Pharm Res (2011) 28:683–687
DOI 10.1007/s11095-010-0328-y

ERRATUM

Erratum: Changes in Gene Expression Pattern of Human Primary Macrophages Induced by Carbosilane Dendrimer 2G-NN16

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Published online: 30 November 2010

Erratum to: Pharm Res
DOI 10.1007/s11095-010-0328-y

ERRORS

- The "Materials and Methods" section stated, "Control and dendrimer probes were labeled, respectively, with Alexa Fluor 647 reactive dye decapack and Alexa Fluor 555 reactive dye decapack." This section should state, "Control and dendrimer probes were labeled, respectively, with Alexa Fluor 555 reactive dye decapack and Alexa Fluor 647 reactive dye decapack."
- There was a mistake in the microarray quantification files, and a new analysis has been done. The new microarray data have been corrected in Gene Expression Omnibus (Series accession number GSE12405). As a consequence of this mistake, Figure 3, Figure 4, Table I, Table II and Supplemental Table have been changed as follows. In spite of this error, conclusions remain valid.

CHANGES AND IMPLICATIONS

Change: The number of genes over-expressed or under-repressed more than twice is 2,706 and 5,560 genes for Dendrimer (DM) and Dendriplex (DX), respectively.
Implication: This change has no effect on discussion, and it is not relevant because the analysis is performed on a selection of these genes.

Change: The number of genes differentially expressed, applying filtering by p-value (<0.05), average signal (>32) and z-score (>1.8 or <-1.8), are 141 and 215 for DM and DX exposure, respectively.
Implication: A number of selected genes by dendrimer or dendriplex exposure is now more homogeneous.

The online version of the original article can be found at doi:10.1007/s11095-008-9776-z.

Electronic Supplementary Material The online version of this article (doi:10.1007/s11095-010-0328-y) contains supplementary material, which is available to authorized users.

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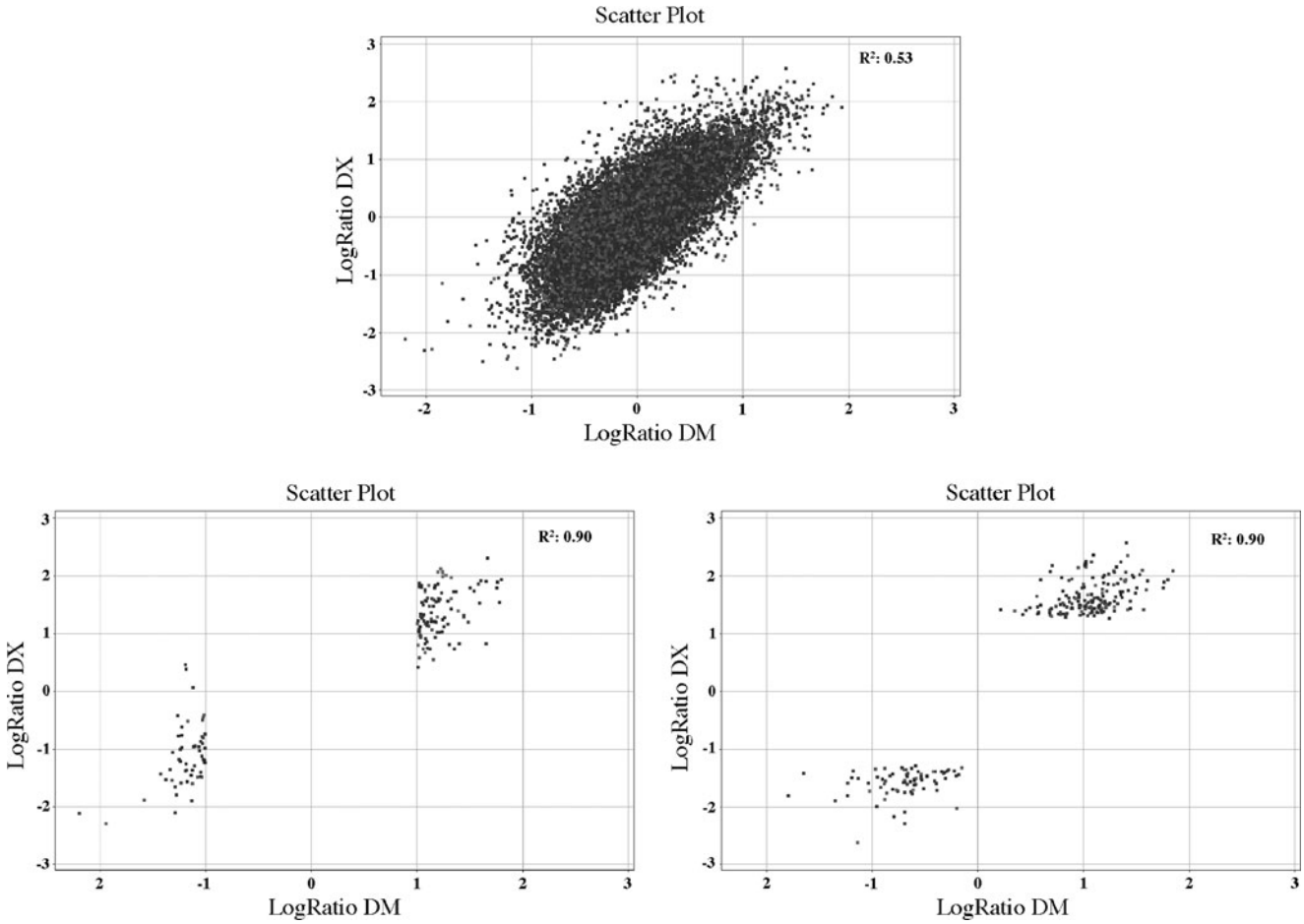

