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Mistaken Identifiers: Gene name errors can be introduced inadvertently when using Excel in bioinformatics

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Abstract

Background: When processing microarray data sets, we recently noticed that some gene names were being changed inadvertently to non-gene names.

Results: A little detective work traced the problem to default date format conversions and floating-point format conversions in the very useful Excel program package. The date conversions affect at least 30 gene names; the floating-point conversions affect at least 2,000 if Riken identifiers are included. These conversions are irreversible; the original gene names cannot be recovered.

Conclusions: Users of Excel for analyses involving gene names should be aware of this problem, which can cause genes, including medically important ones, to be lost from view and which has contaminated even carefully curated public databases. We provide work-arounds and scripts for circumventing the problem.

Text

MatchMiner [1] and GoMiner [2] are two bioinformatics program packages we published recently in another Biomed Central Journal, Genome Biology. When we were beta-testing those programs on microarray data, a frustrating problem occurred repeatedly: Some gene names kept bouncing back as "unknown." A little detective work revealed the reason: Use of one of the research community's most valuable and extensively applied tools for manipulation of genomic data can introduce erroneous names. A default date conversion feature in Excel (Microsoft Corp., Redmond, WA) was altering gene names that it considered to look like dates. For example, the tumor sup-

pressor DEC1 [Deleted in Esophageal Cancer 1] [3] was being converted to '1-DEC.' Figure 1 lists 30 gene names that suffer an analogous fate.

There is another default conversion problem for RIKEN [4] clone identifiers of the form nnnnnnnnEnn, where n denotes a digit. These identifiers are comprised of the serial number of the plate that contains the library, information on plate status, and the address of the clone [5]. A search (using the "DNA sequence length search" functionality at <http://fantom2.gsc.riken.go.jp/db/search/>) identified more than 2,000 such identifiers out of a total set of 60,770. For example, the RIKEN identifier "2310009E13"

The screenshot shows a Microsoft Excel spreadsheet titled "excel.gene2date.xls". The table has 15 rows and 11 columns. The columns are labeled as follows: gene names, internal date format, default date format, gene names, internal date format, default date format, gene names, internal date format, default date format. The first three columns (A, B, C) show the correct gene names. Columns B, F, and J show the underlying internal Excel date representation. Columns C, G, and K show the corresponding default format date conversions. The data consists of 15 rows of gene identifiers and their dates.

	gene names	internal date format	default date format	gene names	internal date format	default date format	gene names	internal date format	default date format
1	APR-1	35885	1-Apr	OCT-1	36068	1-Oct	SEP2	36039	2-Sep
2	APR-2	35886	2-Apr	OCT-2	36069	2-Oct	SEP3	36040	3-Sep
3	APR-3	35887	3-Apr	OCT-3	36070	3-Oct	SEP4	36041	4-Sep
4	APR-4	35888	4-Apr	OCT-4	36071	4-Oct	SEP5	36042	5-Sep
5	APR-5	35889	5-Apr	OCT-6	36073	6-Oct	SEP6	36043	6-Sep
6	DEC-1	36129	1-Dec	OCT1	36068	1-Oct	SEPT1	36038	1-Sep
7	DEC-2	36130	2-Dec	OCT11	36078	11-Oct	SEPT2	36039	2-Sep
8	DEC1	36129	1-Dec	OCT2	36069	2-Oct	SEPT3	36040	3-Sep
9	DEC2	36130	2-Dec	OCT3	36070	3-Oct	SEPT4	36041	4-Sep
10	MAR1	35854	1-Mar	OCT4	36071	4-Oct	SEPT5	36042	5-Sep
11	MAR2	35855	2-Mar	OCT6	36073	6-Oct	SEPT6	36043	6-Sep
12	MAR3	35856	3-Mar	OCT7	36074	7-Oct	SEPT7	36044	7-Sep
13	NOV1	36099	1-Nov	SEP-1	36038	1-Sep	SEPT8	36045	8-Sep
14	NOV2	36100	2-Nov	SEP-2	36039	2-Sep	SEPT9	36046	9-Sep
15				SEP1	36038	1-Sep			
16									

