The UCSC Xena Platform for cancer genomics data visualization and interpretation

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Abstract

UCSC Xena is a web-based visual integration and exploration tool for multi-omic data and associated clinical and phenotypic annotations. The investigator-driven platform consists of a web-based Xena Browser and turn-key Xena Hubs. Xena showcases seminal cancer genomics datasets from TCGA, Pan-Cancer Atlas, PCAWG, ICGC, GTEx, and the GDC; a total of more than 1500 datasets across 50 cancer types. We support virtually any type of functional genomics data modalities, including SNPs, INDELs, large structural variants, CNV, gene and other types of expression, DNA methylation, clinical and phenotypic annotations. A researcher can host their own data securely via private hubs running on a laptop or behind a firewall, with visual and analytical integration occurring only within the Xena Browser. Browser features include the high performance Visual Spreadsheet, dynamic Kaplan-Meier survival analysis, powerful filtering and subgrouping, charts, statistical analyses, genomic signatures, and bookmarks.

Paper

Introduction

Cancer is a complex disease arising from diverse genomic mechanisms (Hanahan 2011). Deciphering how normal cells transform into cancerous ones requires vast amounts of data (Ledford 2010). Recent advances, including high-throughput, whole-genome, and single-cell technologies, are now producing increasingly larger and more comprehensive genomics datasets (Mardis 2008). By 2025, the total amount of genomics data is expected to match the sum of the three other major producers of large data: astronomy, YouTube, and Twitter (Stephens 2015).

Cancer researchers need powerful, interactive visualization and analysis tools to extract knowledge from this deluge of information (Schroeder 2015). As the volume of data reaches the level of many petabytes, it is challenging but imperative that tools continue

to respond rapidly to researcher inquiries. Adding to the data volume, the variety of data modalities, such as gene expression and somatic mutation, are also expanding. Each of these modalities provides a unique window into the genome, which, in concert, give a comprehensive picture of an individual cancers' biology. Integration across these modalities is challenging but necessary togain a more in-depth understanding of the mechanisms for tumorigenesis, metastasis, and treatment response.

The highly distributed nature of this data also poses a significant challenge. Most investigators generate relatively small-scale datasets which are only used by a small number of individuals. In contrast, organized large consortia, such as TCGA (The Cancer Genome Atlas) (Chin 2011, Chin 2011) and the GDC (Genomic Data Commons) (Grossman 2016), generate or host large, high-value datasets that are used by researchers all over the world. Despite data sharing efforts, these two sources of data tend to be “siloed” and cannot be easily integrated or connected.

The UCSC Xena system was developed to enable cancer researchers of all computational backgrounds to explore large public datasets, as well as their own data, no matter where the data is located (Cieślik 2018, Langmead 2018). Xena hosts datasets from landmark cancer genomics resources including TCGA, ICGC (International Cancer Genome Consortium) (The International Cancer Genome Consortium 2010), and the GDC. The system easily supports tens of thousands of samples and has been tested up to as many as a million cells. The simple and flexible architecture supports a variety of common and uncommon genomic and clinical data types. Xena's unique visualizations integrate gene-centric and genomic-coordinate-centric views across multiple data modalities, providing a deep, comprehensive view of genomic events within a cohort of tumors.

Results

UCSC Xena (http://xena.ucsc.edu) is a visual integration and exploration tool for multi-omic data. The Xena platform has two components: the web-based Xena Browser and the back-end Xena Hubs (Figure 1). The Xena Browser empowers biologists to explore data in multiple Xena Hubs using a variety of visualizations and analyses. Each Xena Hub is able to host tens of thousands of samples and supports virtually every modality of functional genomics data. These turn-key hubs can be configured to be public or private and can be installed on laptops, public servers or those behind a firewall, or in the cloud (Figure 1). Any number of Xena hubs can be simultaneously connected to the Xena Browser with integration occurring in the browser. This allows for data to be distributed across multiple Xena Hubs.

The decoupled front-end Xena Browser and back-end Xena Hubs architecture has several advantages. First, researchers can easily view their own private data by installing their own Xena Hub. Data across multiple hubs are combined on the Xena Browser, allowing users to view data from separate hubs as a coherent data resource while keeping private data secure. More importantly, the Xena platform scales easily. As more datasets are generated, more Xena Hubs are added to the network, effectively growing with expanding genomics resources.

Public data resources

Cancer genomics research is increasingly multi-omic. Today, studies commonly collect data on somatic mutations, copy number and gene expression, with other data types such as structural variants and protein expression being relatively rare. However, as genomics technology advances, we expect that these rarer data types to increase in frequency and new data types to be produced. With this in mind we designed Xena to be able to load any tabular or matrix formatted data, giving us exceptional flexibility in the data types we can visualize. Current supported data modalities include somatic and germline SNPs, INDELs, large structural variants, copy number variation, gene-, transcript-, exon-, protein-expression, DNA methylation, phenotype, clinical data, and sample annotations. Additionally, our wrangled data can be downloaded in bulk and used for downstream analyses. We also offer programmatic access to slices of data through the Xena python package (https://github.com/ucscXena/xenaPython), which can be used independently or in a Jupyter Notebook to access any of the public Xena Hubs.

To showcase seminal cancer genomics data resources, we have deployed eight public Xena Hubs in the cloud-computing environment. Together, they host 1512 datasets from more than 50 cancer types, including the latest from TCGA, Pan-Cancer Atlas (Hoadley 2018), ICGC, PCAWG (Pan-Cancer Analysis of Whole Genomes, Campbell 2017), and the GDC (Table 1). Our TCGA hub hosts data from TCGA, the most comprehensive cancer genomics dataset to-date, with full set of data modalities for 12,000+ samples across 30+ cancer types. Xena TCGA hub hosts all public-tier TCGA derived datasets including somatic mutation, copy number variation, gene and exon expression, and more. Our PancanAltas hub hosts data from the latest TCGA project, the Pan-Cancer Atlas, which conducted an integrative molecular analysis of the all tumors in TCGA. In addition to being uniformly analyzed, there are also highly curated datasets such as molecular subtypes and multiple survival endpoints. Our ICGC hub hosts data from the ICGC project, a global effort to create a comprehensive description of genomic, transcriptomic and epigenomic changes in 50 different tumor types. Our PCAWG hub supports the PCAWG project, an analysis of 2,600 ICGC whole-cancer genomes and their matching normal tissues across 39 distinct tumour types (Campbell

2017). Its datasets include somatic mutation data from the whole genome, large structural variants, RNAseq-based data analysis, mutational signatures, curated histology, and more. Our GDC hub hosts data from GDC, where TCGA and TARGET data was uniformly recomputed using state-of-art pipelines and the latest human genome assembly, hg38. In addition to these well-known resources, we also host results from the Toil RNAseq analysis pipeline, a uniformly re-aligned and re-called gene and transcript expression dataset for all TCGA, TARGET and GTEx samples (Vivian 2017). This dataset allows users to compare gene and transcript expression of TCGA 'tumor' samples to corresponding GTEx 'normal' samples. Our Treehouse hub combines data from the Toil hub with Treehouse project (https://treehousegenomics.soe.ucsc.edu/explore-our-data/) pediatric samples to facilitate interpretation of a pediatric sample in a larger context. The UCSC Public hub has data we curated from various literature publications such as CCLE (Cancer Cell Line Encyclopedia, Barretina 2012). Xena complements each of these data sources by not storing any raw sequencing data, but instead, loading derived datasets, such as gene expression estimation and somatic mutation calls, and providing powerful interactive visualizations for these data. All public Xena hubs (https://xenabrowser.net/hub/) are open access, with no account or login required.

Turn-key Xena Hub

Xena Hubs are designed to be turn-key, allowing users who may not be computationally savvy to install and run a Xena Hub on their personal computer. Hubs are easily initiated using a point-and-click interface or through the command line (http://xena.ucsc.edu/private-hubs/). Xena Hubs run on most operating systems, including Windows, MAC and Linux. A dockerized version of the Xena Hub can be used as part of an automated workflow pipeline to visualize computational results.

Xena Hubs can be configured to be private or public. Hubs running on a laptop are private as they only allow connections from the users' own Xena Browser. Users can use a laptop hub to quickly and securely view their own data. Xena Hubs started in the cloud or on a server can be kept private by using a firewall. This enables easy sharing of pre-publication data within a lab, institution, or as part of a larger collaboration. They also can be configured to be public, making the data accessible to the larger community after investigation and publication.