Fig. 3 (*top*) LogRatio Scatter Plot of macrophages exposed to 5 μM 2G-NN16 versus Dendriplex. Spots were filtered by Average intensity higher than 32 units in both conditions. Correlation factor (R2) was 0,53, indicating a high level of correlation. (*bottom left*) Scatter plot (dendrimer vs dendriplex) with significant selected genes differentially expressed in response to dendrimer exposure. (*bottom right*) Scatter plot (dendrimer vs dendriplex) of significant genes differentially expressed in response to dendriplex exposure. High correlations (R2 = 0.90) are observed.

Change: The correlation, measured by a logistic regression, between DM and DX microarray data of all genes with an average signal higher than 2 is 0.53. The correlation for the 141 DM selected genes with the corresponding values in DX arrays was 0.90. The correlation for the 214 DX selected genes with the corresponding values in DM arrays was 0.90.

Implication: The correlation between DM and DX data for genes with an average signal higher than 32 is lower than in our previous publication. However, the most important correlation, concerning genes selected for the functional analysis, still has a high significance ($R^2 = 0.90$). Therefore, the assumption published in our manuscript that dendrimer alone has basically the same effect on gene expression as dendriplex is also valid for the new data.

Change: The unique list with the most significant differentially expressed genes in DM and/or DX exposed now macrophages now includes 336 different genes, instead of 331.

Implication: Obviously, both the lists of selected genes regulated by DM and DX exposure and their corresponding values of Fold Change and p-Value have been modified. However, the most regulated genes published in our manuscript are still selected, principally IL17F, which plays an important role in the discussion and conclusions of our manuscript. RT-PCR of IL17F, IL23R and IL23A are not affected by the new microarray analysis.

Change: The five principal processes identified by Ingenuity with the new list of genes are summarised in the new Table II. "Cellular movement" remains as the highest scored category ($p = 4.07 \times 10^{-7}$), but the rest of them are not in the new top five of the list. Therefore, the rest of the categories published in the previous manuscript are still

