Integrate and understand complex 'omics data

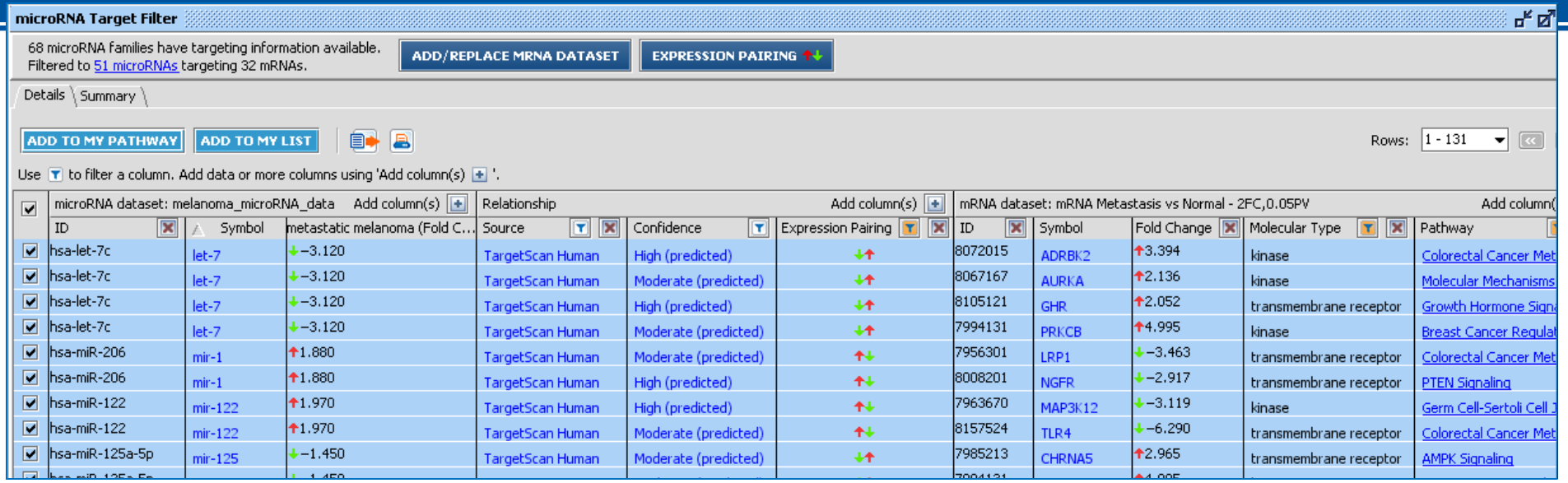
microRNA Target Filter

Workflow for miRNA Target Filter

- Filter miRNA differential expression data set(s) (if corresponding mRNA differential expression data, filter as well)
  - File -> New -> Filtered Data Set
- Start microRNA Target Filter
  - File -> New -> miRNA Target Filter
  - Open miRNA filtered data set
- Using funnel in column headers, filter mapping based on information type/confidence
- Add annotation columns, if desired, by clicking the plus sign in column header and filter as desired
- Perform additional filtering as desired by clicking funnel icon

Workflow for miRNA Target Filter, cont.

- If corresponding mRNA is available, click “ADD/REPLACE MRNA DATA SET” to filter mRNA mappings to genes in the mRNA expression data set
  - Click “EXPRESSION PAIRING” to pair the expression between the miRNA and mRNA
  - Click the funnel in the column header of the expression pairing column to filter for the miRNA-mRNA pairing desired
- Click to summary tab to view a summary of miRNA-mRNA mappings
- For further analysis, select one or more miRNAs from the summary tab and add the miRNA and targets to a new pathway and perform BUILD or OVERLAY actions for interpretation of functions, pathways, drug targets, etc.



88 data points | 13,690 targets | 1,090 targets | 333 targets | 39 targets | 32 targets

Use Pathway tools to build hypothesis for microRNA – target association to melanoma metastasis.

microRNA Content Details:

Ingenuity ® Knowledge Base

- IPA has high-quality microRNA-related findings (including both experimentally validated and predicted interactions)
  - **TarBase**: experimentally validated microRNA-mRNA interactions
  - **Target Scan**: predicted microRNA-mRNA interactions (low-confidence interactions were excluded)
  - **miRecords**: experimentally validated human, rat, and mouse microRNA-mRNA interactions
  - **Literature Findings**: microRNA-related findings manually curated from published literature by scientific experts and structured into the Ingenuity® Knowledge Base
- Single source for microRNA content plus related biology enables biologically relevant target prioritization in minutes vs. weeks
- Extensive human, mouse, and rat coverage

Mapping microRNA IDs in IPA

For Searching, IPA Supports:

- miRBase Identifiers
- Entrez Gene Symbols and Entrez Gene IDs
- Other synonyms used in the literature