Performance is critical for an interactive visualization tool, especially on the web. As the sample size for genomic experiments steadily increases, this has become a challenge for many tools. Knowing this, we optimized Xena to support data queries on tens of thousands of samples and more, serving slices of genomic and clinical data within a few seconds.

Xena Browser

The Xena Browser is an online visual exploration tool for data in one or more Xena Hubs. Our visualizations and analyses include the Xena Visual Spreadsheet, survival analysis, scatter plots, bar graphs, statistical tests and genomic signatures. Sophisticated filtering and searching allows the comparison of dynamically generated subgroups. In addition to Xena's own views, it connects with a variety of complementary visualization tools. The Xena Browser supports dynamic genomic signatures, allowing users to explore correlations between a score and other -omic data. Its shareable bookmarks and high resolution pdfs enhance collaborations and results dissemination. We support modern web browsers such as Chrome, Firefox or Safari.

Visual Spreadsheet

With multi-omic data, it is essential to view different types of data, such as gene expression, copy number, and mutations, on genes or genomic segments side-by-side. Integration across these diverse data modalities provides a more biologically complete understanding of a genomic event. We designed our primary visualization, the Xena Visual Spreadsheet, to facilitate this integration. Analogous to an office spreadsheet application, it is a visual representation of a data grid where each column is a slice of genomic or phenotypic data (e.g. gene expression), and each row is a single entity (e.g. a bulk tumor sample, cell line, or single cells) (Figure 2). Rows of these entities are dynamically sorted by the columns of genomics data, enabling the discovery of patterns and correlations among genomic parameters. Xena's Visual Spreadsheet data grid displays multiple user-requested slices of genomic and phenotypic data over a cohort of samples. It excels at integrating diverse sets of genomics data and dynamically sorting rows and columns to explore patterns, even when the data are hosted across multiple data hubs.

Xena's Visual Spreadsheet displays genomic data in both gene-centric and coordinate-centric views. Gene-centric views show data mapped to a gene or portion of a gene, such as exons, transcripts, or specific CpG islands, and can display only exonic regions or include data mapped to introns. The coordinate-centric view shows data along the genomic coordinate, displaying genomic events such as copy number variation, simple mutations or structural variants (Supplemental Figure 1). Genomic intervals, from base level up to an entire chromosome, can be viewed through entering specific coordinates or through dynamic zooming. Both gene- and coordinate-centric views support coding and non-coding regions (Supplemental Figure 2). Links to the UCSC Genome Browser give genomic context to any chromosome region. In addition to these various genomics views, we also visualize phenotype and clinical data such as age, gender, expression signatures, cell types, and subtype classifications. These crucial phenotypic data enable

users to go beyond the genomic-only discoveries. All these different columns and views can be placed side-by-side in a single Xena Visual Spreadsheet.

The power of the Visual Spreadsheet is its data integration. Integration across different data modalities, such as copy number variation, gene expression and DNA methylation, gives users a more comprehensive view of a genomic event in a tumor sample. For example, higher expression for a gene can be driven by copy number amplification or by promoter hypomethylation. Integration across gene- and coordinate-centric views helps users examine these events in different genomic contexts. For example, a copy number amplification event can be part of chromosomal arm duplication or a focal amplification. Integration across genomic and clinical data gives users the ability to make connections between genomic patterns and clinically relevant phenotypes such as subtype and survival. For example, a mutation in a gene can lead to lower recurrence-free survival. These diverse integrations help researchers harness the power of comprehensive genomics studies, driving discovery and a deeper understanding of cancer biology.

More browser visualizations and functionalities

In addition to the Visual Spreadsheet, we support several other powerful views and analyses. Our Kaplan-Meier analysis allows users to statistically assess survival stratification by any genomic or phenotypic data (Figure 3). Bar charts, box plots and scatter plots, all with statistical tests automatically computed (chi-squared, t-test, or ANOVA as appropriate), provide additional insights into the data (Supplemental Figure 3). The Transcript View enables easy comparison of transcript-level expression between two groups, such as TCGA 'tumor' vs. GTEx 'normal', for all the transcripts of a gene (Figure 4). We also provide context-dependent links to complementary visualizations such as the Tumor Map (https://tumormap.ucsc.edu) (Newton 2017) and MuPIT in CRAVAT (http://mupit.icm.jhu.edu/) (Niknafs 2013), enabling users to easily see a genomic pattern from a different perspective.

Gene-expression signatures have been developed to differentiate distinct subtypes of tumors, identify important cellular responses to their environment (hypoxia), and predict clinical outcomes in cancer (Sotiriou 2009). Xena's genomic signature functionality allows users to enter a signature expressed as a weighted sum of a marker gene set, a common form seen in publications, and dynamically build a new spreadsheet column of the resulting scores. This functionality allows researchers to test existing signatures or build new ones, allowing comparison of the signature score with other genomic and phenotypic data.

Our powerful text-based search allows users to dynamically highlight, filter and group samples (Figure 5). Researchers can search the data on the screen similar to the ‘find’ functionality in Microsoft Word. Samples are matched and highlighted in real-time as the user types. Researchers can filter, focusing the visualization to their samples of interest, or dynamically build a new binary column, where samples are marked as 'true' or 'false', depending if they meet the researcher's search criteria. The new two-group column behaves like any other column and can be used in a Kaplan-Meier analysis, box plot, or other statistical analysis to compare the two sample groups. The find-highlight-new-column functionality is a powerful way to dynamically construct two sub-populations of samples for comparison and analysis.

Being able to share and distribute biological insights is crucial in this era of collaborative genomics. Xena’s bookmark functionality enables the sharing of live views. With a single click, users can generate a URL of their current view, which will take researchers back to the live browser session. The URL can be shared with colleagues or included in reports or publications. If a view contains data from a non-public Xena Hub, we allow users to download the current visualization state as a file. This file can then be appropriately shared and imported into the Xena Browser to recreate the live view. By giving users a file instead of a URL, we ensure that we never have the user's private data on our servers. In addition to bookmarks, researchers can generate a high resolution PDF figure of their current visualization for presentations and publications.

To assist researchers in building a Visual Spreadsheet, we developed a short three-step guided wizard. This ensures that even new users who are unfamiliar with Xena can build basic visualizations. We also provide links to live examples that showcase useful and scientifically interesting visualizations, highlighting the power of Xena. We focus on supporting our users by developing training videos, online and in-person workshops, and help documentation. We keep users up-to-date on new features and datasets through our social media accounts, mailing lists and monthly newsletter.

Discussion

UCSC Xena is a tool for cancer researchers to explore, visualize, and analyze functional genomics data. We host many large public datasets, such as TCGA, Pan-Cancer Atlas, PCAWG, GDC, and ICGC, helping to make these powerful resources accessible to investigators. The Visual Spreadsheet, sophisticated filtering and subgrouping, and Kaplan-Meier analysis enable researchers of all computational backgrounds to investigate complex genomics datasets. We support virtually all data modalities including mutations, copy number, expression, phenotype and clinical data as well as rare data types such as non-coding mutations, large structural variants, and

RNAseq-based gene fusion calls. Integration across different data modalities and visualizations, as well as between genomic and clinical data yield insightful views into cancer biology.

UCSC Xena complements existing tools including the cBio Portal (http://www.cbioportal.org/, Cerami 2012), ICGC Portal (https://dcc.icgc.org/, Zhang 2011), GDC Portal (https://portal.gdc.cancer.gov/, Jensen 2017), IGV (http://software.broadinstitute.org/software/igv/, Thorvaldsdóttir 2013), and St. Jude Cloud (https://stjude.cloud/, Ma 2018), by focusing on providing a federated platform to visualize data across multiple hubs simultaneously. This enables biologists to easily view their own data as well as consortium data while still maintaining data privacy. Additionally, Xena focuses on simultaneous, integrative visualization of multi-omics datasets across different genomic contexts, including gene, genomic element, or any genomic region for both coding and non-coding part of the genome. Finally, Xena is built for performance. It can easily visualize of tens of thousands of samples in a few seconds and has been tested up to a million cells. With single-cell technology becoming more common, functional genomics datasets will increase in size several orders of magnitude larger than traditional bulk tumor samples. Xena is well-positioned to rise to the challenge.