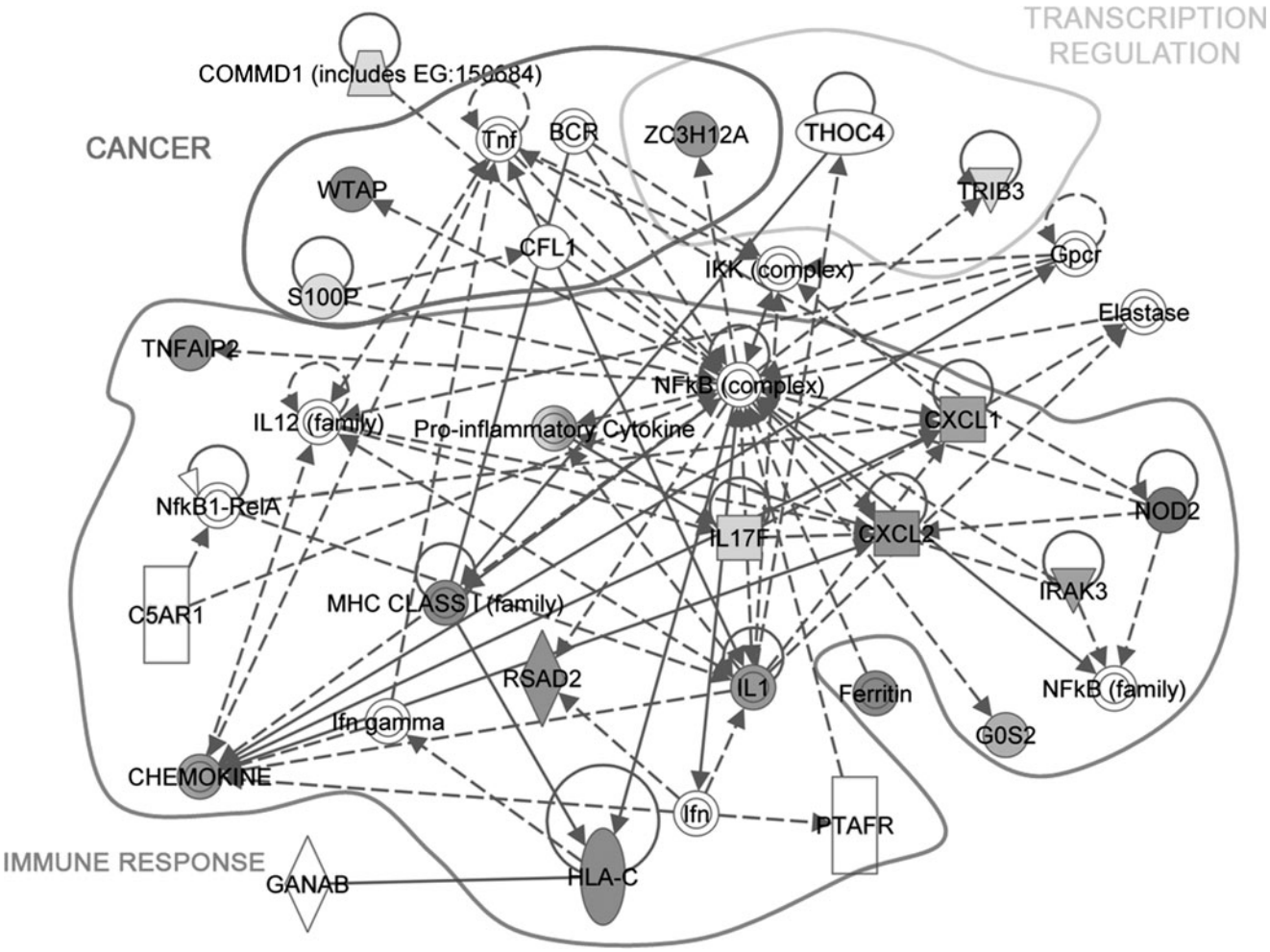

Fig. 4 Graphical representation of Network 1 introducing the list of selected genes in Ingenuity Pathways Analysis. Three principal functions are observed: immune system, cancer and transcriptional regulation.

statistically significant ("Hematological development and function": $p=3.1\times10^{-5}$, "Cell-to-cell signaling and interaction": $p=9.96\times10^{-3}$, "Immune response: $p=9.96\times10^{-3}$", "Inflammatory disease": $p=8.07\times10^{-3}$, "Connective tissue disorders": $p=6.12\times10^{-3}$). It is important to underline that Ingenuity is a dynamic database that continuously incorporates new relations and functions for the different genes.

Implication: The Ingenuity analysis of the principal processes affected reveals that the previously published processes are also significantly affected in the new analysis. However, new processes appear now with a higher score as a consequence of the new list of genes. Basically, cell death, cellular development and proliferation appear now. These categories are closely related, and many of the genes involved are common. In our manuscript we said previously that proliferation was one of the most affected functions by DM/DX exposure in macrophages based on the most significant network found by Ingenuity analysis. Thus, it confirms the previous published conclusions. To test the reproducibility of the data, we analysed the same list of genes of the incorrect microarray data published. Results shown different top-five categories based on the statistical significance. Therefore, in general, results of Ingenuity must be taken with caution.

Change: Immune response, principally, and cancer remain to be over-represented in the most significant network identified by Ingenuity Pathway analysis.

Implication: The most significant gene network found by Ingenuity using the new gene list shows that immune response, cancer and transcription regulation are highly represented. This result is very similar to previously published, in spite of some changes in genes in both old and new list.

Table I List of the 50 Most Regulated Genes in Macrophages by NN16 and Dendriplex Exposition

