927 STREAMLINING CANCER IMMUNOTHERAPY RESEARCH WITH THE CRI IATLAS DATA RESOURCE AND WEB PORTAL

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Background With the increased volume of genomics data from studies involving treatment with immune checkpoint inhibition (ICI) and other immunotherapies, researchers remain unable to to make full use of results due to lack of comprehensive access to data or th ability to compare outcomes across datasets.The Cancer Research Institute (CRI) iAtlas[1] (www.cri-iatlas.org) is a comprehensive web platform for interactive data exploration and discovery in immuno-oncology, originating in a study by The Cancer Genome Atlas (TCGA).[1–3] iAtlas provides topic-oriented analysis modules, each generating visualizations and statistics for studying interactions between tumors and the immune microenvironment (figure 1).

Methods Immunogenomic features from 15 ICI trials encompassing 1,142 samples were processed with a standardized bioinformatics workflow[4] and incorporated into iAtlas, augmenting the 11,535 patient samples from TCGA[1–3] and the Pan-Cancer Analysis of Whole Genomes[5] consortia. A compendium of in-development immunotherapy drug targets[6] and results of a study of germline genetic contribution to immune response in cancer[7] were included. For efficient access, all data were incorporated into a relational database, and programmatic access was made available through an application programming interface (API) (figure 2). The set of available iAtlas modules was vastly extended, and numerous improvements were made to the codebase. Users can now define sample cohorts and sample groups based on any available categorical or numerical variable.

Results iAtlas provides 17 interactive analysis modules (table 1) to explore immune-cancer interactions, immunotherapy treatment, and outcomes in 12,677 patient samples. Six modules are dedicated to ICI studies: dataset overview, immune readouts, immunomodulators, clinical outcome, regression analysis, and a machine learning module to enable identification of factors associated with response to therapy (figure 3). We added modules to explore how germline variation and copy number alterations relate to immune response, and how receptor-ligand interactions mediate interactions among tumor and immune cells (figure 4). Docker images using Common Workflow Language descriptors are provided so that researchers can run iAtlas workflows on their own data. Computational notebooks are provided to illustrate and explain iAtlas code, plots, and functionality and to facilitate integration of iAtlas data with data sourced from a researcher's own study.

Conclusions iAtlas serves as a repository and resource for harmonized data on immune response in cancer and response to immunotherapy. iAtlas enables researchers to readily test hypotheses and access data through multiple modalities: an interactive web portal, data download, tools,[8] and computational workflows and notebooks.

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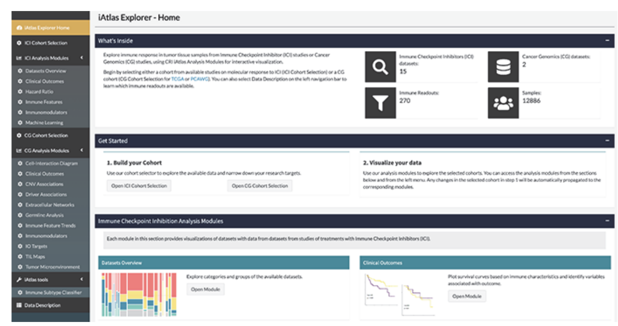
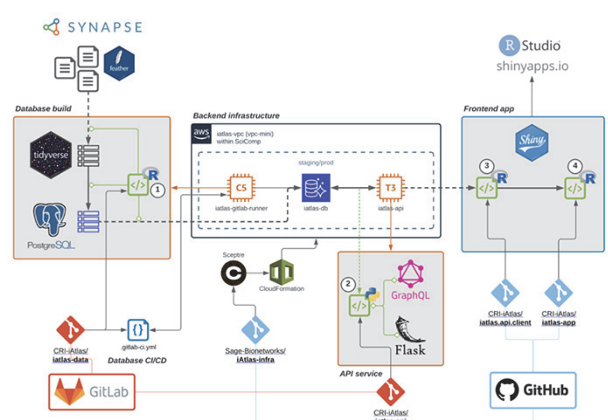
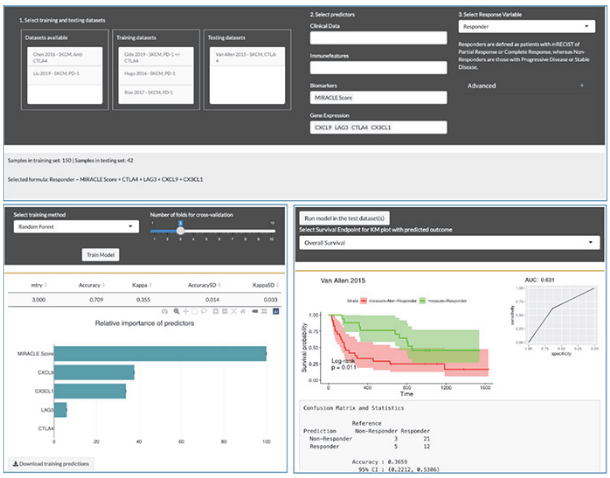


Abstract 927 Figure 1 CRI iAtlas Explorer
Entry into exploration of immune response in cancer with iAtlas. Researchers start by defining cohorts and sample groups, and can then explore and visualize results using any of 17 analysis modules (left navigation bar, and bottom right of image).