While it is widely recognized that data sharing is key to advancing cancer research, how it is shared can impact the ease of data access. UCSC Xena is a designed for cancer researchers both with and without computational expertise to share and access data. Users without a strong computational background can explore their own data by installing a Xena Hub on their personal computer using our point-and-click interface. Bioinformaticians can install a private or public Xena Hub on a server or in the cloud or as part of an analysis pipeline, making the generated data available in a user-friendly manner that requires little extra effort. Data sharing has, and will continue to, advance cancer biology and Xena is part of the technological ecosystem that helps support this priority.

UCSC Xena is a scalable solution to the rapidly expanding and decentralized cancer genomics data. Xena's architecture, with it’s detached data hubs and web-browser-based visualization, allows new projects to easily add their data to the growing compendium that we support. Additionally, by maintaining a flexible tabular and matrix data input format, we support many different data modalities, both current and future. In this age of expanding data resources, Xena's design supports the ongoing needs of the cancer research community.

Xena excels at viewing cohorts of samples, cells, or cell lines and showing trends across those entities, whether they be human or a model organism. While we have focused on cancer genomics, the platform is general enough to host any functional genomics data. We hope to expand Xena to continue to help serve the genomics needs of the biomedical community.

Acknowledgements

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Methods

Data

Functional genomics data are downloaded from each respective source,, wrangled into a generic tabular or matrix format, and then loaded into a corresponding hub. Specific wrangling steps along with any normalization that was performed is listed for each dataset in the Xena Browser dataset pages (https://xenabrowser.net/datapages/). The wrangled data is available for download from the dataset pages.

Xena Hub

The Xena Hub is a JVM-based application, written in Clojure, that serves functional genomic data (http://xena.ucsc.edu/private-hubs/) over HTTP. It exposes a relational query API for metadata and data slicing. Using a query language instead of REST allows us to decouple the client and server. To support interactive visualization REST APIs have to be denormalized for performance (e.g. by joining related objects, and projecting the result). This creates a tight coupling between the REST endpoints and particular views: a novel view requires a novel denormalization. A query language allows us to fetch exactly the data we need, and only the data we need, for quickly evolving visualizations and data shapes, without redeployment of the hubs. This is similar in motivation to Facebook's GraphQL, and Netflix's Falcor, but predates them.

Internally, Xena Hubs use the H2 database for storage. Data is stored in opaque blocks in a column orientation, which allows fast retrieval of a field for all samples of a dataset,

or a subset of samples. A hub can be installed either via the command line or via the point-and-click install4j GUI.

Xena Browser

The Xena Browser is a javascript application to visualize and analyze functional genomics data stored in one or more Xena Hubs. The primary technologies are React, the 2D canvas API, and RxJS. Babel is used for es6 support, and webpack for the build. The application architecture is an asynchronous model similar to redux-observable (https://redux-observable.js.org/), with semantic actions that update application state, and action side-effects creating Rx streams that will dispatch later actions. The redux (https://redux.js.org/), or Om (https://github.com/omcljs/om), pattern of immutable, single-atom state makes it simple to keep multiple views in sync, and provides “time travel” debugging during development.

We prefer the canvas API to SVG libraries such as D3, because it performs better at our data scale. With the advances in javascript JIT compilers, we find that optimized loops over canvas pixel buffers out-perform geometric drawing primitives, such as *rect()*, and *stroke()*, when rendering dense views of large data.

The jsverify property-based testing library (http://jsverify.github.io/) is used for unit and integration testing. Property-based, or "generative" testing is similar to fuzzing -- generating random test cases, and asserting invariants over the results -- but on failure, attempts to find a minimal failing test case. This usually results in more tractable failure cases. Property-based testing allows us to test a much larger portion of the input space than conventional "known-answer" unit tests, and frequently identifies failure cases that we would never think to test.

All of our code is open source and available for reuse under and Apache 2.0 license (https://github.com/ucscXena). We also have contributed two javascript modules to BioJS (Gómez 2013), including a Kaplan-Meier module (https://github.com/ucscXena/kaplan-meier) to compute Kaplan-Meier statistics, and a static-interval-tree library (https://github.com/ucscXena/static-interval-tree) to effectively find overlapping intervals in one dimension.

Public Xena Hubs

We deploy all public-facing hubs in a cloud-computing environment.

Figures and Tables

Figure 1

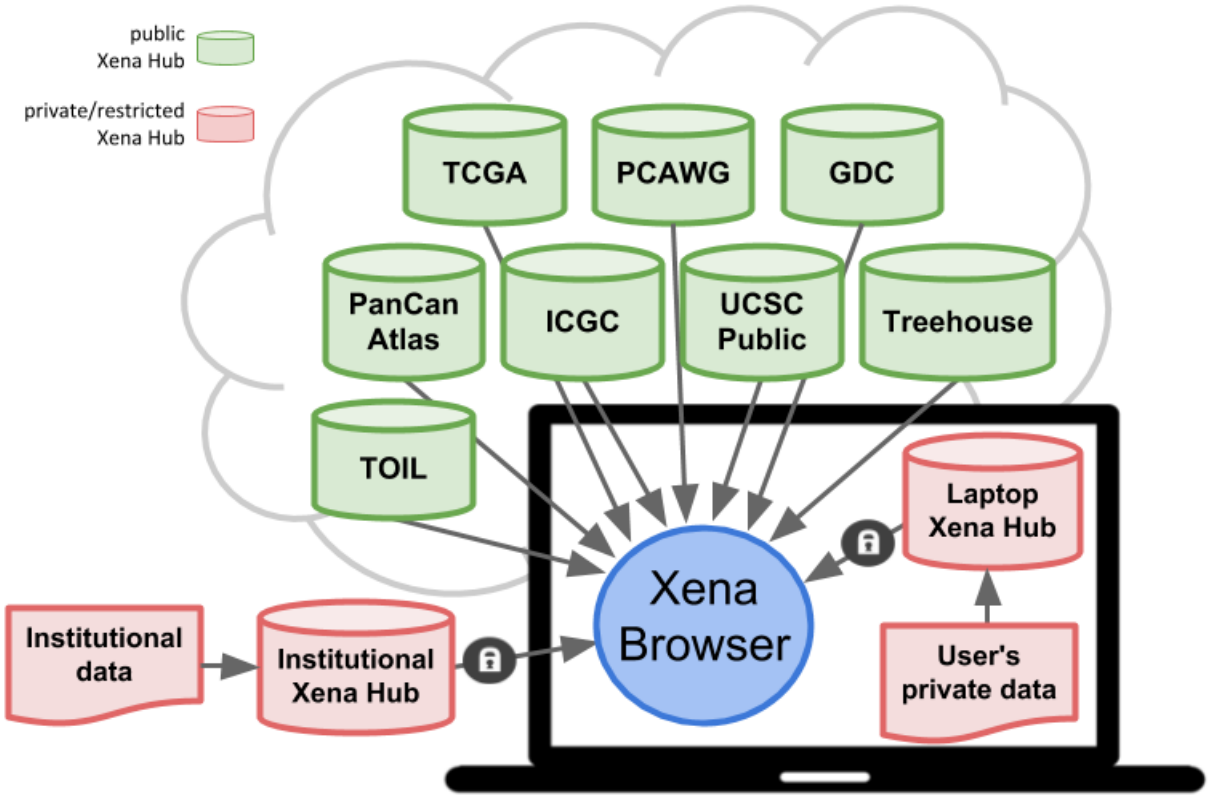


Figure 1. Diagram of the UCSC Xena platform architecture. Multiple Xena Hubs (each shown as a database icon) are connected to the Xena Browser simultaneously. Public Hubs are in green and and private Hubs in red. In this example, private data from an independent research collaboration (in red) can be loaded into their own private Xena Hubs, on their servers or on a researcher's computer. Data integration occurs within the Xena Browser on the user's computer. The lock icon indicates that only authorized users have access to the private Xena Hubs. This design achieves data integration across both public and private resources while maintaining each hub's data confidentiality.