For Data Upload, IPA Supports:

- miRBase Identifiers for mature miRNAs
  - miRBase Accession Numbers (format MIMAT######) are preferred. These are stable identifiers.
  - miRBase Name Identifiers (format: mmu-miR-###) are allowed. Since some miRNA arrays provide annotations only with the name, we have provided mappings for them. These change over time so use MIMAT instead if available.
  - Precursor identifiers are NOT supported
- Entrez Gene IDs (*not* Entrez Gene Symbols)
- HUGO gene symbols (human only)

Mapping microRNA IDs in IPA during Data Upload

- A given ID can only map to a single node in IPA
- miRNA identifiers each map to either a group node or a locus-specific node:
  - miRNA identifiers that correspond to mature miRNAs that do NOT appear in a group (ie, they arise from only one known precursor, and that precursor has no more than one known Entrez Gene ID/locus) are mapped to a locus-specific node.
  - miRNA identifiers corresponding to mature miRNAs that ARE in a group map to that group.
  - No miRNA maps to more than one group node in IPA.

Working with miRNA Groups

Mature miRNAs may arise from multiple precursors:

- A given mature form may arise from multiple distinct miRNA precursors.
- A given precursor may arise from multiple distinct loci.

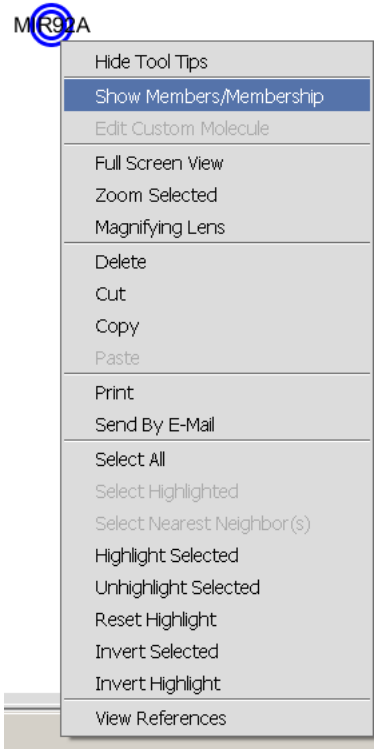
Groups are created in the KB to represent mature miRNA's that may arise from multiple precursors or multiple loci.

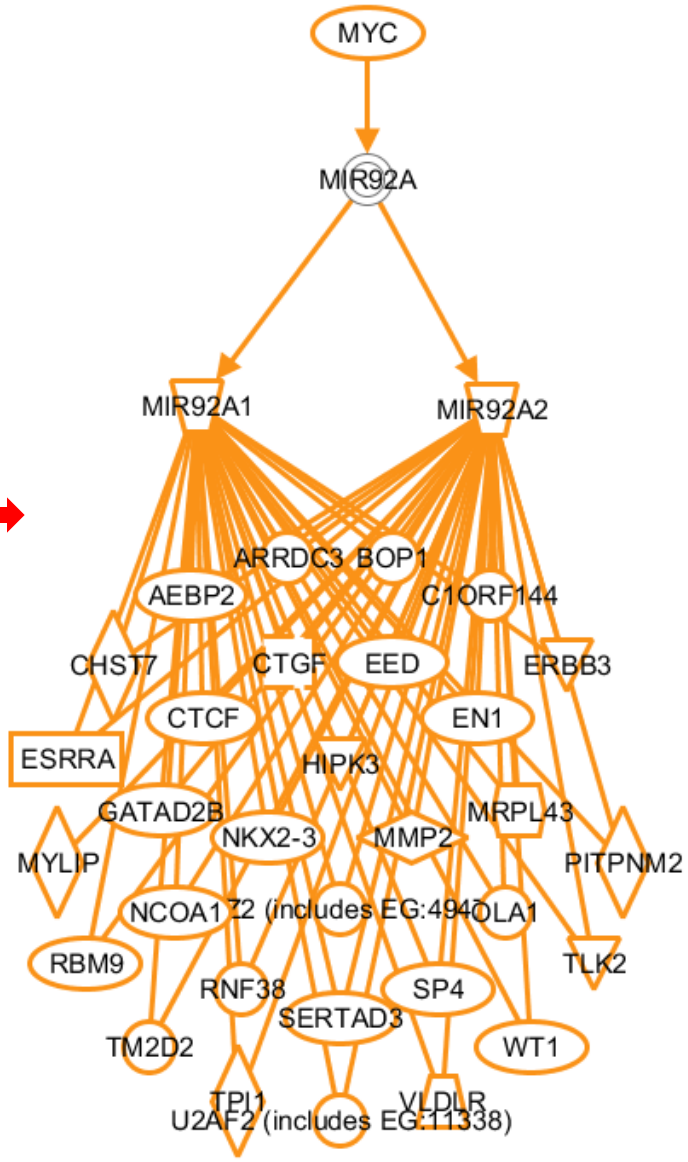
- When authors refer to a particular mature miRNA form that may arise from multiple distinct precursors and/or multiple genetic loci, the finding is mapped to a group concept that contains all potential "parent" precursors.