Figure 1

Screen shot of Microsoft Excel spreadsheet illustrating errors caused by default conversion of gene names to dates. Columns A, E, and I contain the correct gene names. Columns B, F, and J contain the corresponding underlying internal Excel date representation resulting from the forced default date conversion. Columns C, G, and K contain the corresponding default format date conversions. To create this table, we prepared a tab-delimited text file in which each gene name was repeated three times side by side. The correct gene names in columns A, E, and I were retained by opening this text file with Excel, and selecting "text" mode for columns A, E, and I in the Text Import Wizard Step 3 of 3 that appears while opening a file in Excel. Subsequently, the format menu "number" option (with zero decimal places) was applied to columns B, F, and J to display the internal date format.

was converted irreversibly to the floating-point number "2.31E+13." A non-expert user might well fail to notice that approximately 3% of the identifiers on a microarray with tens of thousands of genes had been converted to an incorrect form, yet the potential for 2,000 identifiers to be transmogrified without notice is a considerable concern. Most important, these conversions to an internal date representation or floating-point number format are irreversible; the original gene name cannot be recovered. If one were dealing manually with small numbers of genes, these problems could be detected and then corrected by the tedious, convoluted process described in the legend of Figure 1. But with microarray or other high-throughput data, human proofreading and manual curation are impractical.

The floating-point conversion is not restricted to RIKEN clone identifiers but will affect any clone designation derived from plate coordinates. Although the standard convention is to designate clones officially by library-plate-row-column identification, it is common practice to omit the library reference, particularly if all of the clones come from a single library. Without the library reference in the identifier, all clones from row E of any plate are converted to floating point numbers by Excel. If the library designation is numeric, as it is for RIKEN clones [5], then including it does not solve the problem. Since 96-well plates contain 8 rows and 12 columns, row E represents 12/96 or 12.5% of the clones on the plate; similarly, 6.25% of clones from 384-well plates would be affected. Most libraries contain hundreds of plates, each of which would be subject to this problem.

The screenshot shows the LocusLink Report page for gene NEDD5. The URL in the address bar is <http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=4735>. The main content area displays the gene's official symbol (Homo sapiens Official Gene Symbol and Name (HGNC)), its name (NEDD5: neural precursor cell expressed, developmentally down-regulated 5), and its LocusID (4735). Below this, the 'Relationships' section is highlighted with a red arrow. In the 'Mouse Homology Maps' table, the date '2-Sep' is circled in red, indicating an error in the conversion of a gene name to date.

	NCBI vs. MGD	1 cM	2-Sep	Hs Mm
UCSC vs. MGD	1 cM	Sept2	Hs Mm	
UCSC vs. Hudson et al.	1 1319.34 cR	AW208991	Hs Mm	

Relationships

Mouse Homology Maps:

	NCBI vs. MGD	1 cM	2-Sep	Hs Mm
UCSC vs. MGD	1 cM	Sept2	Hs Mm	
UCSC vs. Hudson et al.	1 1319.34 cR	AW208991	Hs Mm	

Map Information

Chromosome:	2	mv
Cytogenetic:	2q37	RefSeq
Markers:	Chr. 2; D2S2576 D2S2576	mv
	Chr. 2 G19712	mv
	Chr. 2 A001W20	mv
	Chr. 2 D2S2850 D2S2850	mv
	Chr. 2 D2S2704 D2S2704	mv
	Chr. 2 G62117	mv
	Chr. - D15S949 D15S949	