Figure 2

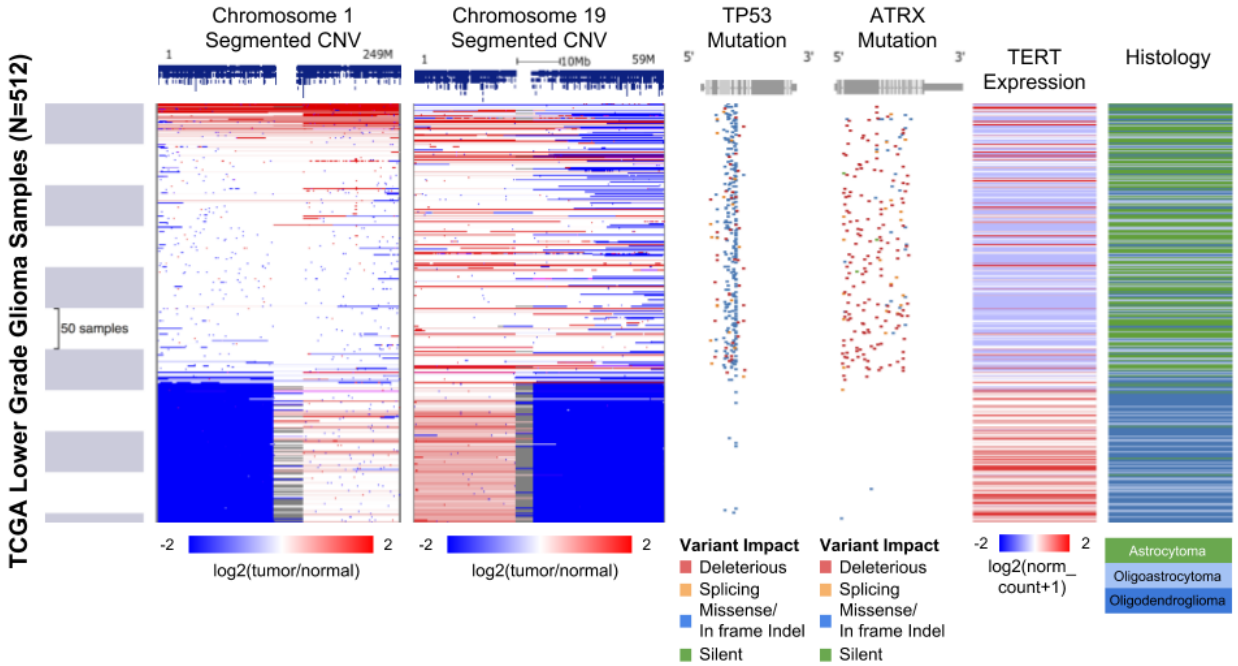


Figure 2. A Xena Visual Spreadsheet showing genetic separation of TCGA lower grade gliomas into two distinct groups with the bottom group being characterized by loss of chromosome arms 1p and 19q, and relatively high expression of TERT and the top one by TP53 and ATRX mutations. Each row in the view corresponds to a single sample. The first column shows the scale of samples and is followed by data columns. The rows are sorted by the left most data column (column B) and sub-sorted on subsequent columns. Starting on the left, data columns are chromosome 1 and 19 copy number segments, TP53 and ATRX mutation status, TERT gene expression, and sample histology. Copy number segments (columns B, C) display genes in dark blue at the top. Amplifications are in red and deletions in blue. Mutations (columns D, E) show a gene diagram at the top with exons in grey boxes with coding regions being taller and untranslated regions being shorter. The position of each mutation is marked in relation to the gene diagram and colored by its functional impact. Deleterious mutations are in red, missense mutations and in-frame indels are in blue, and synonymous mutations are in green. Gene expression (column F) is colored red to blue for high to low expression. Samples at the top of the view are enriched for the astrocytoma histological subtype, while the samples at the bottom tend to be the oligodendroglioma subtype. https://xenabrowser.net/heatmap/?bookmark=6b236d77538128421ee9c32911ce173a

Figure 3

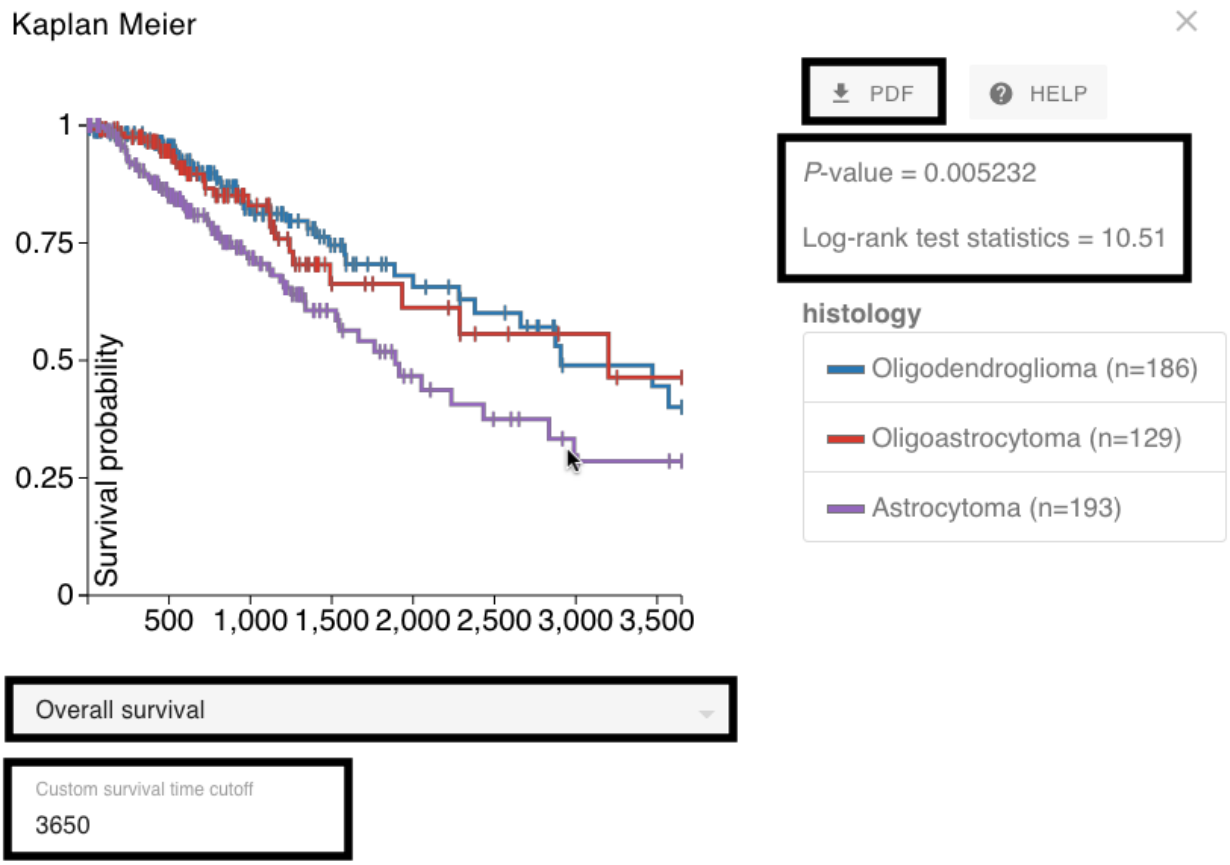


Figure 3. A Xena Kaplan-Meier analysis of overall survival for the TCGA lower grade glioma histological subtypes. Black boxes in the figure highlight, top to bottom, the ability to generate a PDF, statistical analysis results, the ability to select different survival endpoints such as overall or recurrence-free survival, and custom survival time cutoff (currently set to 3,650 days, or 10 years). This figure shows that patients characterized as having the astrocytoma histological subtype have significantly worse 10-year overall survival compared to the oligodendroglioma and oligoastrocytoma subtypes ($p < 0.05$).
https://xenabrowser.net/heatmap/?bookmark=2f9d783982879594dd0f52564058372d

