DATA NOTE

A compendium of monocyte transcriptome datasets to foster biomedical knowledge discovery [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Systems-scale profiling approaches have become widely used in translational research settings. The resulting accumulation of large-scale datasets in public repositories represents a critical opportunity to promote insight and foster knowledge discovery. However, resources that can serve as an interface between biomedical researchers and such vast and heterogeneous dataset collections are needed in order to fulfill this potential. Recently, we have developed an interactive data browsing and visualization web application, the Gene Expression Browser (GXB). This tool can be used to overlay deep molecular phenotyping data with rich contextual information about analytes, samples and studies along with ancillary clinical or immunological profiling data. In this note, we describe a curated compendium of 93 public datasets generated in the context of human monocyte immunological studies, representing a total of 4,516 transcriptome profiles. Datasets were uploaded to an instance of GXB along with study description and sample annotations. Study samples were arranged in different groups. Ranked gene lists were generated based on relevant group comparisons. This resource is publicly available online at <http://monocyte.gxbsidra.org/dm3/landing.gsp>.

Keywords

Monocyte , Transcriptomics , Gene Expression Browser , Immunology , Bioinformatics

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Introduction

Platforms such as microarrays and, more recently, next generation sequencing have been leveraged to generate molecular profiles at the scale of entire systems. The global perspective gained using such approaches is potentially transformative. Transcriptome profiling enabled for instance the characterization of molecular perturbations that occur in the context of a wide range of disease processes^{1–10}. This in turn has provided opportunities for the discovery of biomarkers and for the development of novel therapeutic modalities^{3,11–13}. More recently such systems-scale profiling of the blood transcriptome has also been used to monitor response to vaccines or therapeutic drugs^{14–19}. The democratization of these approaches has led to proliferation of data in public repositories: over 1.7 million individual transcriptome profiles from more than 65,000 studies have been deposited to date in the **NCBI Gene Expression Omnibus** (GEO), a public repository of transcriptome profiles.

Taken together this vast body of “collective data” holds the promise of accelerating the pace of biomedical discovery by creating countless opportunities for identifying and filling critical knowledge gaps. Building tools that provide biomedical researchers with the ability to seamlessly interact with collections of datasets along with rich contextual information is essential in promoting insight and enabling knowledge discovery. To address this need we have developed an interactive data browsing and visualization web application, the Gene Expression Browser (GXB).

GXB was described in a recent publication and is available as open source software on GitHub²⁰. This tool constitutes a simple interface for the browsing and interactive visualization of large volumes of heterogeneous data. Users can easily customize data plots by adding multiple layers of information, modifying the order of samples, and generating links that capture these settings which can be inserted in email communications or in publications. Accessing the tool via these links also provides access to rich contextual information that is essential for data interpretation. This includes access to gene information and relevant literature, study design information, detailed sample information as well as ancillary data²⁰.

In recent years, a large number of transcriptional studies have been conducted aiming at the characterization and functional classification of monocytes in health and disease. Monocytes are a population of immune cells found in the blood, bone marrow, and spleen. They constitute ~10% of the total circulating blood leukocytes in humans. They can remain in the blood circulation for up to 1–2 days, after which time, if they have not been recruited to a tissue, they die and are removed. They are considered the systemic reservoir of myeloid precursors for renewal of tissue macrophages and dendritic cells. Monocytes play a key role during immune response as professional phagocytes^{21,22}, and producers of immune mediators^{23,24}. Indeed, reports show that monocytes are recruited at the site of infections as innate effectors of the inflammatory response to microbes, killing pathogens via phagocytosis, production of reactive oxygen intermediate (ROIs)²⁵, reactive nitrogen intermediate (RNIs)^{26,27}, myeloperoxidase (MPO)^{28,29}, and producing inflammatory cytokines³⁰ that contribute to further amplifying the antimicrobial response³¹.

Human monocytes are derived from hematopoietic stem cells in the bone marrow and are released into peripheral blood circulation upon maturation. They are divided into three major subsets based on the expression of cell surface markers CD14 and CD16. The most prevalent subset in the blood circulation, accounting for 90% of all monocytes, are the classical monocytes that express high levels of CD14 but low levels of CD16. The remaining 10% is divided into two subsets: intermediate monocyte with high expression of CD14 and CD16 (CD14⁺CD16⁺) and non-classical monocytes that express low levels of CD14 but high levels of CD16 (CD14^{dim}CD16⁺⁺ or CD14⁺CD16⁺⁺)^{32–34}.

