

Supplementary Table I. The list of the top 20 differentially expressed genes and a brief description of their functions.

Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide, also known as **FCER1A**, is a protein which in humans is encoded by the *FCER1A* gene (1).

The high affinity IgE receptor plays a central role in allergic disease, coupling allergen and mast cell to initiate the inflammatory and immediate hypersensitivity responses that are characteristic of disorders such as hay fever and asthma. The allergic response occurs when 2 or more IgE receptors are crosslinked via IgE molecules that in turn are bound to an allergen (antigen) molecule. A perturbation occurs that brings about the release of histamine and proteases from the granules in the cytoplasm of the mast cell and leads to the synthesis of prostaglandins and leukotrienes—potent effectors of the hypersensitivity response. The IgE receptor consists of 3 subunits: alpha (this protein), beta, and gamma.

CPA3 is secreted from mast cells and has a pH optimum in the neutral to basic range. It resembles pancreatic carboxypeptidases A1 in cleaving COOH-terminal aromatic and aliphatic amino acid residues (1). CPA3 functions together with endopeptidases secreted from mast cells such as aschymases and trypases to degrade proteins and peptides. Upon mast cell activation and degranulation, CPA3, the chymases, and trypases are released in complexes with heparin proteoglycan

Ring Finger Protein 11 (RNF11). RING finger domains simultaneously bind ubiquitination enzymes and their substrates and hence function as ligases. Ubiquitination in turn targets the substrate protein for degradation. Zinc finger (Znf) domains are relatively small protein motifs that bind one or more zinc atoms, and which usually contain multiple finger-like protrusions that make tandem contacts with their target molecule. They bind DNA, RNA, protein and/or lipid substrates. Their binding properties depend on the amino acid sequence of the finger domains and of the linker between fingers, as well as on the higher-order structures and the number of fingers. Znf domains are often found in clusters, where fingers can have different binding specificities.

KAT2B K(lysine) acetyltransferase 2B

CBP and p300 are large nuclear proteins that bind to many sequence-specific factors involved in cell growth and/or differentiation, including c-jun and the adenoviral oncoprotein E1A. The protein encoded by this gene associates with p300/CBP. It has *in vitro* and *in vivo* binding activity with CBP and p300, and competes with E1A for binding sites in p300/CBP. It has histone acetyl transferase activity with core histones and nucleosome core particles, indicating that this protein plays a direct role in transcriptional regulation.

A kinesin is a protein belonging to a class of motor proteins found in eukaryotic cells. Kinesins move along microtubule filaments, and are powered by the hydrolysis of ATP (thus kinesins are ATPases). The active movement of kinesins supports several cellular functions including mitosis, meiosis and transport of cellular cargo, such as in axonal transport. Most kinesins walk towards the plus end of a microtubule, which, in most cells, entails transporting cargo from the centre of the cell towards the periphery. This form of transport is known as anterograde transport. In contrast, dyneins are motor proteins that move toward the microtubules' minus end

Glutaredoxins are small redox enzymes of approximately one hundred amino-acid residues that use glutathione as a cofactor. Glutaredoxins are oxidized by substrates, and reduced non-enzymatically by glutathione. In contrast to thioredoxins, which are reduced by thioredoxin reductase, no oxidoreductase exists that specifically reduces glutaredoxins. Instead, glutaredoxins are reduced by the oxidation of glutathione. Oxidized glutathione is then regenerated by glutathione reductase. Together these components compose the glutathione system

MARCH8 is a member of the MARCH family of membrane-bound E3 ubiquitin ligases (EC 6.3.2.19). MARCH enzymes add ubiquitin (see MIM 191339) to target lysines in substrate proteins, thereby signaling their vesicular transport between membrane compartments. MARCH8 induces the internalization of several membrane glycoproteins (Goto *et al.*, 2003 [PubMed 12582153]; Bartee *et al.*, 2004 [PubMed 14722266]). [supplied by OMIM, Apr 2010]

Ferrochelatase (FECH, protoheme ferrolyase) is an enzyme that catalyses the terminal (eighth) step in the biosynthesis of heme, converting protoporphyrin IX into heme.

