Microarray-based detection of genomic signatures related with the tumor recurrence in Glioblastoma patients

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ABSTRACT

Glioblastomas tumors, in addition to be the most presented and aggressive brain tumor in humans, are notorious for resistance to therapy. The aim of this work consists, using 80 glioblastomas samples, in the concrete identification of the molecular profiles being related with the treatment resistance by means of the analysis of microarray data given by the reference work (Murat *et al.* 2008). The results show ...

KEYWORDS Microarray; tumour recurrence; glioblastoma.

Introduction

Glioblastoma multiforme is the most presented and aggressive brain tumor in humans, involving glial cells, with an incidence of 2–3 cases per 100,000 person life-years in Europe and North America(Bleeker *et al.* 2012). Its treatment can involve chemotherapy, radiation and surgery. Median survival with standard-of-care radiation and chemotherapy with the alkylating agent temozolomide is 15 months(Johnson *et al.* 2012) while the median survival without treatment is 4 and a half months.

Regretfully glioblastomas are notorious for resistance to therapy, which has been attributed to DNA-repair proficiency, a multitude of deregulated molecular pathways, and, more recently, to the particular biologic behavior of tumor stem-like cells as it is exposed in the work of Anastasia Murat(Murat *et al.* 2008). In that case the HOX and EGFR related pathways were identified as differentially expressed using several cluster procedures. However, a deeper analysis based on more general techniques can be able to determine the molecular profiles specific for treatment resistance. To achieve that goal, the same set of gene expression profiles of 80 patients has been used.

Materials and Methods

Manuscripts submitted to *GENETICS* should contain a clear description of the experimental design in sufficient detail so that the experimental analysis could be repeated by another scientist.

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If the level of detail necessary to explain the protocol goes beyond two paragraphs, give a short description in the main body of the paper and prepare a detailed description for supporting information. For example, details would include indicating how many individuals were used, and if applicable how individuals or groups were combined for analysis. If working with mutants indicate how many independent mutants were isolated. If working with populations indicate how samples were collected and whether they were random with respect to the target population.

Data Access

GENETICS is committed to the open access to all primary data (see Genetics, 184: 1). Please indicate where data can be found (supplemental files, public repository, or published with another paper).

Statistical Analysis

It is important to indicate what statistical analysis has been performed; not just the name of the software and options selected, but the method and model applied. In the case of many genes being examined simultaneously, or many phenotypes, a multiple comparison correction should be used to control the type I error rate, or a rationale for not applying a correction must be provided. The type of correction applied should be clearly stated. It should also be clear whether the p-values reported are raw, or after correction. Corrected p-values are often appropriate, but raw p-values should be available in the supporting materials so that others may perform their own corrections. In large scale data exploration studies (e.g. genome wide expression studies) a

clear and complete description of the replication structure must be provided.

Results and Discussion

The results and discussion should not be repetitive. The results section should give a factual presentation of the data and all tables and figures should be referenced; the discussion should not summarize the results but provide an interpretation of the results, and should clearly delineate between the findings of the particular study and the possible impact of those findings in a larger context. Authors are encouraged to cite recent work relevant to their interpretations. Present and discuss results only once, not in both the Results and Discussion sections. It is sometimes acceptable to combine results and discussion. The text should be as succinct as possible. Heed Strunk and White's dictum: "Omit needless words!"

Additional guidelines

Numbers

In the text, write out numbers nine or less except as part of a date, a fraction or decimal, a percentage, or a unit of measurement. Use Arabic numbers for those larger than nine, except as the first word of a sentence; however, try to avoid starting a sentence with such a number.

Units

Use abbreviations of the customary units of measurement only when they are preceded by a number: "3 min" but "several minutes". Write "percent" as one word, except when used with a number: "several percent" but "75%." To indicate temperature in centigrade, use ° (for example, 37°); include a letter after the degree symbol only when some other scale is intended (for example, 45°K).

Nomenclature and Italicization

Italicize names of organisms even when when the species is not indicated. Italicize the first three letters of the names of restriction enzyme cleavage sites, as in HindIII. Write the names of strains in roman except when incorporating specific genotypic designations. Italicize genotype names and symbols, including all components of alleles, but not when the name of a gene is the same as the name of an enzyme. Do not use "+" to indicate wild type. Carefully distinguish between genotype (italicized) and phenotype (not italicized) in both the writing and the symbolism.

Examples of Article Components

The sections below show examples of different header levels, which you can use in the primary sections of the manuscript (Results, Discussion, etc.) to organize your content.

First level section header

Use this level to group two or more closely related headings in a long article.

Second level section header

Second level section text.

Third level section header: Third level section text. These headings may be numbered, but only when the numbers must be cited in the text.