In this data note we are making available via GXB a curated compendium of 93 public datasets relevant to human monocyte immunobiology, representing a total of 4,516 transcriptome profiles.

Materials and methods

Identification of monocyte datasets

Potentially relevant datasets deposited in GEO were identified using an advanced query based on the Bioconductor package GEOmetadb and the SQLite database that captures detailed information on the GEO data structure; <https://www.bioconductor.org/packages/release/bioc/html/GEOmetadb.html>³⁵. The search query was designed to retrieve entries where the title and description contained the word Monocyte OR Monocytes, were generated from human samples, using Illumina or Affymetrix commercial platforms. The query result is appended with rich metadata from GEOmetadb that allows for manual filtering of the retrieved collection.

The relevance of each entry returned by this query was assessed individually. This process involved reading through the descriptions and examining the list of available samples and their annotations. Sometimes it was also necessary to review the original published report in which the design of the study and generation of the dataset is described in more detail. The datasets cover a broad range of human immunology studies investigating monocyte immunobiology in the context of diseases and through comparison with diverse cell populations and study types as illustrated by a graphical representation of relative occurrences of terms in the list of diseases loaded into our tool (Figure 1). A wide range of cell types and diseases are represented. Ultimately, the collection was comprised of 93 curated datasets. It includes datasets generated from studies profiling primary human CD14⁺ cells isolated from patients with autoimmune diseases (7), bacterial, virus and parasite infections (7), cancer (4), cardiovascular diseases (4), kidney diseases (4), as well as monocytes isolated from healthy subjects (58) (Figure 2). The 58 datasets in which monocytes were isolated from healthy subjects were classified based on whether profiling was conducted *ex vivo* or following *in vitro* experiments. In total 38 datasets were identified in which primary human CD14⁺ cells were stimulated or infected in *in vitro* experiments (Figure 2). Among the many noteworthy datasets, there are 8 datasets investigating differences between monocytes subsets; classical (CD14⁺CD16⁻), intermediate (CD14⁺CD16⁺) and non-classical monocytes (CD14^{dim}CD16⁺⁺)^{32–34} [GXB: [GSE16836](#), [GSE18565](#), [GSE25913](#), [GSE34515](#), [GSE35457](#), [GSE51997](#), [GSE60601](#), [GSE66936](#)]. Another dataset from Banachereau and colleagues investigated responses of monocyte and dendritic cells to 13 different vaccines

Figure 1. Thematic composition of the dataset collection. Word frequencies extracted from text descriptions of the studies loaded into the GXB tool are depicted as a word cloud. The size of the words is proportional to their frequency.

Figure 2. Break down of the dataset collection by category. The pie chart on the left panel indicates dataset frequencies by disease status. The chart on the right panel indicates the type of studies carried out for the 58 datasets consisting of monocyte obtained exclusively from healthy donors.

*in vitro*³⁶ [GXB: [GSE44721](#)]. The datasets that comprise our collection are listed in [Table 1](#) and can be browsed interactively in [GXB](#).

Dataset upload and annotation on GXB

Once a final selection had been made each dataset was downloaded from GEO in the SOFT file format. It was in turn uploaded on an instance of the Gene Expression Browser (GXB) hosted on the Amazon Web Services cloud. Available sample and study information were also uploaded. Samples were grouped according to possible interpretations of study results and ranking based on the different group comparisons that were computed (e.g. comparing monocytes isolated from case vs controls in studies where profiling was performed *ex-vivo*; or stimulated vs medium control in *in vitro* experiments).

Short Gene Expression Brower tutorial

The GXB software has been described in detail in a recent publication²⁰. This custom software interface provides users with a means to easily navigate and filter the dataset collection available at <http://monocyte.gxbsidra.org/dm3/landing.gsp>. A web tutorial is also available online: <http://monocyte.gxbsidra.org/dm3/tutorials.gsp#xbut>. Briefly, datasets of interest can be quickly identified either by filtering using criteria from pre-defined lists on the left or by entering a query term in the search box at the top of the dataset navigation page. Clicking on one of the studies listed in the dataset navigation page opens a viewer designed to provide interactive browsing and graphic representations of large-scale data in an interpretable format. This interface is designed to present ranked gene lists and display expression results graphically in a

Table 1. List of datasets constituting the collection.

