Ingenuity Pathway Analysis (IPA) hands-on workshop

(Introduction and data upload)

by

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IPA use for cancer research: examples

1)

Haematologica. 2015 Jul;100(7):e275-9. doi: 10.3324/haematol.2015.124305. Epub 2015 Mar 20.

Post-transplant molecularly defined Burkitt lymphomas are frequently MYC-negative and characterized by the 11q-gain/loss pattern.

Ferreiro JF[1], Morscio J[2], Dierickx D[3], Marcelis L[2], Verhoef G[3], Vandenberghe P[1], Tousseyn T[2], Wlodarska I[4].

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Genomic and transcriptomic data on PT-mBL.

Julio Finalet Ferreiro et al. Haematologica 2015;100:e275-e279

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Journal of the European Hematology Association
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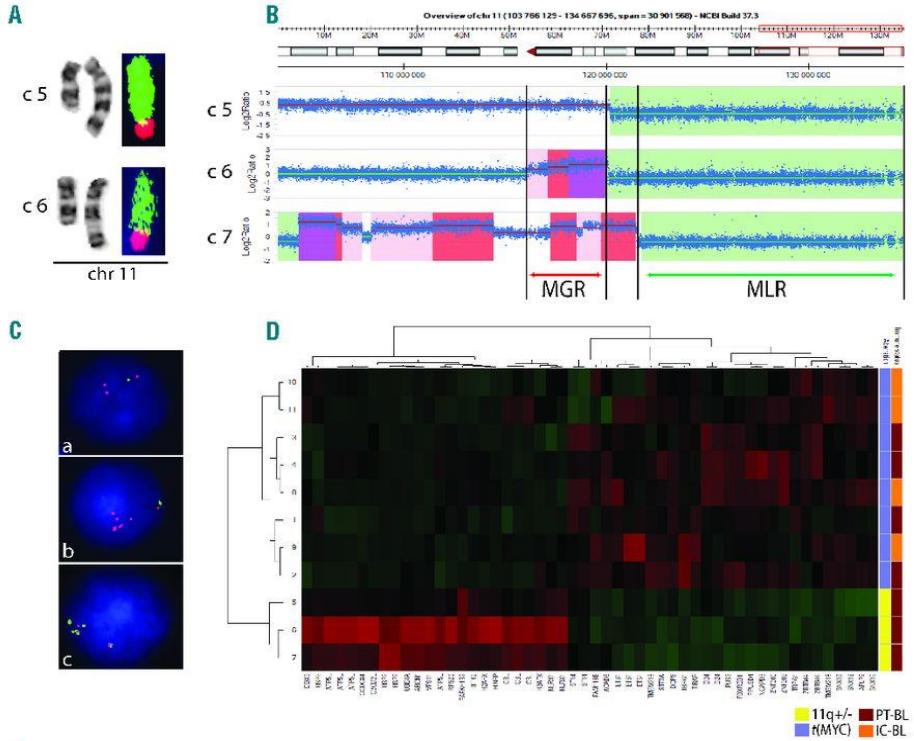

Genomic and transcriptomic data on PT-mBL. (A) Partial karyotype of case 5 (c5) and case 6 (c6) showing chromosome 11 abnormalities and FISH images of both derivative chromosomes painted with WCP11 (green) and WCP8 (red) (case 5), and WCP18 (red) (case 6). The aberrations were eventually described as der(11)(11pter->11q23.3::11q23.3->11q13::8q22q24.3) and der(11)t(11;18)(q23.3;q12), respectively. Note (inverted) duplication of 11q13q23.3 in case 5 and a normal appearance of this region in case 6. (B) Chromosomal view of chromosome 11q23q24 and imbalances identified by array CGH analysis in cases 5–7. Gained regions are highlighted in red-scale (increased intensity reflects an increased amplification level), while lost regions are marked in green. Note a variable level of 11q23.3 gain, a common loss of 11q24qter and the defined MGR (~4 Mb) and MLR (~13.5 Mb). (C) Examples of interphase FISH analysis performed in case 5 (a) and case 6 (b, c). The applied probes include the 11q-MGR/MLR FISH assay (a) (b), and two probes from the duplicated (RP11-284O21-SpectrumOrange) and amplified (RP11-784K23-SpectrumGreen; *Online Supplementary Figure S2*) area in case 6 (c). Note the duplicated and amplified red/11q23.3 signal in (a) and (c), respectively, and loss of the green/11q24 signal in both cases. In (c), note two red and five green signals in the cluster, illustrating various levels of gain within the MGR. (D) Hierarchical clustering of mBL cases using the dysregulated genes located in the MGR and MLR. (E) Interaction network found by Ingenuity Pathway Analysis involving genes targeted by the 11q-gain/loss aberration (bold edges). Solid and interrupted lines represent direct and indirect interactions, respectively. Notably, most of the interactions in this network are direct protein-protein interactions. The molecules with blue and green edges are encoded by MGR- and MLR-associated genes, respectively. The data obtained by comparison of cases 5–7 (PT-mBL with the 11q-gain/loss pattern) (11q+/−) by cases 1–4 (PT-*MYC*-translocation-positive mBL) [(t(*MYC*)] were overlaid in this network. Molecules which are down- and up-regulated in cases with 11q+/− when compared to cases with t(*MYC*) are filled in green and red, respectively.