Groups might have different network connections compared to the individual members of the group.

- Findings might be mapped to the individual members or to the group, depending on information provided by the author.
- 'Grow' functionality does not 'look inside' the groups.
- Additional steps will ensure that all members of group will be considered when applying 'Grow'

Expanding groups prior to Growing will provide information on known molecular interactions for all members of the group.





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Biomarker Analysis

What Is A Biomarker?

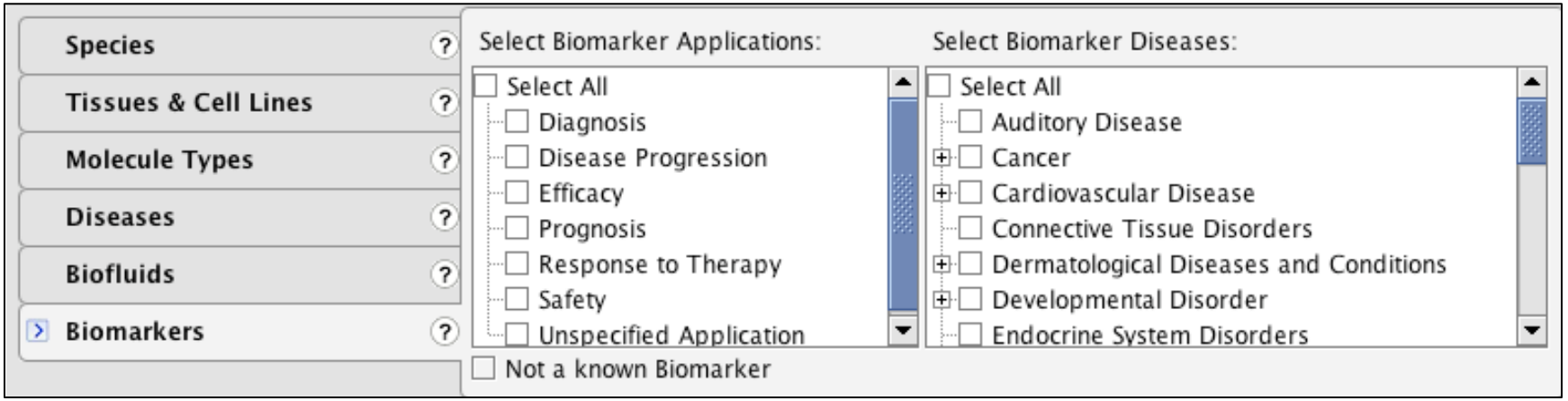
- IPA defines a biomarker as:
  - A biological molecule found in a body fluid or tissue/cell type/cell line that is an indicator of a normal/abnormal process, a specific condition or disease, or other type of phenotype for diagnostic or therapeutic purposes
- IPA-Biomarker™ analysis filters/refines candidate lists based on biological criteria such as association to a disease, normal presence in a fluid, or normal expression in a tissue/cell type/cell line and/or clinical usage.
- Note that there is a Biomarker Overlay tool available for any open pathway
  - OVERLAY in pathway toolbar, select “Biomarkers” in tool pull-down

Introduction to Biomarker Analysis

- IPA's Biomarker Analysis allows you to start with a candidate gene list and filter it based on biological criteria, such as:
  - Species, Tissues and Cell Lines, Biofluids, Diseases
  - Exploratory Clinical Biomarker Use
- The output is a refined list of candidates
  - It does not calculate functions, Canonical Pathways, or networks
- Different observations or datasets can be compared using the Comparison Biomarker Analysis
  - Calculates unique and common molecules

Biomarker Filters

- The Biomarker Filter capability rapidly prioritizes biomarker candidates based on biological characteristics and clinical usage



Clinical Usage (Biomarkers):
Identify biomarkers by their specific application, including markers for Disease Diagnosis and Prognosis, Disease Progression, markers of Drug Efficacy and Safety, and Patient Response to Therapy

Biomarker Workflow with Expression Data

- Upload differential expression data
- To start the Biomarker Filter go to File -> New -> Biomarker Filter
- Set biomarker filter criteria at the top of the settings page
  - Often fluids of interest for assay are selected under “Biofluids”.
  - If you wish to limit to genes/proteins previously identified as potential biomarkers, in the “Biomarkers” filter, select all, or subset of relevant selections for your study
- Set expression cutoffs in middle of the page
  - Similar to core analysis settings
  - Consider filtering expression values for only differentially up-regulated genes using the “Focus on” pull-down next to the expression cut-off entry box.
- Click RUN ANALYSIS