Title	Platforms	Diseases	Number of sample	Experiments	GEO ID	References
Interaction of bone marrow stroma and monocytes: bone marrow stromal cell lines cultured with monocytes	Affymetrix	Healthy	8	<i>In vitro</i>	GSE10595	37
Monocyte gene expression profiling in familial combined hyperlipidemia and its modification by atorvastatin treatment	Affymetrix	Familial combined hyperlipidemia	9	<i>In vitro</i>	GSE11393	38
Performance comparison of Affymetrix and Illumina microarray technologies	Affymetrix	Acute coronary syndrome	10	<i>Ex vivo</i>	GSE11430	39
Gene expression profiling in pediatric meningococcal sepsis reveals dynamic changes in NK-cell and cytotoxic molecules	Affymetrix	Meningococcal sepsis	41	<i>Ex vivo</i>	GSE11755	N/A
Effect of interferon-gamma on macrophage differentiation and response to Toll-like receptor ligands	Affymetrix	Healthy	10	<i>In vitro</i>	GSE11864	40
Human monocyte and dendritic Cell Subtype Gene Arrays	Affymetrix	Healthy	8	<i>Ex vivo</i>	GSE11943	41
Microarray analysis of human monocytes infected with <i>Francisella tularensis</i>	Affymetrix	Healthy	14	<i>In vitro</i>	GSE12108	42
Human blood monocyte profile in Ventilator-Associated Pneumonia patients	Affymetrix	Pneumonia	60	<i>Ex vivo</i>	GSE12838	N/A
Quercetin supplementation and CD14+ monocyte gene expression	Affymetrix	Healthy	6	<i>Ex vivo</i>	GSE13899	43
Effects of PMN-Ectosomes on human macrophages	Affymetrix	Healthy	16	<i>In vitro</i>	GSE14419	N/A
Homogeneous monocytes and macrophages from hES cells following coculture-free differentiation in M-CSF and IL-3	Affymetrix	Healthy	9	<i>Ex vivo</i>	GSE15791	44
Expression data from human macrophages	Affymetrix	Healthy	38	<i>In vitro</i>	GSE16385	45
Transcriptional profiling of CD16+ and CD16- peripheral blood monocytes from healthy individuals	Affymetrix	Healthy	8	<i>Ex vivo</i>	GSE16836	32
COPD-Specific Gene Expression Signatures of Alveolar Macrophages as well as Peripheral Blood Monocytes Overlap and Correlate with Lung Function	Affymetrix	Chronic obstructive pulmonary disease	12	<i>Ex vivo</i>	GSE16972	46
Loss-of-function mutations in REP-1 affect intracellular vesicle transport in fibroblasts and monocytes of CHM patients	Affymetrix	Choroideremia	15	<i>Ex vivo</i>	GSE17549	47
Effect of two weeks erythropoietin treatment on monocyte transcriptomes of cardiorenal patients	Illumina	Cardiorenal syndrome	48	<i>Ex vivo</i>	GSE17582	N/A
Comparison of gene expression profiles between human monocyte subsets	Affymetrix	Healthy	6	<i>Ex vivo</i>	GSE18565	48
Subpopulations of CD163 positive macrophages are classically activated in psoriasis	Illumina	Psoriasis	58	<i>Ex vivo</i>	GSE18686	49
Mycobacterium tuberculosis Chaperonin 60.1 has Bipolar Effects on Human peripheral blood-derived Monocytes	Affymetrix	Healthy	21	<i>In vitro</i>	GSE18794	N/A

