

Supplementary Table S1: Differentially expressed genes in the blood after azithromycin treatment with a fold difference of >1.5.

| Gene Symbol | Gene Name | p-value | Fold Change | Regulation | ProbeID | Accession |
|--------------------|-------------------------------------------------------------------------------------|----------------|--------------------|-------------------|----------------|------------------|
| EPSTI1 | Epithelial stromal interaction 1, transcript variant 2 | 0.009 | 1.9 | down | 5700725 | NM_033255.2 |
| MX1 | Myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 | 0.005 | 1.9 | down | 1690066 | NM_002462.2 |
| STAT1 | Signal transducer and activator of transcription 1, 91kDa, transcript variant alpha | 0.006 | 1.8 | down | 1820750 | NM_007315.2 |
| HERC5 | Hect domain and RLD 5 | 0.004 | 1.8 | down | 5720482 | NM_016323.2 |
| SYK | Spleen tyrosine kinase | 0.038 | 1.8 | down | 110685 | NM_003177.3 |
| HLA-DRB3 | Major histocompatibility complex, class II, DR beta 3 | 0.041 | 1.8 | down | 1770504 | NM_022555.3 |
| NBPF10 | Neuroblastoma breakpoint family, member 10 | 0.022 | 1.8 | down | 1510681 | NM_001039703.1 |
| NBPF20 | Neuroblastoma breakpoint family, member 20 | 0.014 | 1.8 | down | 5310044 | NM_001037675.1 |
| GBP5 | Guanylate binding protein 5 | 0.003 | 1.7 | down | 1510364 | NM_052942.2 |
| TNFRSF1B | Tumor necrosis factor receptor superfamily, member 1B | 0.046 | 1.7 | down | 2490537 | NM_001066.2 |
| PGAM1 | Phosphoglycerate mutase 1 | 0.036 | 1.6 | down | 3940592 | NM_002629.2 |
| XAF1 | XIAP associated factor 1, transcript variant 2 | 0.006 | 1.6 | down | 450189 | NM_199139.1 |
| FCGR1B | Fc fragment of IgG, high affinity Ib, receptor (CD64), transcript variant 1 | 0.015 | 1.6 | down | 2710709 | NM_001017986.1 |
| OAS2 | 2'-5'-oligoadenylate synthetase 2, 69/71kDa, transcript variant 1 | 0.039 | 1.6 | down | 7320561 | NM_016817.2 |
| OAS1 | 2',5'-oligoadenylate synthetase 1, 40/46kDa, transcript variant 3 | 0.004 | 1.6 | down | 1090390 | NM_001032409.1 |

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|----------------|------------------------------------------------------------------------------------|-------|-----|------|---------|-------------|
| PARP14 | Poly (ADP-ribose) polymerase family, member 14 | 0.017 | 1.6 | down | 4150692 | NM_017554.1 |
| NAMPT | Nicotinamide phosphoribosyltransferase | 0.027 | 1.5 | down | 3060523 | NM_005746.2 |
| IL4R | Interleukin 4 receptor (IL4R), transcript variant 1 | 0.024 | 1.5 | down | 5910609 | NM_000418.2 |
| LAP3 | Leucine aminopeptidase 3 | 0.006 | 1.5 | down | 3290292 | NM_015907.2 |
| PFKFB3 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 | 0.034 | 1.5 | down | 4120053 | NM_004566.2 |
| EIF2AK2 | Eukaryotic translation initiation factor 2-alpha kinase 2 | 0.038 | 1.5 | down | 2120079 | NM_002759.1 |
| STAT1 | Signal transducer and activator of transcription 1, 91kDa, transcript variant beta | 0.002 | 1.5 | down | 2570079 | NM_139266.1 |

Supplementary Table S2: Differentially expressed genes in sputum with more than 3 interconnections within the STRING networks

| Gene symbol | Gene name | Gene function | Neighbours |
|-------------|--------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| HLA-B | Major histocompatibility complex, class I, B | Involved in the presentation of foreign antigens to the immune system | 9 |
| HLA-E | Major histocompatibility complex, class I, E | Preferably binds to a peptide derived from the signal sequence of most HLA-A, -B, -C and -G molecules | 9 |
| GBP2 | Guanylate binding protein 2, interferon-inducible | Hydrolyzes GTP to GMP in 2 consecutive cleavage reactions, but the major reaction product is GDP | 8 |
| HLA-A | Major histocompatibility complex, class I, A | Involved in the presentation of foreign antigens to the immune system | 8 |
| HLA-DPA1 | Major histocompatibility complex, class II, DP alpha 1 | Binds peptides derived from antigens that access the endocytic route of antigen presenting cells (APC) and presents them on the cell surface for recognition by the CD4 T-cells | 8 |
| HLA-DRA | Major histocompatibility complex, class II, DR alpha | Binds peptides derived from antigens that access the endocytic route of antigen presenting cells (APC) and presents them on the cell surface for recognition by the CD4 T-cells | 8 |
| GBP1 | Guanylate binding protein 1, interferon-inducible | Hydrolyzes GTP to GMP in 2 consecutive cleavage reactions | 7 |
| IFI30 | Interferon, gamma-inducible protein 30 | Lysosomal thiol reductase that can reduce protein disulfide bonds | 7 |
| IFITM3 | Interferon induced transmembrane protein 3 | IFN-induced antiviral protein which disrupts intracellular cholesterol homeostasis | 4 |

