ONCOMINE™
Training Curriculum

Target Discovery and Validation
Instructor: XXX
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Training Reminders

» Sign-in sheet
» Evaluation forms
» Class format
  » Slides: Introduce training concepts
  » Live Demonstration
    » Training manual available in PDF format
    » Follow along
    » Step-by-step guide
Training Courses

» Introduction to Oncomine
» Target Discovery and Validation
» Pathway and Drug Development

» Additional Support Available
  » 1-1 Sessions—focus on your targets
  » Request training: support@compendiabio.com

Agenda

What We Will Learn
Oncomine Platform
Definitions
Training Objective & Conclusions
Demonstration & Follow Along
What We Will Learn

» Target Discovery
  » Discover new target in breast cancer

» Target Validation
  » Build supporting evidence for the target gene in multiple independent datasets
  » Explore and attempt to validate our observation
  » Identify additional associations
  » Identify models for testing hypothesis

Oncomine Platform: The Data

» World’s largest collection of curated cancer genomics data
  » 499 Datasets
  » 39,500+ Samples

» Samples with key properties for powerful analyses
  » 6,300+ samples with known mutation status
  » 4,600+ samples with biomarker status
Oncomine Platform: Analyses

- Pre-computed analyses
  - Differential Expression
  - Co-Expression
  - Outlier Analysis
- Meta-analysis to compare independent results
  - Meta-Differential Expression
  - Meta-Outlier

The Oncomine Platform

Data
Published cancer genomic data gathered from sources worldwide

Expert Curation
Dedicated team reviewing each sample, each annotation and each publication and mapping the data to The Compendia Ontology

The Compendia Ontology
Multi-threaded hierarchy of terms and synonyms to describe the data

Standardized Analyses
Leveraging The Compendia Ontology, standardized analyses are performed on every Oncomine dataset

The “Computable” Global Collection of Cancer Genomic Data
Oncomine Definitions

» Cancer Outlier Profile Analysis (COPA)
  » Method for scoring & ranking genes based on their high over or under expression in a small subset of cancers (Ex: ERBB2 in 25% BrCa- Outlier profile)

» Outlier
  » A gene having a high COPA score and rank

» Meta-analysis
  » Comparing analyses results across independent datasets to validate an observation

Outlier Analysis & Oncomine

» Why is this useful?
  » Cancer is heterogeneous-many diseases within breast cancers represented by different underlying causes
  » What are the causes at a molecular level?
  » Can we design effective therapies for unique subpopulations by identifying their “Achilles heel” to target with drug?

» What does Oncomine tell us?
  » What genes may be causative in small subpopulations that we can’t detect by differential expression test?
  » What genes can I target with a drug?
  » How strong is the evidence for a particular target?
  » What models can I use in the lab to test my hypothesis?
Outlier Profile

» Outlier
  » High expression in a fraction of total samples
  » Unique & potentially causal in specific disease

Comparing Analysis

» “Meta-analysis”
  » Comparing analyses results across independent datasets to validate an observation
Oncomine Filters

» Filter on drug targets
» Filter on cell line panels
» Filter on results

Training Objective: Target Discovery & Validation of AGTR1

» Are there potential targets in breast cancer that can be identified by an outlier profile?
  » I am interested in novel targets in breast cancer that already have approved compounds, is there an outlier expression profile to define this subset?

» Make associations between novel targets and important biological processes?
  » Are there associations between AGTR1 and known breast cancer biomarkers such as ERBB2 or estrogen receptor status?

» What cell lines harbor high or low expression of my gene of interest?
  » I am ready to further investigate AGTR1 in the laboratory, what breast cancer cell lines express AGTR1?
Training Example Conclusions: What We Will Discover

» Target Discovery & Validation
  » AGTR1, a known drug target, is highly expressed in a subset of breast cancer samples
  » AGTR1 is over-expressed in ER+ samples and it is mutually exclusive with ERBB2
  » The cell line Hs 578T has higher expression of AGTR1

On your own
Training Objective Target Validation: FOXM1

» Can Oncomine help me find over-expression in a specific pathological subset of breast cancers?
  » Is FOXM1 over-expression specific to a pathological subtype of breast cancer?

» Can I use Oncomine to find cancer-specific biological associations?
  » Are there important biological processes that are present in the pathological subset with FOXM1 over-expression?

» Is my gene of interest a drug target?
  » Using the Oncomine drug data, can I find drugs to target FOXM1 over-expression?
On your own
Training Example Conclusions: FOXM1

» FOXM1 is frequently over-expressed in high-grade breast cancers, and is often present in ductal or invasive cancers

» FOXM1 was found to be an important regulator of my cell cycle processes such as cytokinesis and DNA replication

» The tyrosine kinase inhibitors Dasatinib and Gefitinib may target FOXM1 in breast cancer

Oncomine Registration

» Oncomine registration (if not registered)
  » Request registration at www.oncomine.com
  » Training login for today
    USER ID =
    PASSWORD =
Demonstration