Spectrin beta chain, brain 1 is a protein that in humans is encoded by the *SPTBN1* gene (1). Spectrin is an actin crosslinking and molecular scaffold protein that links the plasma membrane to the actin cytoskeleton, and functions in the determination of cell shape, arrangement of transmembrane proteins, and organization of organelles.

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MAX-interacting protein 1 is a protein that in humans is encoded by the *MXI1* gene. Expression of the c-myc gene, which produces an oncogenic transcription factor, is tightly regulated in normal cells but is frequently deregulated in human cancers. The protein encoded by this gene is a transcriptional repressor thought to negatively regulate MYC function, and is therefore a potential tumor suppressor. This protein inhibits the transcriptional activity of MYC by competing for MAX, another basic helix-loop-helix protein that binds to MYC and is required for its function. Defects in this gene are frequently found in patients with prostate tumors.

Interleukin 3 receptor, alpha (low affinity) (IL3RA), also known as CD123 (Cluster of Differentiation 123)

The protein encoded by this gene is an interleukin 3 specific subunit of a heterodimeric cytokine receptor. The receptor is comprised of a ligand specific alpha subunit and a signal transducing beta subunit shared by the receptors for interleukin 3 (IL3), colony stimulating factor 2 (CSF2/GM-CSF), and interleukin 5 (IL5). The binding of this protein to IL3 depends on the beta subunit. The beta subunit is activated by the ligand binding, and is required for the biological activities of IL3. This gene and the gene encoding the colony stimulating factor 2 receptor alpha chain (CSF2RA) form a cytokine receptor gene cluster in a X-Y pseudoautosomal region on chromosomes X or Y.

Tetraspanins are a family of membrane proteins found in all multicellular eukaryotes. There are 34 tetraspanins in mammals, 33 of which have also been identified in humans. Tetraspanins display numerous properties that indicate their physiological importance in cell adhesion, motility, activation and proliferation, as well as their contribution to pathological conditions such as metastasis or viral infection

GATA Binding Protein 2 (GATA2)

The GATA family of transcription factors, which contain zinc fingers in their DNA binding domain, have emerged as candidate regulators of gene expression in hematopoietic cells. GATA1 is essential for normal primitive and definitive erythropoiesis and is expressed at high levels in erythroid cells, mast cells, and megakaryocytes.

GATA2 is expressed in hematopoietic progenitors, including early erythroid cells, mast cells, and megakaryocytes, and also in nonhematopoietic embryonic stem cells. In chicken erythroid progenitors, forced expression of GATA2 promotes proliferation at the expense of differentiation. GATA3 expression is restricted to T-lymphoid cells and some nonhematopoietic cell types, including embryonic stem cells.

MKRN1 makorin ring finger protein 1

This gene encodes a protein that belongs to a novel class of zinc finger proteins. The encoded protein functions as a transcriptional co-regulator, and as an E3 ubiquitin ligase that promotes the ubiquitination and proteasomal degradation of target proteins. The protein encoded by this gene is thought to regulate RNA polymerase II-catalyzed transcription.

Supplementary Table II. Genes differentially expressed in FM that are known drug targets.

Symbol	Gene Name	Targeted drug
MS4A2	membrane-spanning 4-domains, subfamily A, member 2	omalizumab
IL3RA	interleukin 3 receptor, alpha (low affinity)	sargramostim, EPO/sargramostim, rituximab/sargramostim
COL4A6	collagen, type IV, alpha 6	collagenase clostridium histolyticum
MUT	methylmalonyl CoA mutase	hydroxocobalamin, cyanocobalamin
NPY2R	neuropeptide Y receptor Y2	peptide YY 3-36
CPT1A	carnitine palmitoyltransferase 1A (liver)	perhexiline
ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	natalizumab
COL3A1	collagen, type III, alpha 1	collagenase clostridium histolyticum
GGPS1	geranylgeranyl diphosphate synthase 1	zoledronic acid
CA3	carbonic anhydrase III, muscle specific	thiazide diuretics
VWF	von Willebrand factor	Factor 8
ALDH5A1	aldehyde dehydrogenase 5 family	valproic acid
HRH4	histamine receptor H4	tesmilifene, triprolidine, buclizine
YES1	v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1	dasatinib