Figure 4

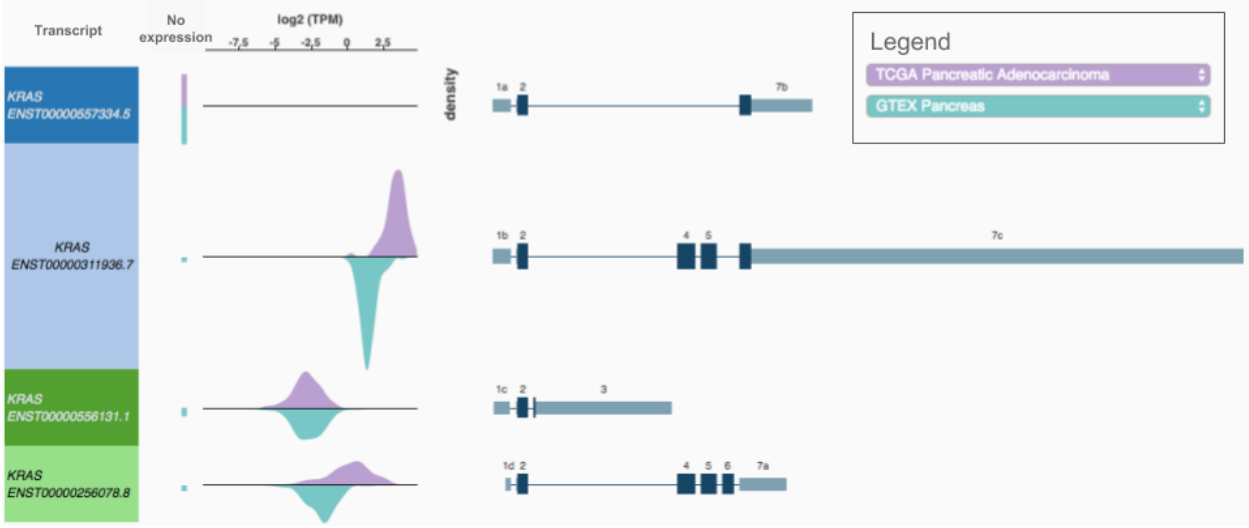
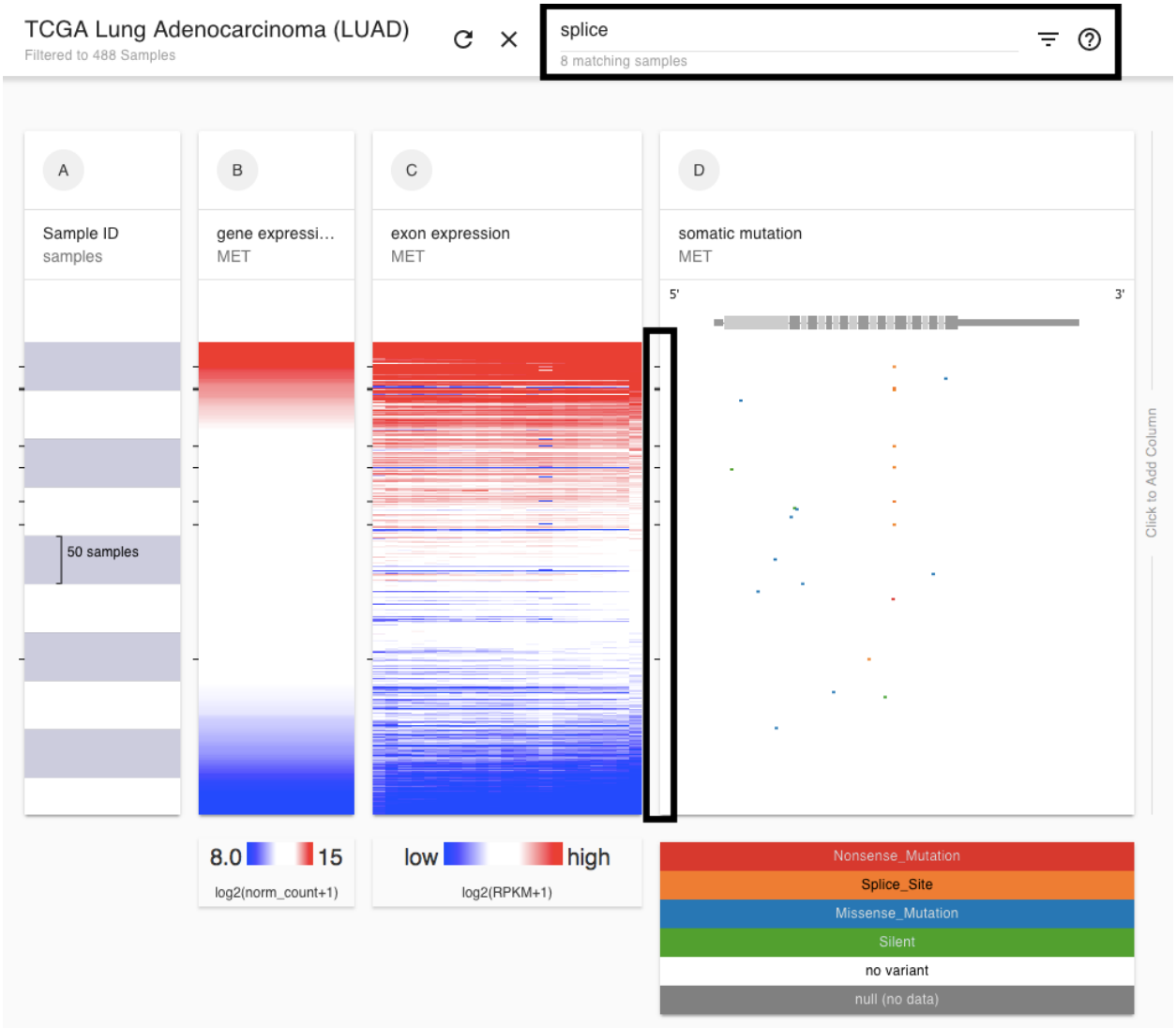


Figure 4. A Xena Transcript View showing four KRAS transcripts' expression for TCGA pancreatic adenocarcinoma and GTEx normal pancreas tissue. To generate a view, a researcher enters a gene and select two populations. The visualization will display, for all transcripts for that gene, a double (top and bottom) density distribution of transcript expression in each population. We see that for KRAS, transcript ENST00000311936.7 (second from the top), has higher expression in pancreatic tumors (TCGA) compared to the normal pancreas tissue (GTEx).
http://dev.xenabrowser.net/transcripts/?bookmark=80d9c57b471b654cc569d4ceb44e6591

Figure 5

a.


TCGA Lung Adenocarcinoma (LUAD)
Filtered to 488 Samples
splice
8 matching samples
A
Sample ID
samples
50 samples
B
gene expressi...
MET
C
exon expression
MET
D
somatic mutation
MET
5'
3'
Click to Add Column
8.0
15
log2(norm_count+1)
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Missense_Mutation
Silent
no variant
null (no data)

b.