Title	Platforms	Diseases	Number of sample	Experiments	GEO ID	References
Blood Transcriptional Profiles of Active TB (Separated cell)	Illumina	Tuberculosis	44	Ex vivo	GSE19443	11
Filaria induced monocyte dysfunction and its reversal following treatment	Affymetrix	Filariasis	14	Ex vivo	GSE2135	50
Ubiquitinol-induced gene expression signatures are translated into reduced erythropoiesis and LDL cholesterol levels in humans	Affymetrix	Healthy	6	Ex vivo	GSE21351	51
Monocyte vs Macrophage Study	Affymetrix	Healthy	6	In vitro	GSE22373	52
Monocyte gene expression patterns distinguish subjects with and without atherosclerosis	Illumina	Carotid atherosclerosis	95	Ex vivo	GSE23746	N/A
Deconvoluting Early Post-Transplant Immunity Using Purified Cell Subsets Reveals Functional Networks Not Evident by Whole Blood Analysis	Affymetrix	Kidney transplantation	179	Ex vivo	GSE24223	53
Cooperative and redundant signaling of leukotriene B4 and leukotriene D4 in human monocytes	Affymetrix	Healthy	10	In vitro	GSE24869	54
Gene expression profiling of the classical (CD14++CD16-), intermediate (CD14++CD16+) and nonclassical (CD14+CD16+) human monocyte subsets	Illumina	Healthy	24	Ex vivo	GSE25913	34
Direct Cell Conversion of Human Fibroblasts to Monocytic phagocytes by Forced Expression of Monocytic Regulatory Network Elements	Illumina	Dermatomyositis	15	Ex vivo	GSE27304	N/A
cMyb and vMyb in human monocytes	Affymetrix	Healthy	6	In vitro	GSE2816	55
Temporal transcriptional changes in human monocytes following acute myocardial infarction: The GerMIFs monocyte expression study	Illumina	Acute myocardial infarction	76	Ex vivo	GSE28454	N/A
mRNA expression profiling of human immune cell subset (Roche)	Affymetrix	Healthy	47	Ex vivo	GSE28490	56
mRNA expression profiling of human immune cell subsets (HUG)	Affymetrix	Healthy	33	Ex vivo	GSE28491	56
Changes in gene expression profiles in patients with 5q- syndrome in CD14+ monocytes caused by lenalidomide treatment	Illumina	5q- syndrome	17	Ex vivo	GSE31460	N/A
Genome-wide analysis of lupus immune complex stimulation of purified CD14+ monocytes and how this response is regulated by C1q	Illumina	Healthy	8	In vitro	GSE32278	57
Transcriptome analysis of circulating monocytes in obese patients before and three months after bariatric surgery	Illumina	Obesity	48	Ex vivo	GSE32575	58
CD4 on human monocytes	Affymetrix	Healthy	6	In vitro	GSE32939	59
Peripheral Blood Monocyte Gene Expression in Recent-Onset Type 1 Diabetes	Illumina	Type 1 Diabetes	22	Ex vivo	GSE33440	60
Traffic-related Particulate Matter Upregulates Allergic Responses by a Notch-pathway Dependent Mechanism	Affymetrix	Healthy	16	In vitro	GSE34025	N/A