Symbol	Fold Change DM	p-value DM	Fold Change DX	p-value DX
IL17F	−4.59	0.0180	−4.31	0.0608
EFHB	−3.86	0.0443	−4.89	0.1250
TEX261	−3.48	0.0755	−3.48	0.0357
FUT7	−3.15	0.1849	−2.67	0.0224
A_24_P170309	−3.01	0.0200	−3.68	0.0659
X58329	−2.70	0.0069	−2.68	0.0745
A_24_P212605	−2.60	0.0116	−2.88	0.0841
TRIB3	−2.56	0.2185	−3.70	0.0276
LOC441238	−2.53	0.0017	−2.54	0.0882
CXCR6	−2.50	0.0265	−2.90	0.1773
PTPLAD2	−2.49	0.0079	−2.08	0.1983
LRRN3	−2.45	0.0254	−4.30	0.0965
LOC441893	−2.45	0.0139	−3.14	0.2581
D31828	−2.42	0.0125	−3.45	0.1973
C9orf119	−2.41	0.0128	−1.33	0.1766
A_24_P884915	−2.40	0.0166	−1.70	0.0497
A_24_P233560	−2.38	0.0120	−2.27	0.1361
CSTF3	−2.37	0.0455	−2.31	0.0402
RPS10	−2.36	0.0392	−2.00	0.0782
ZMAT5	−2.36	0.0216	−3.00	0.0398
HPGD	−2.35	0.1171	−3.49	0.0217
LOC392221	−2.35	0.0309	−1.69	0.0027
ANKRD2	−2.35	0.0285	−1.53	0.4301
MGC17330	−2.35	0.1701	−3.01	0.0420
SEDLP	−2.34	0.0490	−1.96	0.0393
STAM2	2.68	0.1513	2.67	0.0489
AK094950	2.68	0.1714	5.12	0.0156
AK000420	2.69	0.0618	3.37	0.0441
MICALCL	2.71	0.0247	2.50	0.0214
ANKRD12	2.72	0.1705	2.96	0.0379
BTN2A2	2.72	0.0658	2.72	0.0035
PDE4DIP	2.72	0.0451	2.44	0.0386
A_23_P136849	2.80	0.0478	2.29	0.0471
THC2694735	2.81	0.2077	3.27	0.0245
THC2623234	2.83	0.0379	3.45	0.0388
THC2719547	2.90	0.0381	3.33	0.0503
A_23_P136013	2.95	0.0748	4.28	0.0461
ZFYVE16	2.97	0.0807	2.66	0.0487
THC2559651	2.99	0.0289	3.63	0.1231
NBPF15	3.01	0.0789	3.39	0.0193
FLJ11292	3.02	0.0489	2.89	0.0812
STRN3	3.04	0.0348	3.77	0.0338
NOD2	3.14	0.0452	3.73	0.0643
COX1	3.15	0.0214	1.77	0.3774
NBPF11	3.17	0.0141	4.96	0.0648
THC2476126	3.37	0.0444	3.46	0.0083
AB040974	3.38	0.0290	3.70	0.0016
BTN2A1	3.44	0.0225	2.90	0.0596
THC2545558	3.47	0.0255	3.81	0.0184
USP54	3.59	0.0844	4.26	0.0447

Table II Results of Analysis using the Ingenuity Pathway Analysis SoftwareShowing the Functions with the Highest Probability to be Affected in Macrophages by Dendrimer/Dendriplex Exposure

Category	Function Annotation	Significance	Molecules
Cellular Movement	movement of eukaryotic cells	0	APBB1, ARHGAP24, BAX, C5AR1, CCDC88A, CFL1, CKLF, CXCL1, CXCL2, DOCK4, EBF1, EREG, FUT7, HBEGF, HIF1A, HOXB2, IL7, IL1B, ITGB2, LYST, MAPK3, MARCKS (includes EG:4082), MET, MXD1, NFKBIA, PDLIM2, PIM1, PLD1, PPARG, S100P, SDCBP, SERPINB2, SHC1, SLC1A2, SOD2, SPI1, VEGFA, WNT5A, ZEB2
Cell Death	cell viability of cell lines	0	BAX, CD7, CLN3, FTH1, IL7, IL1B, MET, NFAT5, NFKBIA, OGG1, SHC1, SOD2, VEGFA
Cellular Development	developmental process of fibroblast cell lines	0	CCND3, DYRK1A, EBF1, EREG, HBEGF, IL1B, MET, MLLT6, MXD1, NFKBIA, PPARG, RASGRP4, RB1, SHC1, TRIB3, WNT5A
Cellular Growth and Proliferation	growth of cell lines	0	BAX, CCND3, CLN3, CXCL1, CXCL2, EIF5A, ELOVL7, EREG, FTH1, HBEGF, HIF1A, HPGD, IL7, IL1B, KIF13A, MAPK3, MET, MLLT6, NFKBIA, PIM1, PPARG, RASGRP4, RB1, RPS6KB1, SAT1, SGMS1, SOD2, SPI1, VEGFA, WNT5A, ZMYM2
Skeletal and Muscular System Development and Function	skeletal and muscular process of cell lines	0	IL1B, MET, NFKBIA, PLD1, PPARG, RPS6KB1, SHC1

Selected genes were included in Ingenuity to have this result. In the table, parameters such as Category, Function Annotation, Significance and Molecules are presented.