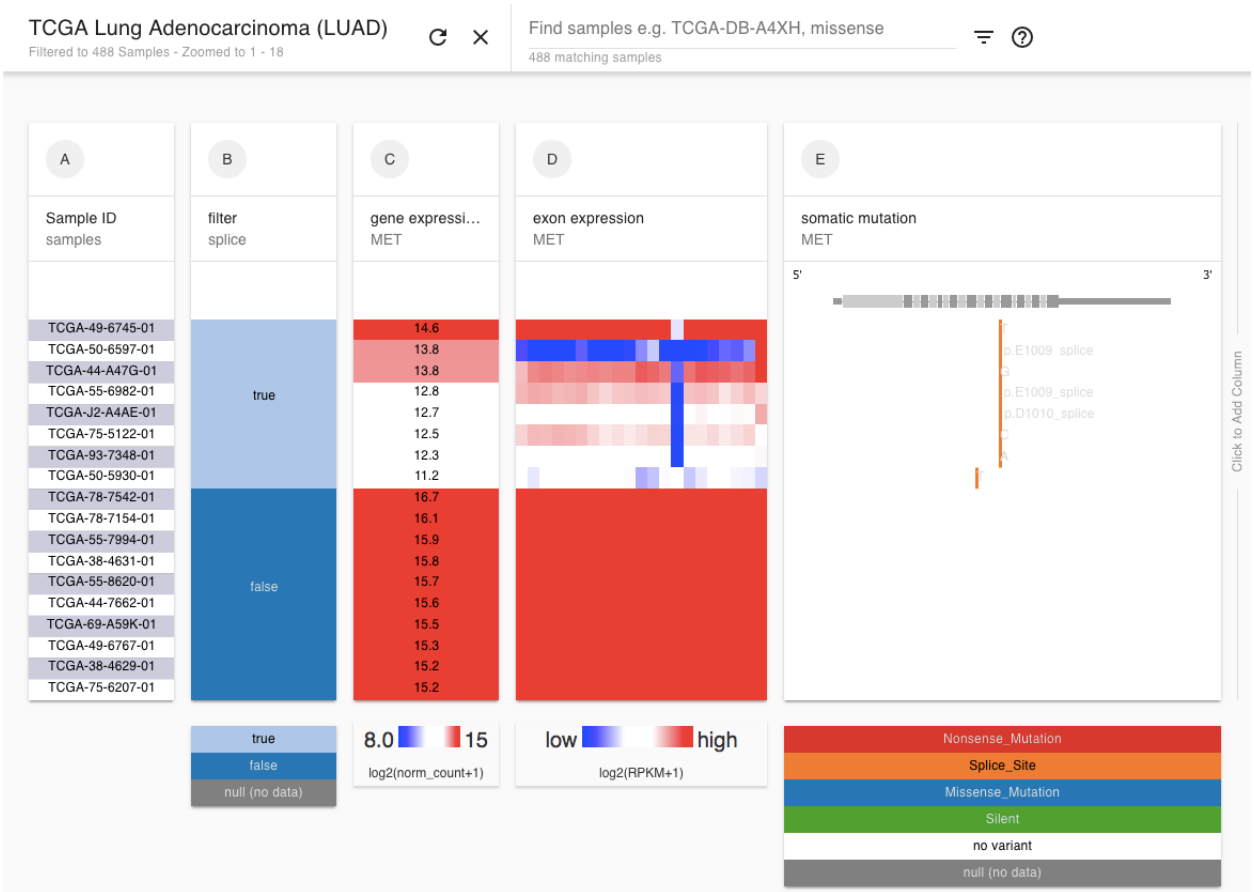


Figure 5. Xena Browser text-based find, highlight, filter, and subgroup samples functionality. **(a)** Finding and highlighting samples in TCGA lung adenocarcinoma cohort that have a splice mutation in MET. Similar to the 'find in document' feature in Microsoft Word, users can search all data on the screen. In this figure, the Xena Browser searched all columns for the user's search term 'splice' and highlighted those samples with a 'splice' mutation with black tick marks (indicated by the black box). Other supported operations include 'AND', 'OR', '>', '<', '=', and more. Users can dynamically filter, zoom, and create subgroups based on the search results. Columns from left to right are MET gene expression, MET exon expression and MET somatic mutation status.
https://xenabrowser.net/heatmap/?bookmark=d145daa18123218d4a37af0ec214b95c
(b) After creating a new column with two subgroups. Columns left to right are same as (a) with an additional user-generated column on the left created from the search. Samples that matched the query of 'splice' were assigned a value of "true" and those that do not "false". The researcher has zoomed to the few samples at the top for a more detailed view. The figure shows that samples that have the splice site mutation (orange, column E) have lower expression of exon 14 within the MET gene (column D). The splice mutation causes exon 14 skipping and results in the activation of MET (Kong-

Beltran 2006, The Cancer Genome Atlas Research Network 2014).
https://xenabrowser.net/heatmap/?bookmark=2239102135132b7fbd482204aa723a95

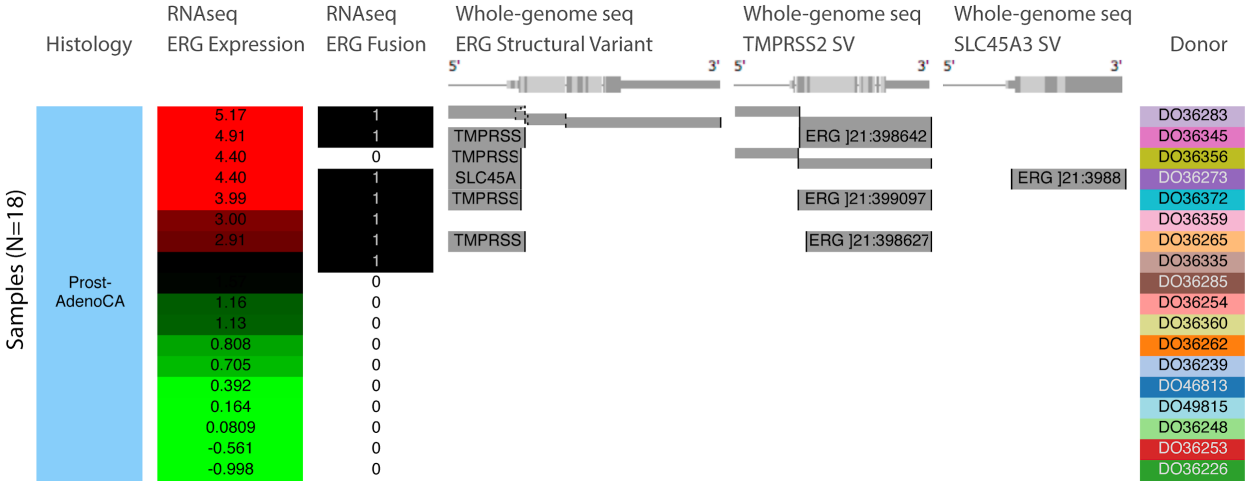
Table 1

Data Hub	Samples	List of Data Types
TCGA	12,811	copy number, gene-, exon-, miRNA-, and protein-expression, somatic mutation, DNA methylation, survival, and clinical data
Pancan Atlas	12,591	copy number, gene-, miRNA-, and protein-expression, somatic mutation, DNA methylation, molecular subtypes, curated survival, and clinical data
ICGC	17,677	copy number, gene expression, somatic coding mutation, and somatic whole-genome mutation (non-TCGA only)
PCAWG	3,205	whole-genome copy number, somatic mutations, large structural variants, gene- and miRNA-expression, RNAseq based gene fusion, alternative promoter usage, RNAseq based slicing events, purity, ploidy, mutational signature, survival, and curated histology
Toil	19,340	TCGA, TARGET and GTEx gene and transcript expression
GDC	20,157	copy number, somatic mutations, gene and miRNA expression, overall survival, and phenotypes
Treehouse	11,078	TCGA, TARGET and Treehouse partnering clinical studies gene and transcript expression
UCSC Public	*	Somatic mutation, gene expression, copy number, and clinical data on adult and pediatric cancer, cell lines and mouse models

Table 1. Summary of data hosted on Public Xena Hubs. *Number of samples is not listed for the UCSC Public Hub because each of the 44 cohorts are individual studies.