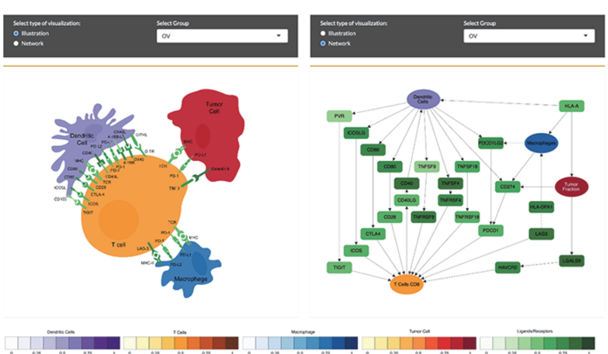


Abstract 927 Figure 2 iAtlas 2.0 infrastructureThe infrastructure underlying the iAtlas web application (top right) has four main components: 1. R scripts to (i) download data files from Synapse; (ii) extract tables from files and perform any transformations to fit database schema; and (iii) build PostgreSQL database tables, which are stored in Aurora DB. 2. Python package that implements a GraphQL API service using Flask; GraphQL query requests are resolved to SQL database queries using SQLAlchemy. 3. R package that implements a GraphQL API client to retrieve data (and transform JSON responses into tables) within the app, or as part of a regular R session. 4. Shiny/R app

code, including a set of reusable Shiny modules in the iatlas.modules R package; app is hosted using shinyapps.io and deployed manually using the rsconnect package



Abstract 927 Figure 3 iAtlas ICI Machine Learning ModuleTo identify factors that may be associated with response to Immune Checkpoint Inhibition (ICI), users choose test and training sets, factors of interest, and the response variable (top). After selection of the modeling method (here, Random Forest – other choices are Elastic Net, Logistic regression and Gradient Boosting) and parameters, the model can be trained (bottom left) and statistics are reported after running on the test set (bottom right)



Abstract 927 Figure 4 Interactions in the Tumor Immune Microenvironment
In this iAtlas analysis module, Cell-Interaction Diagram, the estimated levels of cells and associated ligands and receptors that bind are shown within a selected group of samples, in this case ovarian (OV) tumor samples in the TCGA. Users can elect to show interactions superimposed on an illustration (left) or on a node-edge network diagram (right). A related module, Extracellular Networks, infers from data the likely ligand-receptor-mediated cellular interactions in the microenvironment and displays those as a node-edge network diagram.

Abstract 927 Table 1 Interactive analysis modules available in iAtlas

Data Source	Module Name	Module Description
Immune Checkpoint Inhibition	Datasets Overview	Explore categories and groups of the available datasets.
	Clinical Outcomes	Plot survival curves based on immune characteristics and identify variables associated with outcome.
	Hazard Ratio	Create Cox Proportional Hazard Regression Models and visualize Hazard Ratio in a heatmap and a forest plot.
	Immune Features	See how immune readouts vary across your groups and ICI datasets.
	Immunomodulators	Explore the expression of genes that code for immunomodulating proteins, including checkpoint proteins.
	Machine Learning	Train and run multivariable models with cross-validation on ICI genomics and immunogenomics data.
Cancer Genomics	Cell-Interaction Diagram	Explore cell and protein abundance on an illustration.
	Clinical Outcomes	Quantify the relationship between immune response and disease outcome, in terms of either overall survival (OS) or progression free interval (PFI).
	CNV Associations	Explore associations of microenvironment with gene copy number.
	Driver Associations	Explore associations of microenvironment with cancer driver mutations.
	Extracellular Networks	Explore the extracellular networks modulating tumoral immune response.
	Germline Analysis	Explore the germline genetic contribution to the immune landscape of cancer.
	Immune Feature Trends	Visualize how immune readouts vary across sample groups.
	Immunomodulators	Explore the expression of genes that code for immunomodulating proteins, including checkpoint proteins.
	IO Targets	Explore the expression of genes that code for immuno-oncological (IO) targets.
	TIL Maps	Explore the characteristics of maps of tumor infiltrating lymphocytes obtained from analysis of H&E images.
	Tumor Microenvironment	Explore the immune cell proportions in sample groups.

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