Figures and Tables

Figures and Tables should be labelled and referenced in the standard way using the `\label{}` and `\ref{}` commands.

Sample Figure

Figure 1 shows an example figure.

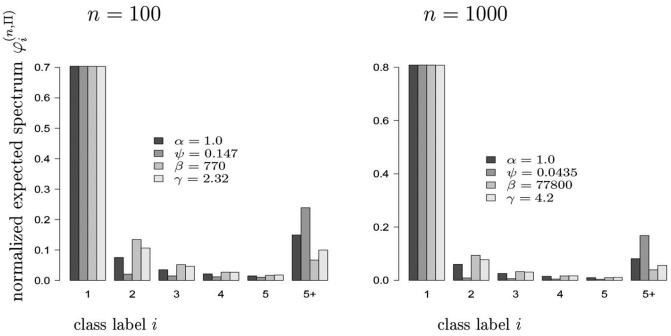

Figure 1 Example figure from 10.1534/genetics.114.173807. Please include your figures in the manuscript for the review process. You can upload figures to Overleaf via the Project menu. Upon acceptance, we'll ask for your figure files to be uploaded in any of the following formats: TIFF (.tiff), JPEG (.jpg), Microsoft PowerPoint (.ppt), EPS (.eps), or Adobe Illustrator (.ai). Images should be a minimum of 300 dpi in resolution and 500 dpi minimum if line art images. RGB, CMYK, and Grayscale are all acceptable. Halftones should be high contrast with sharp detail, because some loss of detail and contrast is inevitable in the production process. Figures should be 10-20 cm in width and 1-25 cm in height. Graph axes must be exactly perpendicular and all lines of equal density. Label multiple figure parts with A, B, etc. in bolded type, and use Arrows and numbers to draw attention to areas you want to highlight. Legends should start with a brief title and should be a self-contained description of the content of the figure that provides enough detail to fully understand the data presented. All conventional symbols used to indicate figure data points are available for typesetting; unconventional symbols should not be used. Italicize all mathematical variables (both in the figure legend and figure) , genotypes, and additional symbols that are normally italicized.

Sample Video

Figure 2 shows how to include a video in your manuscript.

Sample Table

Table 1 shows an example table. Avoid shading, color type, line drawings, graphics, or other illustrations within tables. Use tables for data only; present drawings, graphics, and illustrations as separate figures. Histograms should not be used to present data that can be captured easily in text or small tables, as they take up much more space.

Tables numbers are given in Arabic numerals. Tables should not be numbered 1A, 1B, etc., but if necessary, interior parts of the table can be labeled A, B, etc. for easy reference in the text.

Sample Equation

Let $X_1, X_2, \ldots, X_n$ be a sequence of independent and identically distributed random variables with $\mathrm{E}[X_i] = \mu$ and $\mathrm{Var}[X_i] =$

Table 1 Students and their grades

Student	Grade[a]	Rank	Notes
Alice	82%	1	Performed very well.
Bob	65%	3	Not up to his usual standard.
Charlie	73%	2	A good attempt.

[a] This is an example of a footnote in a table. Lowercase, superscript italic letters (a, b, c, etc.) are used by default. You can also use *, **, and *** to indicate conventional levels of statistical significance, explained below the table.

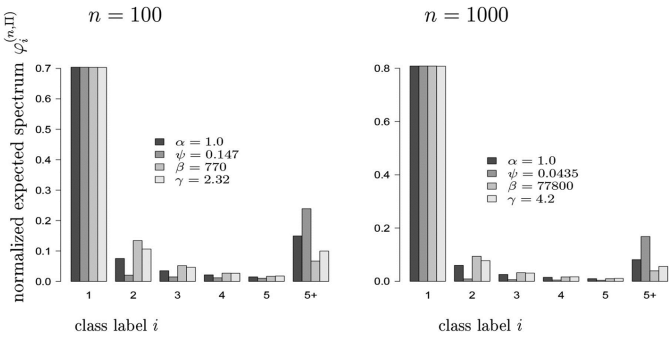

Figure 2 Example movie (the figure file above is used as a placeholder for this example). *GENETICS* supports video and movie files that can be linked from any portion of the article - including the abstract. Acceptable formats include .asf, avi, .wav, and all types of Windows Media files.

$\sigma^2 < \infty$, and let

$$S_n = \frac{X_1 + X_2 + \cdots + X_n}{n} = \frac{1}{n}\sum_i^n X_i \qquad (1)$$

denote their mean. Then as n approaches infinity, the random variables $\sqrt{n}(S_n - \mu)$ converge in distribution to a normal $\mathcal{N}(0, \sigma^2)$.

Literature Cited

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