Title	Platforms	Diseases	Number of sample	Experiments	GEO ID	References
Human monocyte activation with NOD2L vs. TLR2/1L	Affymetrix	Healthy	45	<i>In vitro</i>	GSE34156	61
Bacillus anthracis' lethal toxin induces broad transcriptional responses in human peripheral monocyte	Affymetrix	Healthy	8	<i>In vitro</i>	GSE34407	62
Gene expression profiles of human blood classical monocytes (CD14++CD16-), CD16 positive monocytes (CD14+16+++ and CD14++CD16+), and CD1c+ CD19- dendritic cells	Affymetrix	Healthy	9	<i>Ex vivo</i>	GSE34515	N/A
Genome-wide analysis of monocytes and T cells' response to interferon beta	Illumina	Healthy	12	<i>In vitro</i>	GSE34627	63
Highly pathogenic influenza virus inhibit Inflammatory Responses in Monocytes via Activation of the Rar-Related Orphan Receptor Alpha (RORalpha)	Affymetrix	Healthy	12	<i>In vitro</i>	GSE35283	N/A
Transcriptome profiles of human monocyte and dendritic cell subsets	Illumina	Healthy	49	<i>Ex vivo</i>	GSE35457	64
Influenza virus A infected monocytes	Illumina	Healthy	6	<i>In vitro</i>	GSE35473	65
PGE2-induced OSM expression	Affymetrix	Chronic wound	6	<i>Ex vivo</i>	GSE36995	66
Inflammatory Expression Profiles in Monocyte to Macrophage Differentiation amongst Patients with Systemic Lupus Erythematosus and Healthy Controls with and without an Atherosclerosis Phenotype	Illumina	Systemic lupus erythematosus	72	<i>Ex vivo</i>	GSE37356	N/A
New insights into key genes and pathways involved in the pathogenesis of HLA-B27-associated acute anterior uveitis	Affymetrix	Acute anterior uveitis	6	<i>In vitro</i>	GSE37588	N/A
Analysis of blood myelomonocytic cells from RCC patients	Illumina	Renal cell carcinoma	8	<i>Ex vivo</i>	GSE38424	67
Nanotoxicogenomic study of ZnO and TiO2 responses	Illumina	Healthy	90	<i>In vitro</i>	GSE39316	N/A
Macrophage Microvesicles Induce Macrophage Differentiation and miR-223 Transfer	Affymetrix	Healthy	24	<i>In vitro</i>	GSE41889	68
TREM-1 is a novel therapeutic target in Psoriasis	Affymetrix	Psoriasis	15	<i>In vitro</i>	GSE42305	69
Comparison study between Uremic patient with Healthy control	Affymetrix	Chronic kidney disease	6	<i>Ex vivo</i>	GSE43484	N/A
Microarray analysis of IL-10 stimulated adherent peripheral blood mononuclear cells	Affymetrix	Healthy	8	<i>In vitro</i>	GSE43700	70
Monocytes and Dendritic cells stimulated by 13 human vaccines and LPS	Illumina	Vaccination	128	<i>In vitro</i>	GSE44721	36
Gene expression profile of human monocytes stimulated with all-trans retinoic acid (ATRA) or 1,25a-dihydroxyvitamin D3 (1,25D3)	Affymetrix	Healthy	12	<i>In vitro</i>	GSE46268	71
Transcriptome analysis of blood monocytes from sepsis patients	Illumina	Sepsis	44	<i>Ex vivo</i>	GSE46955	72
Tumor-educated circulating monocytes are powerful specific biomarkers for diagnosis of colorectal cancer	Illumina	Colorectal cancer	93	<i>Ex vivo</i>	GSE47756	73

Title	Platforms	Diseases	Number of sample	Experiments	GEO ID	References
Similarities and differences between macrophage polarized gene profiles	Illumina	Healthy	12	<i>In vitro</i>	GSE49240	74
The effect of cell subset isolation method on gene expression in leukocytes.	Illumina	Healthy	50	<i>Ex vivo</i>	GSE50008	N/A
Transcriptome analysis of HIV-infected peripheral blood monocytes	Illumina	HIV	86	<i>Ex vivo</i>	GSE50011	75
Gene expression profiles in T-lymphocytes and Monocytes of participants of the Tour de France 2005	Affymetrix	Healthy	66	<i>Ex vivo</i>	GSE5105	N/A
Effects of exercise on gene expression level in human monocytes	Affymetrix	Healthy	24	<i>Ex vivo</i>	GSE51835	76
T helper lymphocyte- and monocyte-specific type I interferon (IFN) signatures in autoimmunity and viral infection.	Affymetrix	Autoimmune diseases	36	<i>Ex vivo</i>	GSE51997	77
Longitudinal comparison of monocytes from an HIV viremic vs aviremic state	Affymetrix	HIV	16	<i>Ex vivo</i>	GSE5220	78
Expression data from monocytes and monocyte derived macrophages	Affymetrix	Healthy	12	<i>In vitro</i>	GSE52647	N/A
Transcriptome analysis of primary monocytes from HIV+ patients with differential responses to therapy	Illumina	HIV	14	<i>Ex vivo</i>	GSE52900	79
Human blood monocyte response to IL-17A in culture	Affymetrix	Healthy	6	<i>In vitro</i>	GSE54884	N/A
Divergent genome wide transcriptional profiles from immune cell subsets isolated from SLE patients with different ancestral backgrounds	Illumina	Systemic lupus erythematosus	208	<i>Ex vivo</i>	GSE55447	80
Cell Specific Expression & Pathway Analyses Reveal Novel Alterations in Trauma-Related Human T-Cell & Monocyte Pathways	Affymetrix	Trauma patients	42	<i>Ex vivo</i>	GSE5580	81
Immune Variation Project (ImmVar) [CD14]	Affymetrix	Healthy	485	<i>Ex vivo</i>	GSE56034	N/A
Transcriptomics of human monocytes	Illumina	Healthy	1202	<i>Ex vivo</i>	GSE56045	82
Effect of vitamin D treatment on human monocyte	Affymetrix	Healthy	16	<i>In vitro</i>	GSE56490	N/A
Monocytes of patients with familial hypercholesterolemia show alterations in cholesterol metabolism	Affymetrix	Hypercholesterolemia	23	<i>Ex vivo</i>	GSE6054	83
Gene expression data from CD14++ CD16- classical monocytes from healthy volunteers and patients with pancreatic ductal adenocarcinoma	Affymetrix	Pancreatic ductal adenocarcinoma	12	<i>Ex vivo</i>	GSE60601	N/A
Activation of the JAK/STAT pathway in Behcet's Disease	Affymetrix	Behcet's disease	29	<i>Ex vivo</i>	GSE61399	N/A
Alarmins MRP8 and MRP14 induce stress-tolerance in phagocytes under sterile inflammatory conditions	Illumina	Sterile inflammation	12	<i>In vitro</i>	GSE61477	N/A