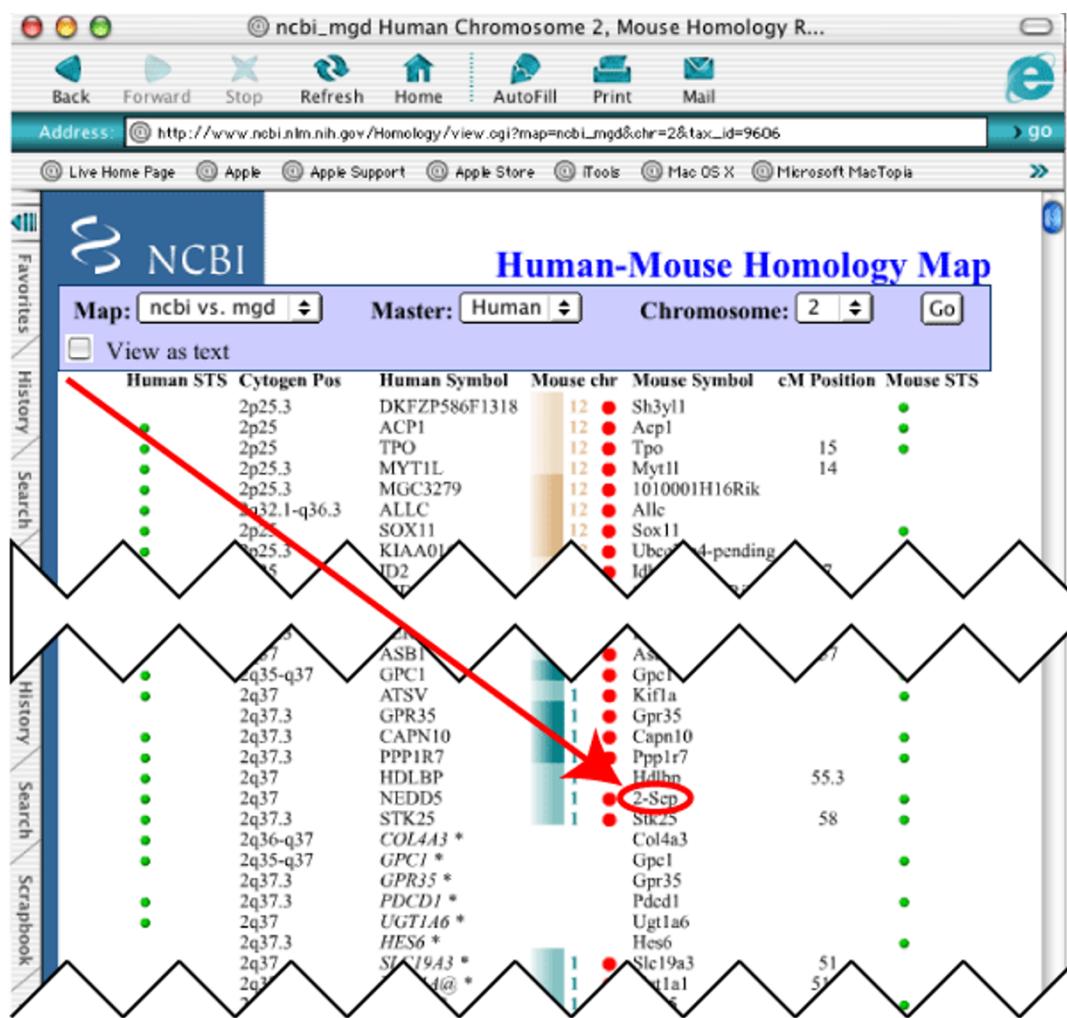
NCBI Reference Sequences (RefSeq)

Category: PROVISIONAL

mRNA: NM_004404

Figure 2

Screen shot of LocusLink from November 12, 2002 illustrating an error caused by default conversion of a gene name to date that had propagated from the human-mouse homology map data (Figure 3).

**Figure 3**

Screen shot of the human-mouse homology map from November 14, 2003 illustrating an error caused by default conversion of a gene name to date.

