Mining Human Prostate Cancer Datasets: The "camcAPP" Shiny App

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In Focus

Mining Human Prostate Cancer Datasets: The “camcAPP” Shiny App


Abstract

Obtaining access to robust, well-annotated human genomic datasets is an important step in demonstrating the relevance of experimental findings and, often, in generating the hypotheses that led to those experiments being conducted in the first place. We recently published data from the CamCaP Study Group which comprised two cohorts of men with prostate cancer who had undergone prostatectomy in Cambridge, UK and Stockholm, Sweden. We searched for other web-tools that are already available for this purpose. Although no such site exists for assessment of subgroup patterns or combined expression and copy number profiles, the Memorial Sloane Kettering Cancer Centre (MSKCC) and Michigan data can be analysed as part of cBioPortal. Here we introduce the camcAPP (http://bioinformatics.cruk.cam.ac.uk/apps/camcAPP/); a bespoke web interface to multiple prostate cancer genomics datasets. The interface was created with Shiny (https://www.rstudio.com/products/shiny/), and allows the non-specialist Bioinformatician to create publication-ready figures and tables through an intuitive interface to the underlying computer code. After selecting a dataset of interest, and uploading a list of genes, the following analyses can be performed:

1. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

2. Following analyses can be performed:

   a. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   b. Following analyses can be performed:

   i. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   ii. Following analyses can be performed:

   a. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   b. Following analyses can be performed:

   i. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   c. Following analyses can be performed:

   i. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   d. Following analyses can be performed:

   i. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.

   e. Following analyses can be performed:

   i. Boxplots and analysis of variance for expression of genes of interest grouped by clinical group, sample type, Gleason grade or copy number status of a single gene or gene-set in prostates from men divided either according to clinical categories (Gleason score, biochemical relapse status or tumour type) or according to molecular subgroups. These subgroups could either be pre-defined molecular groups published in the relevant papers, or de novo subgroups generated by hierarchical clustering based on an uploaded gene set.
number cluster (N.B. not all covariates available for all data sets) (see Supplementary Fig. 2).
2) A recursive partitioning-based survival analysis and Kaplan-Meier plots on a gene-by-gene basis (Supplementary Fig. 3).
3) Pairwise-correlations of gene expression across whole studies and within clinical subgroups.
4) Clustering and heatmaps of gene expression data, with options to interrogate associations between clinical covariates and newly-derived clusters (Supplementary Fig. 4).
5) Tabulating the number of copy-number amplifications and deletions observed across whole studies or within a particular clinical covariate, and making a heatmap of copy-number calls (Supplementary Fig. 5) (Lalonde et al., 2014).

One of the challenges in constructing such a tool is delivering an output format that is readily transferable to slides for presentations or panels of a figure for publication. We recognise that this is, in part, a matter of axis typesetting and plot configuration but also of delivering an output file which permits further adjustment of the figure in, for example, Adobe Illustrator™. To this end, all plots can be exported as PDF or PNG files with configurable dimensions. Furthermore, for those that are well-versed in R, the code to produce a particular plot can be downloaded and modified as required. A further challenge that we seek to address with this interface is merging datasets for combined analysis. We hope to offer this option in due course, as we include further datasets that include samples analysed on compatible platforms.

Strategies to address the Big Data problem have focused on making the ever-increasing volume of genomic data accessible to scientists and on opening up the possibility of engaging non-specialists (Keener, 2015). This approach embodies a responsible attitude to science both in terms of patient input and financial resource and we believe that tools such as this are an important step to maximising the value of these landmark studies. We take pleasure in making this platform available to the prostate cancer community by means of this ‘In Focus’ article in EBioMedicine, a journal that we believe champions this responsible attitude to science both in terms of patient input and further afield (Taudien et al., 2016).

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Authors’ contribution

Study concept: MD, AGL, ADL.

Study design: MD, AGL, ADL.
CamCaP Study Group leads: ADL, HRA.
Data programming: MD, SV, AGL.
Programme contributions: EL.
Beta testing: IGM, EL, PB.
Oversight: AGL, ADL.

Disclosure

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ebiom.2017.02.022. This includes a ‘manual’ for the Shiny App which can also be downloaded from the app itself.

References


Table 1

<table>
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<th>Dataset</th>
<th>Paper</th>
<th>Platform: gene expression</th>
<th>Platform: copy number</th>
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