IPA (hands-on) workshop

GENOMICS CORE | UZ LEUVEN

2)

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PLOS | ONE

Integrative Genomic and Transcriptomic Analysis Identified Candidate Genes Implicated in the Pathogenesis of Hepatosplenic T-Cell Lymphoma

Julio Finalet Ferreiro[1], Leila Rouhigharabaei[1], Helena Urbankova[1], Jo-Anne van der Krogt[1], Lucienne Michaux[1], Shashirekha Shetty[2], Laszlo Krenacs[3], Thomas Tousseyn[4], Pascale De Paepe[5], Anne Uyttebroeck[6], Gregor Verhoef[7], Tom Taghon[8], Peter Vandenberghe[1], Jan Cools[1,9], Iwona Wlodarska[1]*

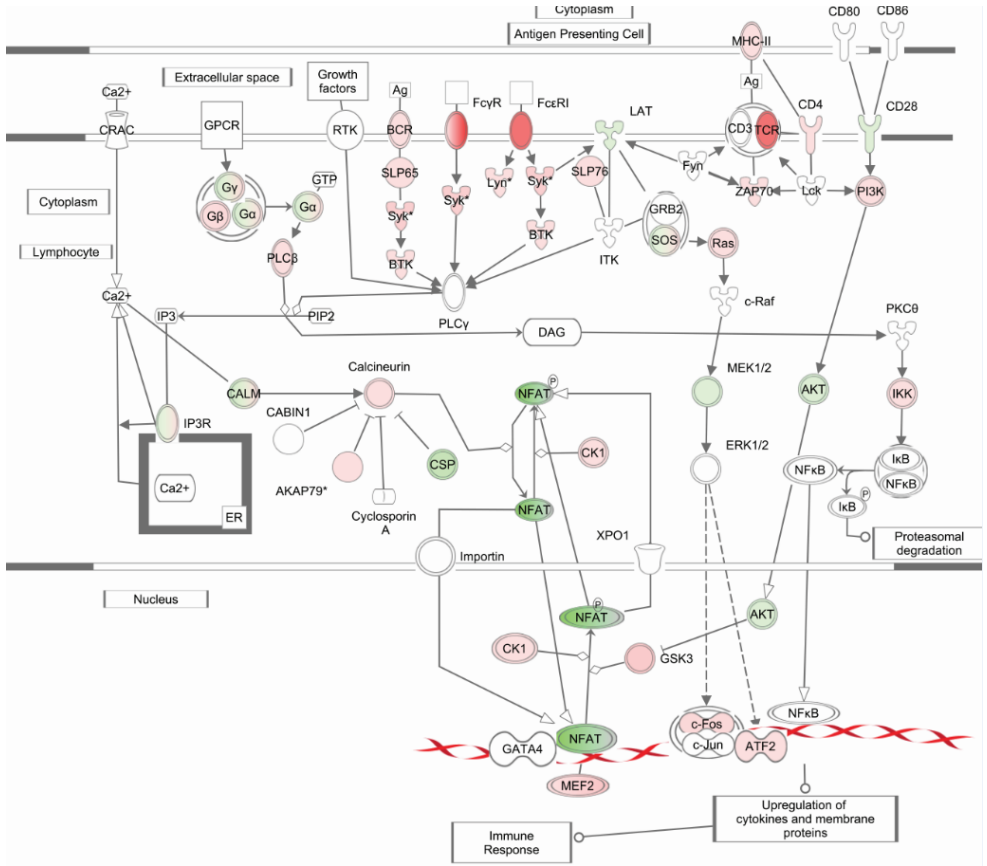

Figure S3

http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0102977

3)

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PLOS ONE

Non-*IG* Aberrations of *FOXP1* in B-Cell Malignancies Lead to an Aberrant Expression of N-Truncated Isoforms of FOXP1