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| CD86 | CD86 molecule | Receptor involved in the costimulatory signal essential for T-lymphocyte proliferation and interleukin-2 production, by binding CD28 or CTLA-4 | 3 |
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Supplementary Table S3: Differentially expressed genes in blood with more than 3 interconnections within the STRING networks

| Gene symbol | Gene name | Gene function | Neighbours |
|-------------|---------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| OAS1 | 2'-5'-oligoadenylate synthetase 1 | Interferon-induced, dsRNA-activated antiviral enzyme which plays a critical role in cellular innate antiviral response | 20 |
| OAS2 | 2'-5'-oligoadenylate synthetase 2 | Interferon-induced, dsRNA-activated antiviral enzyme which plays a critical role in cellular innate antiviral response | 20 |
| TRIM25 | Tripartite motif-containing 25 (TRIM25) | Functions as a ubiquitin E3 ligase and as an ISG15 E3 ligase. Involved in innate immune defense against viruses by mediating ubiquitination of DDX58. Mediates 'Lys-63'-linked polyubiquitination of the DDX58 N-terminal CARD-like region which is crucial for triggering the cytosolic signal transduction that leads to the production of interferons in response to viral infection. Promotes ISGylation of 14-3-3 sigma (SFN), an adapter protein implicated in the regulation of a large spectrum signaling pathway. Mediates estrogen action in various target organs | 20 |
| HLA-F | Major histocompatibility complex, class I, F | Involved in the presentation of foreign antigens to the immune system | 19 |
| HLA-G | Major histocompatibility complex, class I, G | Involved in the presentation of foreign antigens to the immune system | 19 |
| GBP1 | Guanylate binding protein 1, interferon-inducible | Hydrolyzes GTP to GMP in 2 consecutive cleavage reactions | 18 |
| IRF9 | Interferon regulatory factor 9 | Transcription factor that mediates signalling by type I IFNs (IFN-alpha and IFN-beta). Following type I IFN binding to cell surface receptors, Jak kinases (TYK2 and JAK1) are activated, leading to tyrosine phosphorylation of STAT1 and STAT2. IRF9/ISGF3G associates with the phosphorylated STAT1:STAT2 dimer to form a complex termed ISGF3 transcription factor, that enters the nucleus. ISGF3 binds to | 18 |

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| | | the IFN stimulated response element (ISRE) to activate the transcription of interferon stimulated genes, which drive the cell in an antiviral state | |
| MX1 | Myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 | Interferon-induced dynamin-like GTPase with antiviral activity against a wide range of RNA viruses and some DNA viruses | 18 |
| OASL | 2'-5'-oligoadenylate synthetase-like | Does not have 2'-5'-OAS activity, but can bind double- stranded RNA | 18 |
| STAT1 | Signal transducer and activator of transcription 1 | Signal transducer and transcription activator that mediates cellular responses to interferons (IFNs), cytokine KITLG/SCF and other cytokines and other growth factors | 18 |
| IFIT1 | Interferon-induced protein with tetratricopeptide repeats 1 | Interferon-induced antiviral RNA-binding protein that specifically binds single-stranded RNA bearing a 5'-triphosphate group (PPP-RNA), thereby acting as a sensor of viral single- stranded RNAs and inhibiting expression of viral messenger RNAs | 17 |
| IRF1 | Interferon regulatory factor 1 | Transcriptional regulator which displays a remarkable functional diversity in the regulation of cellular responses. These include the regulation of IFN and IFN-inducible genes, host response to viral and bacterial infections, regulation of many genes expressed during hematopoiesis, inflammation, immune responses and cell proliferation and differentiation, regulation of the cell cycle and induction of growth arrest and programmed cell death following DNA damage | 17 |
| IRF7 | Interferon regulatory factor 7 | Key transcriptional regulator of type I interferon (IFN)-dependent immune responses and plays a critical role in the innate immune response against DNA and RNA viruses | 17 |
| GBP2 | Guanylate binding protein 2, interferon-inducible | Hydrolyzes GTP to GMP in 2 consecutive cleavage reactions, but the major reaction product is GDP | 16 |