Title	Platforms	Diseases	Number of sample	Experiments	GEO ID	References
GM-CSF induced gene-regulation in human monocytes	Affymetrix	Healthy	6	<i>In vitro</i>	GSE63662	84
Treatment of human monocytes with TLR7 or TLR8 agonists	Affymetrix	Healthy	9	<i>In vitro</i>	GSE64480	85
Restricted Dendritic Cell and Monocyte Progenitors in Human Cord Blood and Bone Marrow	Illumina	Healthy	36	<i>Ex vivo</i>	GSE65128	86
Interleukin-1- and Type I Interferon-Dependent Enhanced Immunogenicity of an NYVAC-HIV-1 Env-Gag-Pol-Nef Vaccine Vector with Dual Deletions of Type I and Type II Interferon-Binding Proteins	Illumina	Vaccination	20	<i>In vitro</i>	GSE65412	N/A
Comparative analysis of monocytes from healthy donors, patients with metastatic breast cancer, sepsis or tuberculosis.	Illumina	Breast cancer and Bacterial infection	13	<i>Ex vivo</i>	GSE65517	87
Expression data from intermediate monocytes from healthy donors and autoimmune uveitis patients	Affymetrix	Autoimmune uveitis	21	<i>Ex vivo</i>	GSE66936	88
Induction of Dendritic Cell-like Phenotype in Macrophages during Foam Cell Formation	Affymetrix	Healthy	22	<i>In vitro</i>	GSE7138	89
Genome Wide Gene Expression Study of Circulating Monocytes in human with extremely high vs. low bone mass	Affymetrix	Healthy	26	<i>Ex vivo</i>	GSE7158	N/A
Genomic profiles for human peripheral blood T cells, B cells, natural killer cells, monocytes, and polymorphonuclear cells: comparisons to ischemic stroke, migraine, and Tourette syndrome	Affymetrix	Healthy	18	<i>Ex vivo</i>	GSE72642	90
Expression data from monocytes of individuals with different collateral flow index CFI	Affymetrix	Coronary artery disease	160	<i>Ex vivo</i>	GSE7638	91
Leukotriene D4 induces gene expression in human monocytes through cysteinyl leukotriene type 1 receptor	Affymetrix	Healthy	8	<i>In vitro</i>	GSE7807	92
Gene expression profile during monocytes to macrophage differentiation	Affymetrix	Healthy	9	<i>In vitro</i>	GSE8286	N/A
Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response	Affymetrix	Healthy	50	<i>In vitro</i>	GSE8921	93
TRAIL Is a Novel Antiviral Protein against Dengue Virus	Affymetrix	Dengue	10	<i>In vitro</i>	GSE9378	N/A
Gene Expression-Based High Throughput Screening: APL Treatment with Candidate Compounds	Affymetrix	Leukemia	24	<i>Ex vivo</i>	GSE976	94
Innate immune responses to TREM-1 activation	Affymetrix	Healthy	11	<i>In vitro</i>	GSE9988	95