Leila Rouhigharabaei[1☯], Julio Finalet Ferreiro[1☯], Thomas Tousseyn[2], Jo-Anne van der Krogt[1], Natalie Put[1], Eugenia Haralambieva[3], Carlos Graux[4], Brigitte Maes[5], Carmen Vicente[1,6], Peter Vandenberghe[1], Jan Cools[1,6], Iwona Wlodarska[1]*

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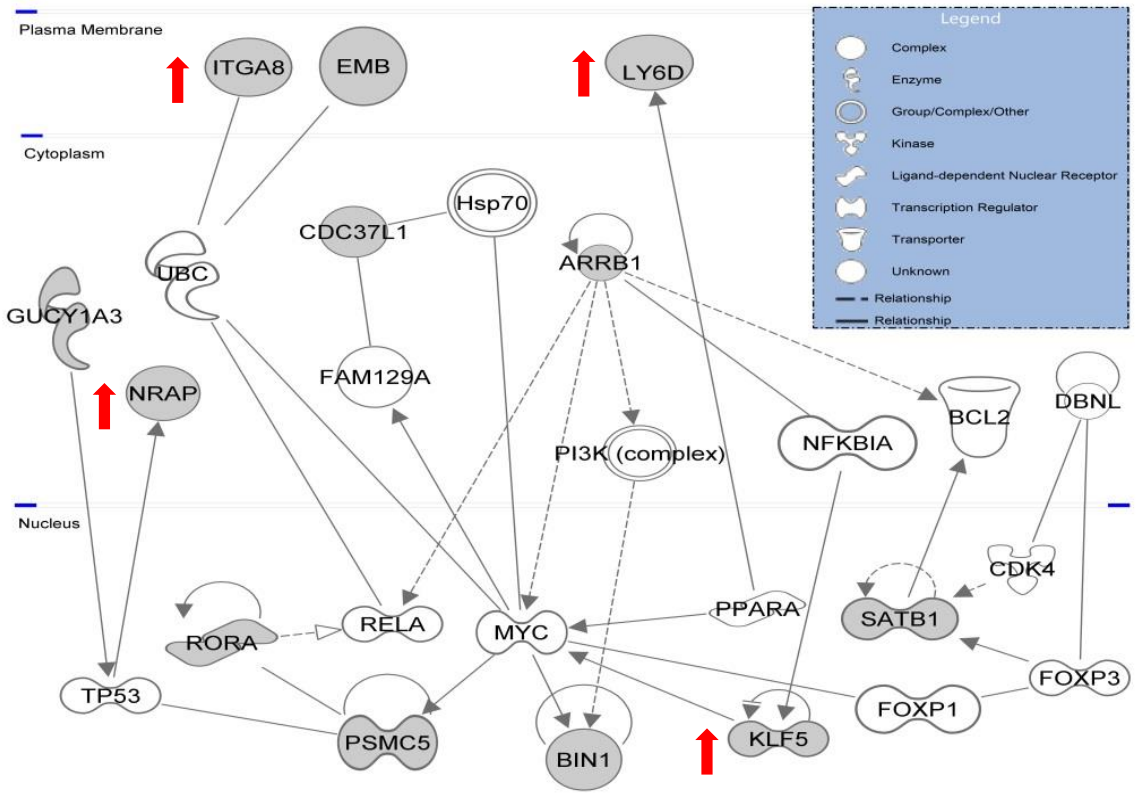


Figure S4.

Interaction network of genes exclusively mutated in t(3;14)-positive case 5 (in grey) with the well know cancer genes specified by IPA. Continuous and discontinues lines indicate direct and indirect interactions, respectively. Red arrows mark genes found to be upregulated in $FOXP1_{FL}$ expressing case 5 when compared with cases expressing $FOXP1_{NT}$.

doi:10.1371/journal.pone.0085851.s004

(PPTX)

Summary of the dataset and research objective (1)

Disease and control samples:

Disease: Peripheral T-cell lymphoma :

A rare Lymphoproliferative disorder of T cell origin

Controls: Normal lymph nodes and other T-cell tumor (HSTL)

Research objective:

To gain insight into the biology of the disease

Summary of the dataset and research objective (2)

Research questions:

which:

- molecules (from our dataset) are involved in well characterized biological (canonical) pathways
- canonical pathways are relevant to the disease
- cancer-related genes are relevant for the disease
- genes might define the gene signature of the disease
- genes not present in my dataset are linked, directly or indirectly, to the genes in my dataset
- Publications supports my findings

