27401672> |
| CD83 | 1 | * STAT6 & NFKB2 & IRF4 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDCs have been reported to express cel lsurface markers CD80, CD83, CD86,and CD1a in vitro   1. <https://pubmed.ncbi.nlm.nih.gov/27401672> |
| CD209 | 1 | * AP1 & CREB & ELK4 & IRF4 & PU1 & STAT6 & FOXO1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  PMID: 29262348. CD209 was exclusively expressed by MOs GMCS IL4 (0 tp 72h). CD11b didnot discriminate between the cell populations.   moDC marker accoding with Radford et al 2014   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348>   <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| CD141 | 1 | * (CEBPa | CREB) & USF1 & ATF1 & IRF4 | |
| Gene THBD.  Sites found using matrix-scan with the regulatory regions of moDC in this study.  CD141 phenotypic markers for moDC   1. <https://www.genecards.org/cgi-bin/carddisp.pl?gene=THBD&keywords=CD141>   <https://pubmed.ncbi.nlm.nih.gov/29448070> |
| CD226 | 1 | * (BATF3 | CEBPa) & FOXO1 & IRF4 & PRDM1 & PU1 & STAT3 & STAT5 & STAT6 & USF1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  All 11 subpopulations expressed the moDC markers CD1c, CD226, CD48, and CD11c.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| DEC205 | 1 | * FOXO1 & AP1 & PRDM1 | |
| Sites found using matrix-scan with the regulatory regions of moDC in this study.  Gene LY75  moDC marker accoding with Radford et al 2014   1. <https://www.genecards.org/cgi-bin/carddisp.pl?gene=LY75&keywords=ly75>   <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| DCIR | 1 | * STAT6 & PU1 | |
| CLEC4A Gene  Sites found using matrix-scan with the regulatory regions of moDC in this study.  moDC marker accoding with Radford et al 2014   1. <https://www.genecards.org/cgi-bin/carddisp.pl?gene=CLEC4A&keywords=DCIR>   <https://pubmed.ncbi.nlm.nih.gov/24513968> |
| Tet2 | 1 | * PU1 | |
| Demethylation is TET2 dependent and is essential for acquiring proper dendritic cell and macrophage identity.   1. <https://pubmed.ncbi.nlm.nih.gov/26758199> |
| PTPN1 | 1 | * AhR | |
| PMID: 11694501. The presence of a second aryl phosphate binding site in PTP1B has also been reported by others.   1. <https://www.ncbi.nlm.nih.gov/pubmed/11694501> |
| SOCS | 1 | * STAT3 | |
| PMID: 30578415. However, by far the most important negative regulation occurs at the level of receptor mediated STAT3 activation and is conferred by suppressor of cytokine signalling (SOCS) E3 ubiquitin ligases that enable the degradation of cytokine receptor complexes. SOCS proteins are themselves encoded by STAT target genes and thus provide a transcription dependent negative feedback mechanism.   1. <https://www.ncbi.nlm.nih.gov/pubmed/30578415> |
| CD14 | 1 | * STAT3 & FOXO1 & KLF4 & !STAT5 | |
| Sites found using matrix-scan with the regulatory regions of Mo in this study.  PMID: 17762869. We observed an B30 fold induction of the CD14 promoter by KLF4 (Figure 3A).   1. <https://www.ncbi.nlm.nih.gov/pubmed/17762869> |
| SELL | 1 | * STAT6 & FOXO1 & !PRDM1 | |
| PRDM1 is a putative negative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.  Monocyte associated genes (AHR, SELL, CLEC4D)   1. <https://pubmed.ncbi.nlm.nih.gov/29262348> |
| CD163 | 1 | * MAFB & IRF8 & !PRDM1:1 | |