DEC1, a possible target for cancer therapy, was incorrectly rendered, and it could potentially be missed in downstream data analysis. The same type of error can infect, and propagate through, the major public data resources. For example, this type of error occurs several times in even the immaculately curated LocusLink database (Figure 2). This error in LocusLink originated from the human-mouse homology map data (Figure 3).

There are a number of work-arounds to these behaviors in Excel, but all of them require continued attention on the

part of the user to avoid introducing errors. The appropriate solutions depend on the context in which Excel is opened:

If Excel is configured to open a test file automatically from another application, then the data must be pre-processed in the upstream application. For example, a space character or an apostrophe can be placed in front of the gene name. That is the solution implemented in the Excel output format option of MatchMiner [1] and the primary

```

#! /bin/csh

foreach arg ($*)
echo $arg

tr "\r" "\n" < $arg | sed '1,$s/\^M/\\\
/g' | gawk
'(/ [0-9] \-
(JAN|FEB|MAR|APR|MAY|JUN|JUL|AUG|SEP|OCT|NOV|DEC|Jan|Feb|
Mar|Apr|M
ay|Jun|Jul|Aug|Sep|Oct|Nov|Dec|jan|feb|mar|
apr|may|jun|jul|aug|sep|oct|nov|dec) / ||
apr|may|jun|jul|aug|sep|oct|nov|/[0-9]\.[0-9][0-9]E\+[0-
9][0-9]/)
{print NR,$0}'
end

```

Figure 4
Script to scan for SymbolMutation error.

approach recommended by Microsoft in their Knowledge Base Article on the issue [6].

If a text file is to be opened by Excel, open Excel first and then select the text file to read. Then select "text" mode for the column(s) containing potentially affected symbols in the Text Import Wizard Step 3 of 3.

If text is to be copied from another application (such as a text processor) and pasted into a pre-opened Excel spreadsheet, the formatting must be set in the spreadsheet. Within the pre-opened spreadsheet, prior to pasting, use Format -> cells to specify which columns of the recipient spreadsheet are to be treated as text [6]. That procedure works for copying from several text processors tested on Mac OS 10.2. However, changing the format of the spreadsheet column to text fails to solve the conversion problem when pasting data from a Microsoft Word file. In that case, in addition to the formatting, use the Paste Special -> Paste: As: Text command to insert the text.

Despite the work-arounds, even the most vigilant investigator can inadvertently introduce conversion errors, and it is often necessary to screen data received from other sources. For that reason, we have provided the text of a Unix C shell program that detects possible gene-to-date

and floating-point conversion problems (Figure 4). A downloadable version is available in the Supplementary Materials (see Additional file 1) and on our companion web site [7]. We have implemented a version in Match-Miner [1] and are releasing a version of GoMiner [2] that includes a quality check that uses the script.

We hope the date and floating-point conversions will be made non-default options – in deference to the large bio-informatics and biotechnology communities if not for other users. Even if that is done, however, there will be a lag time before all researchers have the new program version and an even longer time of confusion before the existing errors and inconsistencies have been expunged from all public and private databases. In the meantime, it is important to be alert to the problem.

The twin aims of this paper are (i) to minimize additional contamination of the public databases and literature, and (ii) to provide a cautionary note to the many researchers who put their microarray data through the exceptionally useful medium of an Excel spreadsheet, then map the clone identifiers or GenBank accession numbers into human-readable gene names. There is no way to know how many times and in how many laboratories the default date and floating point conversions to non-gene

names have adversely affected an experiment or caused genes to "disappear" from view.

Additional material

Additional File 1

Symbol Mutation Scan: Shell file in downloadable format Companion Website: <http://discover.nci.nih.gov/symbolmutation>

Click here for file [NOTE: to correct an error, this file was updated on 20 August 2004]
[\[http://www.biomedcentral.com/content/supplementary/1471-2105-5-80-S1.sh\]](http://www.biomedcentral.com/content/supplementary/1471-2105-5-80-S1.sh)

7. **Mistaken Identifiers Companion** [<http://discover.nci.nih.gov/symbolmutation>]

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