Dataset after inference analysis with DEseq V2

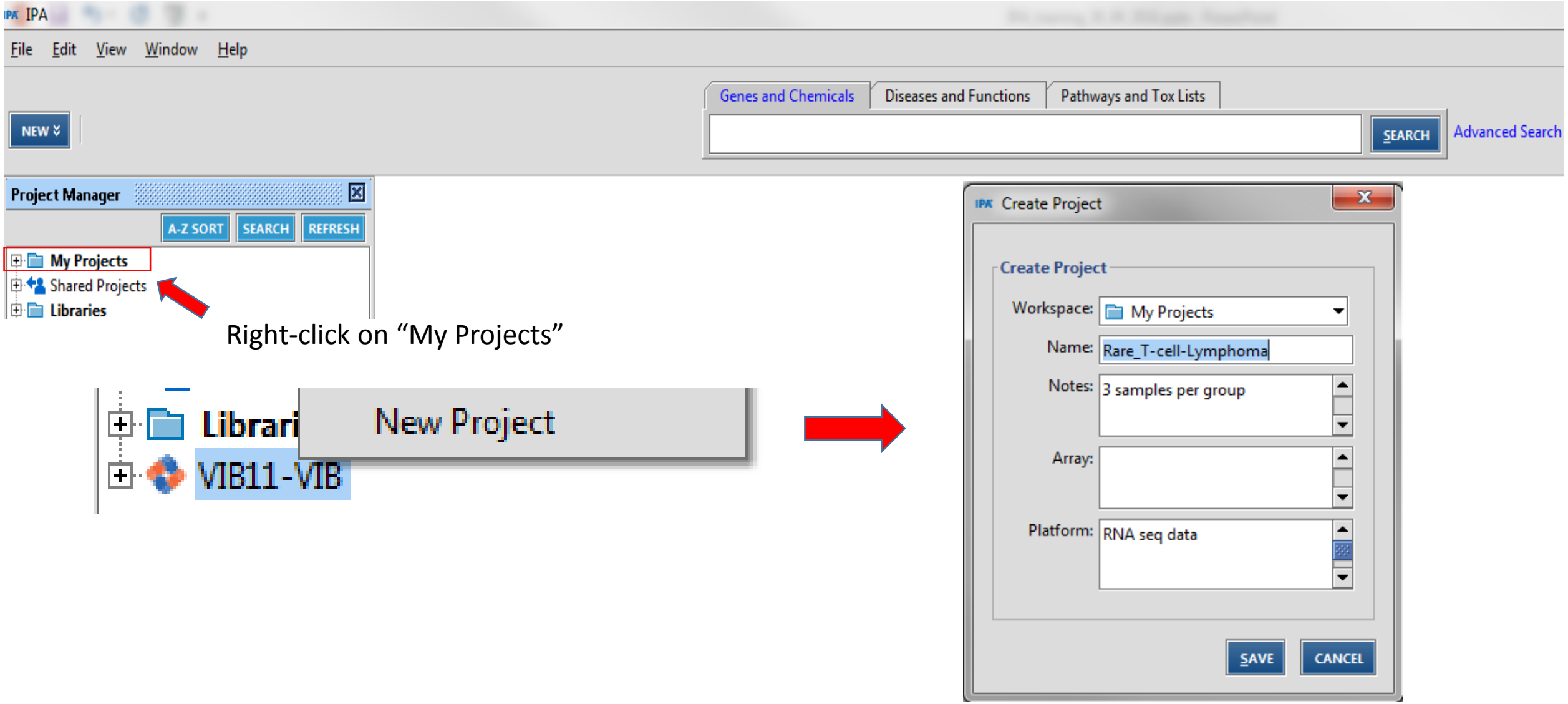
Tumor_type_A vs Normal Tissue

ID	Exp Fold Change	Exp False Discovery Rate (q-value)
ENSG00000008311	-8.838	0.011000
ENSG00000108846	10.928	0.159000
ENSG00000160179	10.467	0.075000
ENSG00000176244	-65.239	0.002000
ENSG00000103740	-11.742	0.073000
ENSG00000114739	-10.31	0.028000
ENSG00000197381	-10.105	0.004000
ENSG00000152990	-12.15	0.009000
ENSG00000169129	-7.488	0.078000
ENSG00000163568	10.918	0.084000
ENSG00000129474	-6.589	0.089000
ENSG00000112294	-6.396	0.032000
ENSG00000012779	45.744	0.023000
ENSG00000139211	28.862	0.063000