Supplemental Figures

Supplemental Figure 1

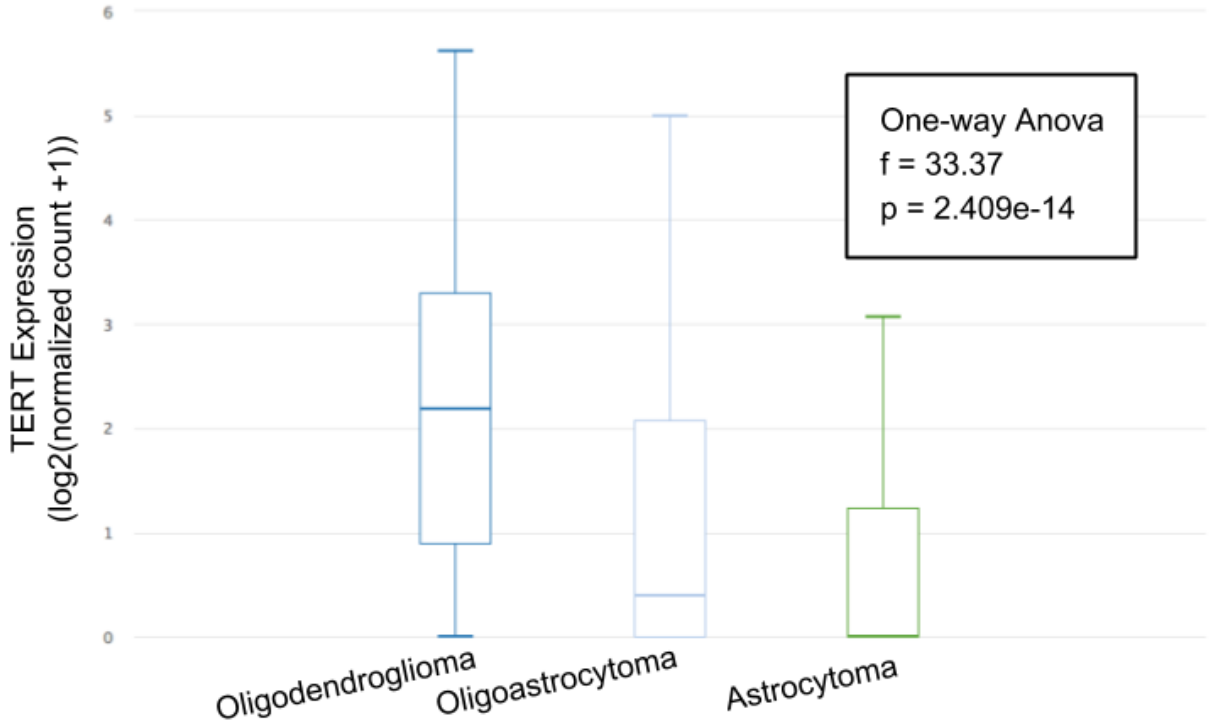


Supplemental Figure 1. Visualization of large structural variants. This figure shows the frequent ERG fusion in PCAWG prostate cancer detected by both RNA-seq and DNA-seq analysis. Columns, starting at the left, correspond to histology, ERG gene expression, and ERG fusion based on RNA-seq data. Gene expression is colored red to green for high to low expression. In the ERG fusion column samples that have a fusion are marked with 1 and those that do not are marked with 0. The next three columns show structural variant calls made using whole-genome DNA-seq data for ERG, TMPRSS2, and SLC45A3. Precise breakpoints are mapped to gene annotations. A grey bar indicates an external piece of DNA that is fused at the breakpoint. Gene names on the grey bars show the origin of the external DNA that is joined. This figure shows that TMPRSS2 and SLC45A3 are fusion partners for ERG, and that these fusions correlate with over-expression of ERG. Fusions detected by RNA-seq and whole-genome sequencing are not always consistent. Here, even using a consensus of DNA-based detection methods, one fusion detected by a consensus of RNA-based detectors is missed, and the converse is also seen. This example shows that an integrated visualization across multiple data types and algorithms provides a more accurate model of a genomic event.
https://xenabrowser.net/heatmap/?bookmark=24ad428d0f3bf3bf3205bcffab64d276

Supplemental Figure 2

Supplemental Figure 2. Visualization of both coding and non-coding mutations from a gene-centric perspective in ICGC lymphoma. The columns left to right are cancer type, BCL2, BCL7A, BIRC3 and ST6GAL1 mutation status, respectively. Gene diagrams are shown at the top of each column with exons in light and dark grey boxes with coding regions being taller and untranslated regions being shorter. The position of each mutation is marked in relation to the gene diagram and colored by its functional impact, with deleterious mutations in red, missense mutations and in-frame indels in blue, synonymous mutations in green, splice site mutations in orange, and mutations with an unknown functional impact in grey. This figure shows the frequent intronic mutations in these genes, which are visible via our dynamic toggle to show or hide introns. These mutation 'pile-ups' would be not be visible if viewing exomes only. While the majority of the intronic mutations in this view have an unknown impact (shown in grey), they do overlap with known enhancers regions (Mathelier 2015).
https://xenabrowser.net/heatmap/?bookmark=d2a79e46e22456036a732c49c2e4c5b3

Supplemental Figure 3



Supplemental Figure 3. Xena Chart View showing a box plot of TERT expression for each of the TCGA lower grade glioma histological subtypes. Columns created in the Visual Spreadsheet (Figure 2) are used to construct the chart. Statistical analyses are automatically computed. This view shows a significant expression difference for TERT between oligodendroglioma, oligoastrocytoma and astrocytoma histologies (one-way ANOVA, $p < 0.05$).
https://xenabrowser.net/heatmap/?bookmark=ae1a7f260e8d95bd3c1742503de32192

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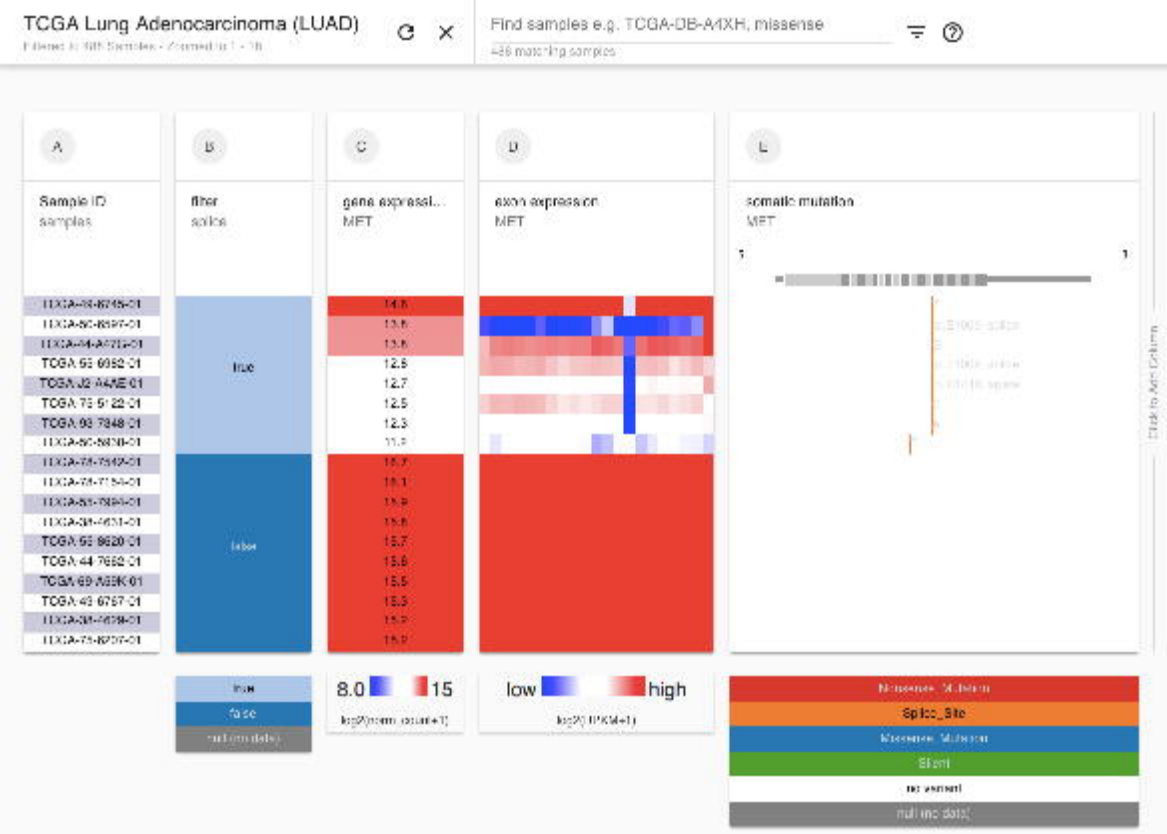
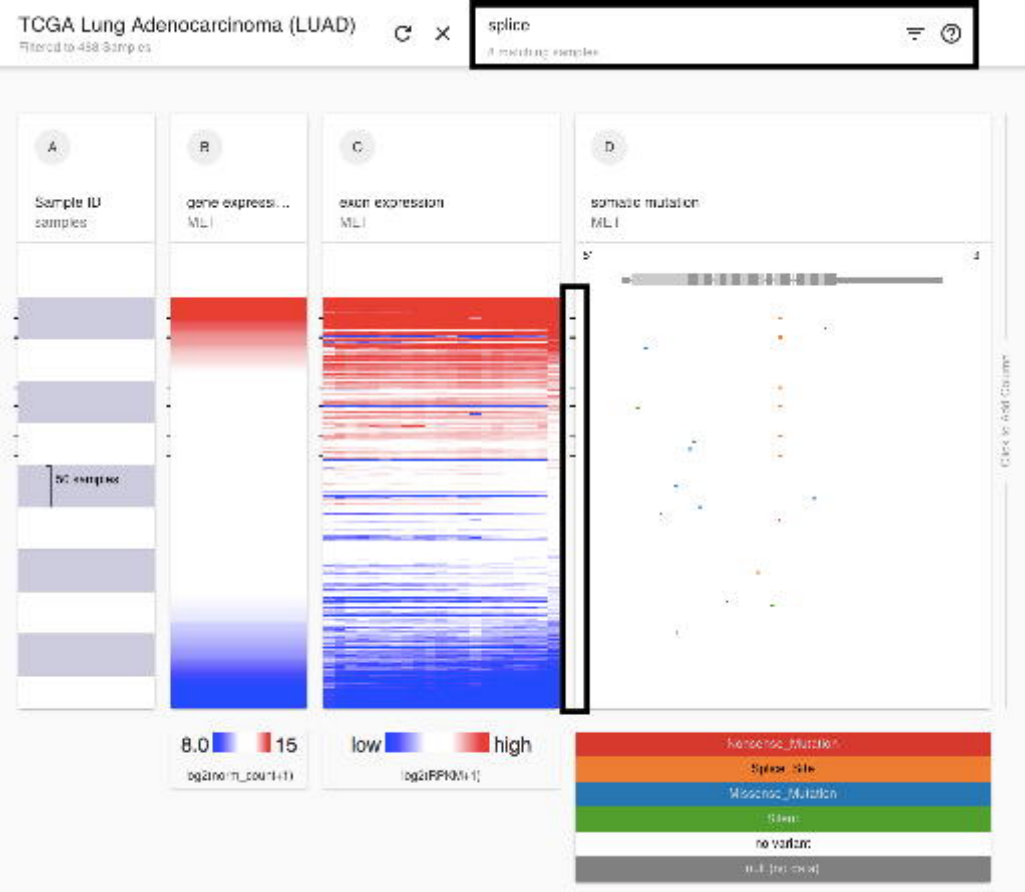
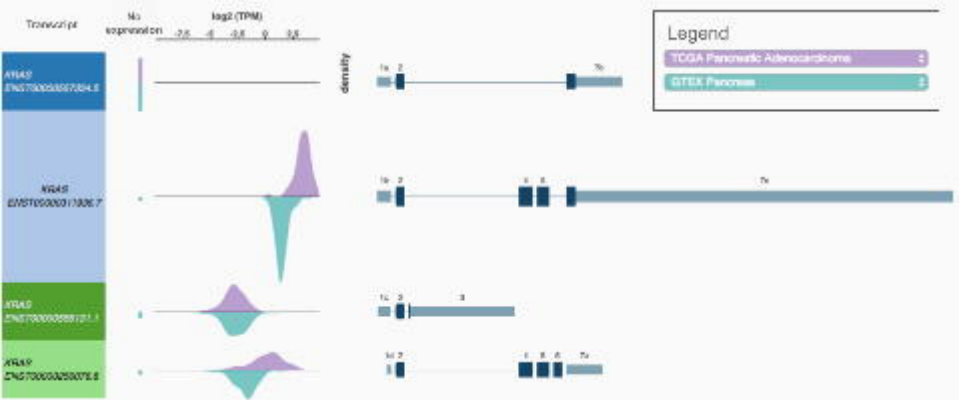