context-rich environment. Selecting a gene from the rank ordered list on the left of the data-viewing interface will display its expression values graphically in the screen's central panel. Directly above the graphical display drop down menus give users the ability: a) To change how the gene list is ranked; this allows the user to change the method used to rank the genes, or to include only genes that are selected for specific biological interest; b) To change sample grouping (Group Set button), in some datasets a user can switch between groups based on cell type to groups based on disease type, for example; c) To sort individual samples within a group based on associated categorical or continuous variables (e.g. gender or age); d) To toggle between the bar chart view and a box plot view, with expression values represented as a single point for each sample. Samples are split into the same groups whether displayed as a bar chart or box plot; e) To provide a color legend for the sample groups; f) To select categorical information that is to be overlaid at the bottom of the graph. For example, the user can display gender or smoking status in this manner; g) To provide a color legend for the categorical information overlaid at the bottom of the graph; and h) To download the graph as a png image or csv file for performing a separate analysis. Measurements have no intrinsic utility in absence of contextual information. It is this contextual information that makes the results of a study or experiment interpretable. It is therefore important to capture, integrate and display information that will give users the ability to interpret data and gain new insights from it. We have organized this information under different tabs directly above the graphical display. The tabs can be hidden to make more room for displaying the data plots, or revealed by clicking on the blue "show info panel" button on the top right corner of the display. Information about the gene selected from the list on the left side of the display is available under the "Gene" tab. Information about the study is available under the "Study" tab. Information available about individual samples is provided under the "Sample" tab. Rolling

the mouse cursor over a bar chart's element while displaying the "Sample" tab lists any clinical, demographic, or laboratory information available for the selected sample. Finally, the "Downloads" tab allows advanced users to retrieve the original dataset for analysis outside this tool. It also provides all available sample annotation data for use alongside the expression data in third party analysis software. Other functionalities are provided under the "Tools" dropdown menu located in the top right corner of the user interface. Some of the notable functionalities available through this menu include: a) Annotations, which provides access to all the ancillary information about the study, samples and dataset organized across different tabs; b) Cross-project view, which provides the ability for a given gene to browse through all available studies; c) Copy link, which generates a mini-URL encapsulating information about the display settings in use and that can be saved and shared with others (clicking on the envelope icon on the toolbar inserts the url in an email message via the local email client); and d) Chart options, which gives user the option to customize chart labels.

Dataset validation

Quality control checks were performed with the examination of profiles of relevant biological indicators. Known leukocyte markers were used, such as CD14, which is expressed by monocytes and macrophages; as well as markers that would indicate significant contamination of the sample by other leukocyte populations: such as CD3, a T-cells marker; CD19, a B-cell marker; CD56, an NK cell marker (Figure 3; The expression of the CD14 marker across all studies can be checked using the cross project functionality of GXB: http://monocyte.gxbsidra.org/dm3/geneBrowser/crossProject?probeID=201743_at&geneSymbol=CD14&geneID=929). In addition, expression of the XIST transcripts, in which expression is gender-specific, was also examined to determine its concordance with demographic information provided with the GEO submission.

Figure 3. Illustrative example showing the abundance levels of CD14 transcripts across samples in a given study. The expression of this gene is indicative of the purity of primary human monocyte preparation; this marker is expected to be high in monocyte preparations and low in other leukocyte populations. In this view of the GXB expression of CD14 can be visualized across projects listed on the left.

Data availability

All datasets included in our curated collection are also available publically via the NCBI GEO website: <http://www.ncbi.nlm.nih.gov/geo/>; and are referenced throughout the manuscript by their GEO accession numbers (e.g. [GSE25913](#)). Signal files and sample description files can also be downloaded from the GXB tool under the “downloads” tab.

Author contributions

DR: curated, uploaded and annotated datasets, and drafted the manuscript. **SB:** installed the software, uploaded datasets, programmed portions of the web application, and tested the software, and assisted in drafting the manuscript. **SP:** participated in the design of the software, programmed portions of the original web application, installed the software, and tested the software, and assisted in drafting the manuscript. **CQ:** participated in designed and programmed

portions of the original web application, tested the software, and assisted in drafting the manuscript. **DC:** participated in software design, tested the software, and drafted the manuscript.

Competing interests

No competing interests were disclosed.