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| FCGR1A | Fc fragment of IgG, high affinity Ia, receptor (CD64) | High affinity receptor for the Fc region of immunoglobulins gamma | 15 |
| FCGR1B | Fc fragment of IgG, high affinity Ib, receptor (CD64) | May bind to the Fc region of immunoglobulins gamma with a low affinity compared to FCGR1A | 15 |
| XAF1 | XIAP associated factor 1 | Seems to function as a negative regulator of members of the IAP (inhibitor of apoptosis protein) family | 15 |
| GBP5 | Guanylate binding protein 5 | As an activator of NLRP3 inflammasome assembly, plays a role in innate immunity and inflammation | 13 |
| HERC5 | HECT and RLD domain containing E3 ubiquitin protein ligase 5 | Major E3 ligase for ISG15 conjugation. Acts as a positive regulator of innate antiviral response in cells induced by interferon | 12 |
| UBE2L6 | Ubiquitin-conjugating enzyme E2L 6 | Catalyzes the covalent attachment of ubiquitin or ISG15 to other proteins. Functions in the E6/E6-AP-induced ubiquitination of p53/TP53. Promotes ubiquitination and subsequent proteasomal degradation of FLT3 | 11 |
| FYN | FYN oncogene related to SRC, FGR, YES | Non-receptor tyrosine-protein kinase that plays a role in many biological processes including regulation of cell growth and survival, cell adhesion, integrin-mediated signalling, cytoskeletal remodelling, cell motility, immune response and axon guidance | 6 |
| EIF2AK2 | Eukaryotic translation initiation factor 2-alpha kinase 2 | IFN-induced dsRNA-dependent serine/threonine-protein kinase which plays a key role in the innate immune response to viral infection and is also involved in the regulation of signal transduction, apoptosis, cell proliferation and differentiation | 6 |
| LILRB2 | Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 2; Receptor for class I MHC antigens | Recognizes a broad spectrum of HLA-A, HLA-B, HLA-C and HLA-G alleles. Involved in the down-regulation of the immune response and the development of tolerance | 5 |

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| SP110 | NFSP110 nuclear body protein | Transcription factor. May be a nuclear hormone receptor coactivator. Enhances transcription of genes with retinoic acid response elements (RARE) | 5 |
| STAT6 | Signal transducer and activator of transcription 6, interleukin-4 induced | Carries out a dual function: signal transduction and activation of transcription. Involved in IL4/interleukin-4- and IL3/interleukin-3-mediated signalling | 5 |
| SYK | Spleen tyrosine kinase | Non-receptor tyrosine kinase which mediates signal transduction downstream of a variety of transmembrane receptors including classical immunoreceptors like the B-cell receptor (BCR) | 5 |
| LAP3 | Leucine aminopeptidase 3 | Presumably involved in the processing and regular turnover of intracellular proteins. Catalyzes the removal of unsubstituted N-terminal amino acids from various peptides | 4 |
| FBXO6 | F-box protein 6 | Substrate-recognition component of some SCF (SKP1-CUL1- F-box protein)-type E3 ubiquitin ligase complexes. Involved in endoplasmic reticulum-associated degradation pathway (ERAD) for misfolded luminal proteins by recognizing and binding sugar chains on unfolded glycoproteins that are retrotranslocated into the cytosol and promoting their ubiquitination and subsequent degradation | 3 |
| PSME2 | Proteasome (prosome, macropain) activator subunit 2 (PA28 beta) | Implicated in immunoproteasome assembly and required for efficient antigen processing. The PA28 activator complex enhances the generation of class I binding peptides by altering the cleavage pattern of the proteasome | 3 |
| SNAP23 | Synaptosomal-associated protein, 23kDa | Essential component of the high affinity receptor for the general membrane fusion machinery and an important regulator of transport vesicle docking and fusion | 3 |
| TNFRSF1B | Tumor necrosis factor receptor superfamily, member 1B | Receptor with high affinity for TNFSF2/TNF-alpha and approximately 5-fold lower affinity for homotrimeric TNFSF1/lymphotoxin-alpha. The TRAF1/TRAF2 complex recruits the apoptotic suppressors BIRC2 and BIRC3 to TNFRSF1B/TNFR2. This receptor mediates most of the metabolic effects of TNF-alpha | 3 |
| ZNF364 | Ring finger protein 115 | E3 ubiquitin-protein ligase that mediates E2-dependent, 'Lys-48'- and/or 'Lys-63'-linked polyubiquitination of substrates and may play a role in diverse biological | 3 |

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| | | processes. Through their polyubiquitination, may play a role in the endosomal trafficking and degradation of membrane receptors including EGFR, FLT3, MET and CXCR4 | |
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