| PRDM1 is a putative negative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.  MOs M CSF (macrophages) expressed high amounts of CD163, CD169, and MERTK.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| CD206 | 1 | * MAFB & IRF8 & USF1 & !PRDM1 | |
| PRDM1 is a putative negative regulation, through the sites found using matrix-scan with the regulatory regions of moDC in this study.  MOs GM CSF (macrophage) were defined by two subclusters (clusters 7 and 8). Both clusters expressed CD14, CD64, CD68, and CD206.  MR, mannose receptor   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348>   <https://pubmed.ncbi.nlm.nih.gov/27401672>  <https://pubmed.ncbi.nlm.nih.gov/10085160> |
| MERTK | 1 | * IRF8 & MAFB | |
| Sites found using matrix-scan with the regulatory regions of Mac in this study.  MOs M CSF (macrophages) expressed high amounts of CD163, CD169, and MERTK.   1. <https://www.ncbi.nlm.nih.gov/pubmed/29262348> |
| CCDC151 | 1 | * PU1:1 & AP1 & CEBPb | |
| Sites found using matrix-scan with the regulatory regions of Mac in this study.  According with Cuevas et al 2017, CCDC151 is an specific gene for macrophages.   1. <https://pubmed.ncbi.nlm.nih.gov/28093525> |
| BCL2 | 1 | * !JNK & STAT3:2 | |
| These results indicate that GM CSF likely induces autophagy by activating JNK and, subsequently, the release of Beclin1 from Bcl2 during monocyte differentiation.  STAT3 blocks the formation of autophagosomes by driving increased expression of antiautophagic genes Bcl2, Bcl2l1 and Mcl1 and suppression of the proautophagic gene Becn1, which encodes beclin 1.   1. <https://www.ncbi.nlm.nih.gov/pubmed/30578415>   <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |
| BECN1 | 1 | * !STAT3 & !BCL2 & JNK | |
| These results indicate that GM CSF likely induces autophagy by activating JNK and, subsequently, the release of Beclin1 from Bcl2 during monocyte differentiation.  STAT3 blocks the formation of autophagosomes by driving increased expression of antiautophagic genes Bcl2, Bcl2l1 and Mcl1 and suppression of the proautophagic gene Becn1, which encodes beclin 1.   1. <https://www.ncbi.nlm.nih.gov/pubmed/30578415>   <https://www.ncbi.nlm.nih.gov/pubmed/22323450> |

Bibliography

1. [Aguilera-Montilla, Noemí, Sonia Chamorro, Concha Nieto, Fátima Sánchez-Cabo, Ana Dopazo, Pedro Maria Fernández-Salguero, Jose Luis Rodríguez-Fernández, et al. 2013. “Aryl Hydrocarbon Receptor Contributes to the MEK/ERK-Dependent Maintenance of the Immature State of Human Dendritic Cells.” *Blood* 121 (15): e108–17.](http://paperpile.com/b/goh7ky/zv1w)
2. [Bhattacharjee, Ashish, Meenakshi Shukla, Valentin P. Yakubenko, Anny Mulya, Suman Kundu, and Martha K. Cathcart. 2013. “IL-4 and IL-13 Employ Discrete Signaling Pathways for Target Gene Expression in Alternatively Activated Monocytes/macrophages.” *Free Radical Biology & Medicine* 54 (January): 1–16.](http://paperpile.com/b/goh7ky/kBGq)
3. [Carotta, Sebastian, Aleksandar Dakic, Angela D’Amico, Swee Heng Milon Pang, Kylie T. Greig, Stephen L. Nutt, and Li Wu. 2010. “The Transcription Factor PU.1 Controls Dendritic Cell Development and Flt3 Cytokine Receptor Expression in a Dose-Dependent Manner.” *Immunity* 32 (5): 628–41.](http://paperpile.com/b/goh7ky/yKSQ)