TCGA Lung Adenocarcinoma (LUAD)
Find samples e.g. TCGA-DB-A4XH, missense
A
B
C
D
E
Sample ID
samples
filter
solid
gene expressi...
MET
exon expression
MET
somatic mutation
MET
true
false
14.6
13.6
13.6
12.6
12.7
12.5
12.3
8.0
15
low
high
Missense_Mutation
Splice_Site
Missense_Mutation
Silent
no variant
multiple data


TCGA Lung Adenocarcinoma (LUAD)
Filtered to 458 Samples
splice
A
Sample ID
samples
B
gene express...
MLI
C
exon expression
MLI
D
somatic mutation
MLI
8.0
15
low
high
Nonsense_Mutation
Splice_Site
Missense_Mutation
Silent
no variant


Transcript
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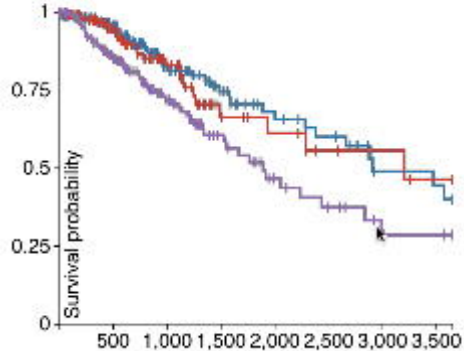
log2 (TPM)
density
Legend
TCGA Pancreatic Adenocarcinoma
GTEX Pancreas

Kaplan Meier



PDF

HELP

P-value = 0.005232

Log-rank test statistics = 10.51

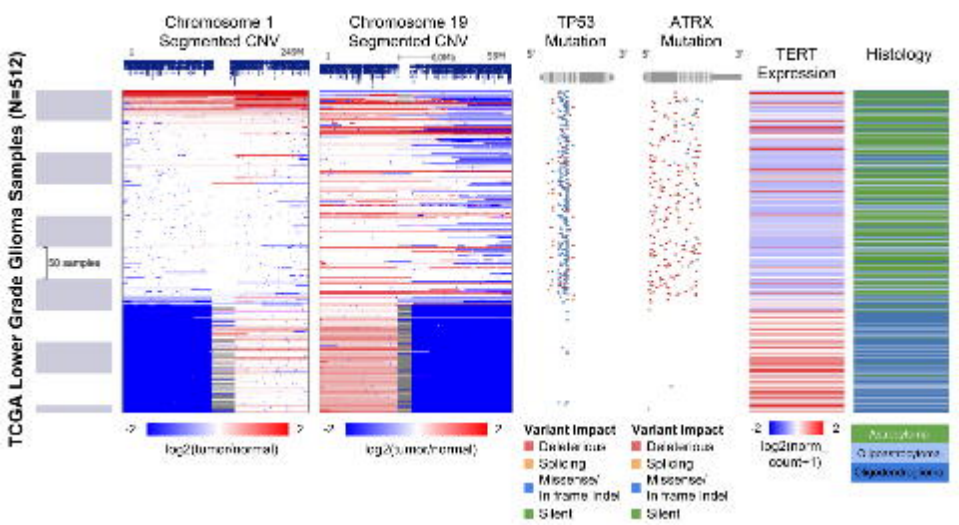
histology

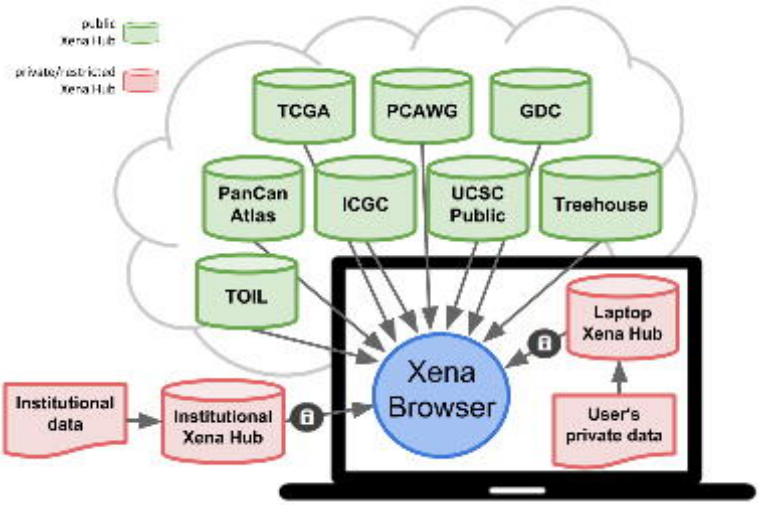
- Oligodendroglioma (n=186)
- Oligoastrocytoma (n=129)
- Astrocytoma (n=193)

Overall survival

Custom survival time point

3650


Chromosome 1
Segmented CNV
Chromosome 19
Segmented CNV
TP53
Mutation
ATRX
Mutation
TERT
Expression
Histology
TCGA Lower Grade Glioma Samples (N=512)
50 samples
log2(tumor/normal)
log2(tumor/normal)
Variant Impact
Deleterious
Splicing
Missense/
In frame indel
Silent
Variant Impact
Deleterious
Splicing
Missense/
In frame indel
Silent
log2(norm.
count+1)


public
Xena Hub
private/restricted
Xena Hub
TCGA
PCAWG
GDC
PanCan
Atlas
ICGC
UCSC
Public
Treehouse
TOIL
Laptop
Xena Hub
Xena
Browser
Institutional
data
Institutional
Xena Hub
User's
private data