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General Comments

Modern genomics, especially with the emergence of high-throughput next-generation sequencing, is generating data at such a rapid rate that new tools for organizing, visualizing, sharing, and integrating heterogeneous data in the context of scientific information are needed for scientists to efficiently use these published data. The Chaussabel group has recently developed an interactive data browsing and visualization web application, the Gene Expression Browser (GXB), to address this problem.

In this data note, Dr. Rinchai *et al.* report a compendium of ninety-six curated human monocyte transcriptome datasets from GEO spanning a broad range of diseases, cell types, and experiments. These datasets were then uploaded to the Gene Expression Browser for exploratory data analysis and dataset validation. The Gene Expression Browser should prove very useful for investigating large datasets; however, I have several questions and comments regarding the curated data itself:

Title:

The novel aspect and apparent emphasis of this data note is using the Gene Expression Browser to more easily explore the curated ninety-six datasets. But the current title emphasizes the key information on fostering the knowledge discovery. Please consider rephrasing it by focusing on the monocyte datasets and web application.

Introduction:

As the Gene Expression Browser has been described in detail previously, the emphasis of this data note should be on the curated data. It would be helpful to discuss the motivation for creating this

particular compendium of monocyte transcriptome datasets as well as the intended use of the curated data given the breadth and heterogeneity of diseases, cell types, and experiments that it includes.

Methods:

1. Please elaborate more specifically on how the datasets were curated. What were the eligibility criteria for inclusion into the compendium?
2. The table summarizing the published data can difficult to read due to its landscape orientation. Consider rotating the table from a landscape orientation to a portrait orientation.
3. In the right pie chart of Figure 2, there are twelve datasets studying primary monocytes; however, datasets classified as *in vitro* stimulation, infection, and monocyte subsets may also contain primary monocytes. Better categorization is needed.
4. Data validation is critical for verifying that a dataset is acceptable for use. The authors mention performing dataset validation but do not report the related results or summary of their validation. On page 9, the process of assessing contamination by other leukocyte populations using surface markers should be done carefully as CD14⁺ monocytes do share surface marker CD4.
5. In Fig. 3, it is unclear whether the orange bar plot is referring to CD4⁺ T cells or CD4⁺ cells in general. They are different cell types.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 29 Mar 2016

Darawan Rinchai, Sidra Medical and Research Center, Doha, Qatar

We thank the reviewers for their valuable feedback and suggestions to improve our manuscript.

Title:

Following the suggestion of the reviewers we changed the title of the manuscript to "A curated compendium of transcriptome datasets of relevance to human monocyte immunobiology research".

Introduction:

Thanks for raising this point. We added a long paragraph and new references in the introduction to emphasize the role of monocyte across different diseases and the motivation for creating this compendium of monocyte transcriptome datasets.

Methods:

1. *We have added information about how datasets were selected for inclusion in the collections in*

the methods section under the title "Identification of monocyte datasets"... "Using the search query, the results also returned a number of datasets that did not include profiles of monocytes but instead of "monocyte-derived dendritic cells" or "monocyte-derived macrophages". During our manual screen these were excluded as were studies employing monocytic cell lines. Only studies including primary human monocyte profiles were retained."

2. We agree with the reviewer that presenting the table using landscape orientation makes it difficult to read. We therefore changed table format from landscape to portrait orientation.

3. Thank you for pointing this out. We changed the label on this figure to read "ex-vivo, no treatment". These include studies where monocytes were isolated from healthy subjects for comparison with other cell types, or evaluation of variation among healthy individuals.

4. Assessing contamination can indeed be difficult, especially using this type of data where cell-level information is lacking. We plan to explore with our bioinformatics collaborators the development of a "scoring" approach to better quantify potential contamination but this is not a simple matter to address. At this point we have simply verified for each dataset that expression of markers was consistent with grouping labels provided by depositors. We have added language in the manuscript to clarify this point.

5. Thank you for pointing out this typo on this label. This dataset focuses on genomic profile of human blood both CD4+ and CD8+ T cells, B cells, NK cells monocytes and neutrophil. Figure 3 was corrected accordingly as shown in the new Figure 3.

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 March 2016

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Marc Pellegrini

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In this short descriptive report the authors put their published Gene Expression Browser tool to work in arranging several thousand transcriptome profiles obtained from public datasets that looked at monocyte immunology. They were able to compare groups of monocytes based on phenotypic attributes and rank gene expression. The authors provide a nice summary of the technique and validation.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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