4. [Cuevas, Víctor D., Laura Anta, Rafael Samaniego, Emmanuel Orta-Zavalza, Juan Vladimir de la Rosa, Geneviève Baujat, Ángeles Domínguez-Soto, et al. 2017. “MAFB Determines Human Macrophage Anti-Inflammatory Polarization: Relevance for the Pathogenic Mechanisms Operating in Multicentric Carpotarsal Osteolysis.” *Journal of Immunology*  198 (5): 2070–81.](http://paperpile.com/b/goh7ky/so9U)
5. [Dickensheets, H. L., C. Venkataraman, U. Schindler, and R. P. Donnelly. 1999. “Interferons Inhibit Activation of STAT6 by Interleukin 4 in Human Monocytes by Inducing SOCS-1 Gene Expression.” *Proceedings of the National Academy of Sciences of the United States of America* 96 (19): 10800–805.](http://paperpile.com/b/goh7ky/kszl)
6. [Egan, B. S., K. B. Lane, and V. L. Shepherd. 1999. “PU.1 and USF Are Required for Macrophage-Specific Mannose Receptor Promoter Activity.” *The Journal of Biological Chemistry* 274 (13): 9098–9107.](http://paperpile.com/b/goh7ky/xRt0)
7. [Feinberg, Mark W., Akm Khyrul Wara, Zhuoxiao Cao, Maria A. Lebedeva, Frank Rosenbauer, Hiromi Iwasaki, Hideyo Hirai, et al. 2007. “The Kruppel-like Factor KLF4 Is a Critical Regulator of Monocyte Differentiation.” *The EMBO Journal* 26 (18): 4138–48.](http://paperpile.com/b/goh7ky/Ubpu)
8. [Furukawa, T., T. Yatsuoka, E. M. Youssef, T. Abe, T. Yokoyama, S. Fukushige, E. Soeda, et al. 1998. “Genomic Analysis of DUSP6, a Dual Specificity MAP Kinase Phosphatase, in Pancreatic Cancer.” *Cytogenetics and Cell Genetics* 82 (3-4): 156–59.](http://paperpile.com/b/goh7ky/hZs9)
9. [Goudot, Christel, Alice Coillard, Alexandra-Chloé Villani, Paul Gueguen, Adeline Cros, Siranush Sarkizova, Tsing-Lee Tang-Huau, et al. 2017. “Aryl Hydrocarbon Receptor Controls Monocyte Differentiation into Dendritic Cells versus Macrophages.” *Immunity* 47 (3): 582–96.e6.](http://paperpile.com/b/goh7ky/hML2)
10. [Gutsch, Romina, Judith D. Kandemir, Daniel Pietsch, Christian Cappello, Johann Meyer, Kathrin Simanowski, René Huber, and Korbinian Brand. 2011. “CCAAT/enhancer-Binding Protein Beta Inhibits Proliferation in Monocytic Cells by Affecting the Retinoblastoma protein/E2F/cyclin E Pathway but Is Not Directly Required for Macrophage Morphology.” *The Journal of Biological Chemistry* 286 (26): 22716–29.](http://paperpile.com/b/goh7ky/hXTw)
11. [Hebenstreit, Daniel, Gerald Wirnsberger, Jutta Horejs-Hoeck, and Albert Duschl. 2006. “Signaling Mechanisms, Interaction Partners, and Target Genes of STAT6.” *Cytokine & Growth Factor Reviews* 17 (3): 173–88.](http://paperpile.com/b/goh7ky/LPck)
12. [Hsu, Amy T., Tanya J. Lupancu, Ming-Chin Lee, Andrew J. Fleetwood, Andrew D. Cook, John A. Hamilton, and Adrian Achuthan. 2018. “Epigenetic and Transcriptional Regulation of IL4-Induced CCL17 Production in Human Monocytes and Murine Macrophages.” *The Journal of Biological Chemistry* 293 (29): 11415–23.](http://paperpile.com/b/goh7ky/6RXY)
13. [Huynh, Jennifer, Ashwini Chand, Daniel Gough, and Matthias Ernst. 2019. “Therapeutically Exploiting STAT3 Activity in Cancer - Using Tissue Repair as a Road Map.” *Nature Reviews. Cancer* 19 (2): 82–96.](http://paperpile.com/b/goh7ky/CUrd)
14. [Ikizawa, K., K. Kajiwara, K. Izuhara, and Y. Yanagihara. 2001. “PKCdelta and Zeta Mediate IL-4/IL-13-Induced Germline Epsilon Transcription in Human B Cells: A Putative Regulation via PU.1 Phosphorylation.” *Biochemical and Biophysical Research Communications* 288 (1): 34–41.](http://paperpile.com/b/goh7ky/ax6T)
15. [Laar, Lianne van de, Paul J. Coffer, and Andrea M. Woltman. 2012. “Regulation of Dendritic Cell Development by GM-CSF: Molecular Control and Implications for Immune Homeostasis and Therapy.” *Blood* 119 (15): 3383–93.](http://paperpile.com/b/goh7ky/zRYT)
16. [Lehtonen, Anne, Helena Ahlfors, Ville Veckman, Minja Miettinen, Riitta Lahesmaa, and Ilkka Julkunen. 2007. “Gene Expression Profiling during Differentiation of Human Monocytes to Macrophages or Dendritic Cells.” *Journal of Leukocyte Biology* 82 (3): 710–20.](http://paperpile.com/b/goh7ky/kBn3)
17. [Marecki, S., M. L. Atchison, and M. J. Fenton. 1999. “Differential Expression and Distinct Functions of IFN Regulatory Factor 4 and IFN Consensus Sequence Binding Protein in Macrophages.” *Journal of Immunology*  163 (5): 2713–22.](http://paperpile.com/b/goh7ky/4y1a)
18. [Menetrier-Caux, C., M. C. Thomachot, L. Alberti, G. Montmain, and J. Y. Blay. 2001. “IL-4 Prevents the Blockade of Dendritic Cell Differentiation Induced by Tumor Cells.” *Cancer Research* 61 (7): 3096–3104.](http://paperpile.com/b/goh7ky/6KL5)
19. [Mumtaz, Peerzada Tajamul, Shakil Ahmad Bhat, Syed Mudasir Ahmad, Mashooq Ahmad Dar, Raashid Ahmed, Uneeb Urwat, Aadil Ayaz, Divya Shrivastava, Riaz Ahmad Shah, and Nazir Ahmad Ganai. 2017. “LncRNAs and Immunity: Watchdogs for Host Pathogen Interactions.” *Biological Procedures Online* 19 (April): 3.](http://paperpile.com/b/goh7ky/3yHr)
20. [Myers, M. P., J. N. Andersen, A. Cheng, M. L. Tremblay, C. M. Horvath, J. P. Parisien, A. Salmeen, D. Barford, and N. K. Tonks. 2001. “TYK2 and JAK2 Are Substrates of Protein-Tyrosine Phosphatase 1B.” *The Journal of Biological Chemistry* 276 (51): 47771–74.](http://paperpile.com/b/goh7ky/bQrZ)
21. [Pham, Thu-Hang, Christopher Benner, Monika Lichtinger, Lucia Schwarzfischer, Yuhui Hu, Reinhard Andreesen, Wei Chen, and Michael Rehli. 2012. “Dynamic Epigenetic Enhancer Signatures Reveal Key Transcription Factors Associated with Monocytic Differentiation States.” *Blood* 119 (24): e161–71.](http://paperpile.com/b/goh7ky/sj0a)
22. [Radford, Kristen J., Kirsteen M. Tullett, and Mireille H. Lahoud. 2014. “Dendritic Cells and Cancer Immunotherapy.” *Current Opinion in Immunology* 27 (1): 26–32.](http://paperpile.com/b/goh7ky/0Y5R)
23. [Ranasinghe, Charani, Shubhanshi Trivedi, Danushka K. Wijesundara, and Ronald J. Jackson. 2014. “IL-4 and IL-13 Receptors: Roles in Immunity and Powerful Vaccine Adjuvants.” *Cytokine & Growth Factor Reviews* 25 (4): 437–42.](http://paperpile.com/b/goh7ky/i4fn)
24. [Sallusto, F., and Antonio Lanzavecchia. 1994. “Efficient Presentation of Soluble Antigen by Cultured Human Dendritic Cells Is Maintained by Granulocyte/macrophage Colony-Stimulating Factor plus Interleukin 4 and Downregulated by Tumor Necrosis Factor Alpha.” *The Journal of Experimental Medicine* 179 (4): 1109–18.](http://paperpile.com/b/goh7ky/PEQF)
25. [Sander, Jil, Susanne V. Schmidt, Branko Cirovic, Naomi McGovern, Olympia Papantonopoulou, Anna-Lena Hardt, Anna C. Aschenbrenner, et al. 2017. “Cellular Differentiation of Human Monocytes Is Regulated by Time-Dependent Interleukin-4 Signaling and the Transcriptional Regulator NCOR2.” *Immunity* 47 (6): 1051–66.e12.](http://paperpile.com/b/goh7ky/v38v)
26. [Seillet, Cyril, and Gabrielle T. Belz. 2013. “Terminal Differentiation of Dendritic Cells.” *Advances in Immunology* 120: 185–210.](http://paperpile.com/b/goh7ky/wiSp)
27. [Tamura Tomohiko. 2017. “Regulation of mononuclear phagocyte development by IRF8.” *[Rinsho ketsueki] The Japanese journal of clinical hematology* 58 (7): 798–805.](http://paperpile.com/b/goh7ky/5Qmn)
28. [Tang-Huau, Tsing-Lee, and Elodie Segura. 2019. “Human in Vivo-Differentiated Monocyte-Derived Dendritic Cells.” *Seminars in Cell & Developmental Biology* 86 (February): 44–49.](http://paperpile.com/b/goh7ky/uYFd)
29. [Ul-Haq, Zaheer, Sehrish Naz, and M. Ahmed Mesaik. 2016. “Interleukin-4 Receptor Signaling and Its Binding Mechanism: A Therapeutic Insight from Inhibitors Tool Box.” *Cytokine & Growth Factor Reviews* 32 (December): 3–15.](http://paperpile.com/b/goh7ky/Aq3s)
30. [Vento-Tormo, Roser, Carlos Company, Javier Rodríguez-Ubreva, Lorenzo de la Rica, José M. Urquiza, Biola M. Javierre, Radhakrishnan Sabarinathan, et al. 2016. “IL-4 Orchestrates STAT6-Mediated DNA Demethylation Leading to Dendritic Cell Differentiation.” *Genome Biology* 17 (January): 4.](http://paperpile.com/b/goh7ky/byOr)
31. [Wang, Pin, Yiquan Xue, Yanmei Han, Li Lin, Cong Wu, Sheng Xu, Zhengping Jiang, Junfang Xu, Qiuyan Liu, and Xuetao Cao. 2014. “The STAT3-Binding Long Noncoding RNA Lnc-DC Controls Human Dendritic Cell Differentiation.” *Science* 344 (6181): 310–13.](http://paperpile.com/b/goh7ky/lt5m)
32. [Williams, Keneeshia N., Andrea Szilagyi, Li-Ke He, Peggie Conrad, Marcia Halerz, Richard L. Gamelli, Ravi Shankar, and Kuzhali Muthumalaiappan. 2012. “Dendritic Cell Depletion in Burn Patients Is Regulated by MafB Expression.” *Journal of Burn Care & Research: Official Publication of the American Burn Association* 33 (6): 747–58.](http://paperpile.com/b/goh7ky/IOoS)
33. [Yashiro, Takuya, Kazumi Kasakura, Yoshihito Oda, Nao Kitamura, Akihito Inoue, Shusuke Nakamura, Hokuto Yokoyama, et al. 2017. “The Hematopoietic Cell-Specific Transcription Factor PU.1 Is Critical for Expression of CD11c.” *International Immunology* 29 (2): 87–94.](http://paperpile.com/b/goh7ky/MOUV)
34. [Zarif, Jelani C., James R. Hernandez, James E. Verdone, Scott P. Campbell, Charles G. Drake, and Kenneth J. Pienta. 2016. “A Phased Strategy to Differentiate Human CD14+monocytes into Classically and Alternatively Activated Macrophages and Dendritic Cells.” *BioTechniques* 61 (1): 33–41.](http://paperpile.com/b/goh7ky/cHBz)
35. [Zhou, Jimmy Jianheng, Yuan Min Wang, Vincent Ws Lee, Richard Ks Phoon, Geoff Yu Zhang, Ya Wang, Thian Kui Tan, et al. 2012. “DEC205-DC Targeted DNA Vaccines to CX3CR1 and CCL2 Are Potent and Limit Macrophage Migration.” *International Journal of Clinical and Experimental Medicine* 5 (1): 24–33.](http://paperpile.com/b/goh7ky/wbLy)
36. [Zmajkovicova, Katarina, Veronika Jesenberger, Federica Catalanotti, Christian Baumgartner, Gloria Reyes, and Manuela Baccarini. 2013. “MEK1 Is Required for PTEN Membrane Recruitment, AKT Regulation, and the Maintenance of Peripheral Tolerance.” *Molecular Cell* 50 (1): 43–55.](http://paperpile.com/b/goh7ky/xpPj)