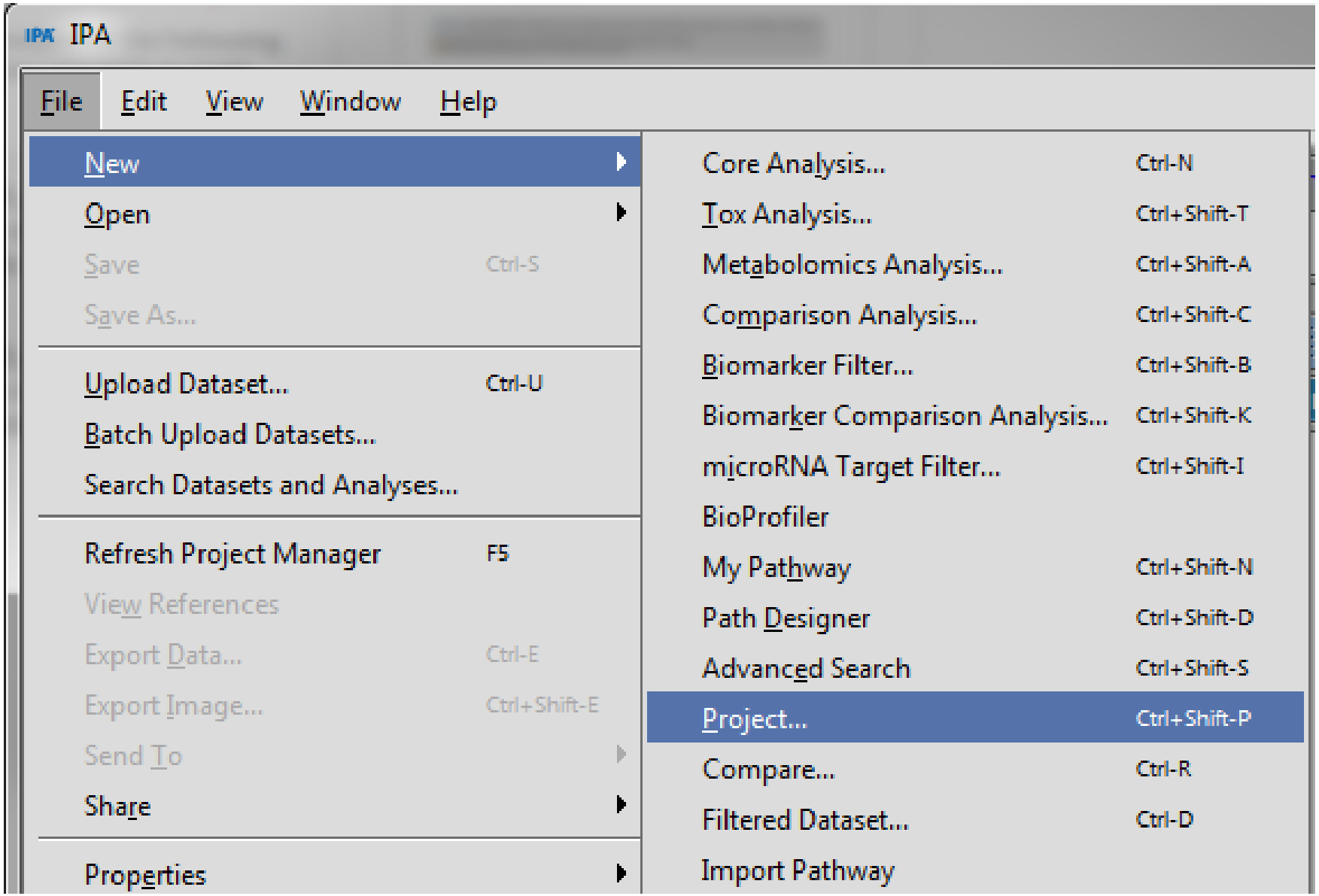
Tumor_type_A vs Tumor_type_B

ID	Exp Fold Change	Exp False Discovery Rate (q-value)
ENSG00000175985	-2.832	0.058
ENSG00000204262	2.529	0.058
ENSG00000138080	2.04	0.057
ENSG00000158715	-2.253	0.057
ENSG00000245680	-2.123	0.056
ENSG00000174292	-2.364	0.056
ENSG00000115457	2.795	0.056
ENSG00000154920	2.603	0.056
ENSG00000182054	2.103	0.055
ENSG00000171246	-2.86	0.055
ENSG00000079215	2.132	0.055
ENSG00000141576	-2.378	0.055
ENSG00000164086	-2.072	0.055
ENSG00000105664	2.793	0.055
ENSG00000008394	2.872	0.055

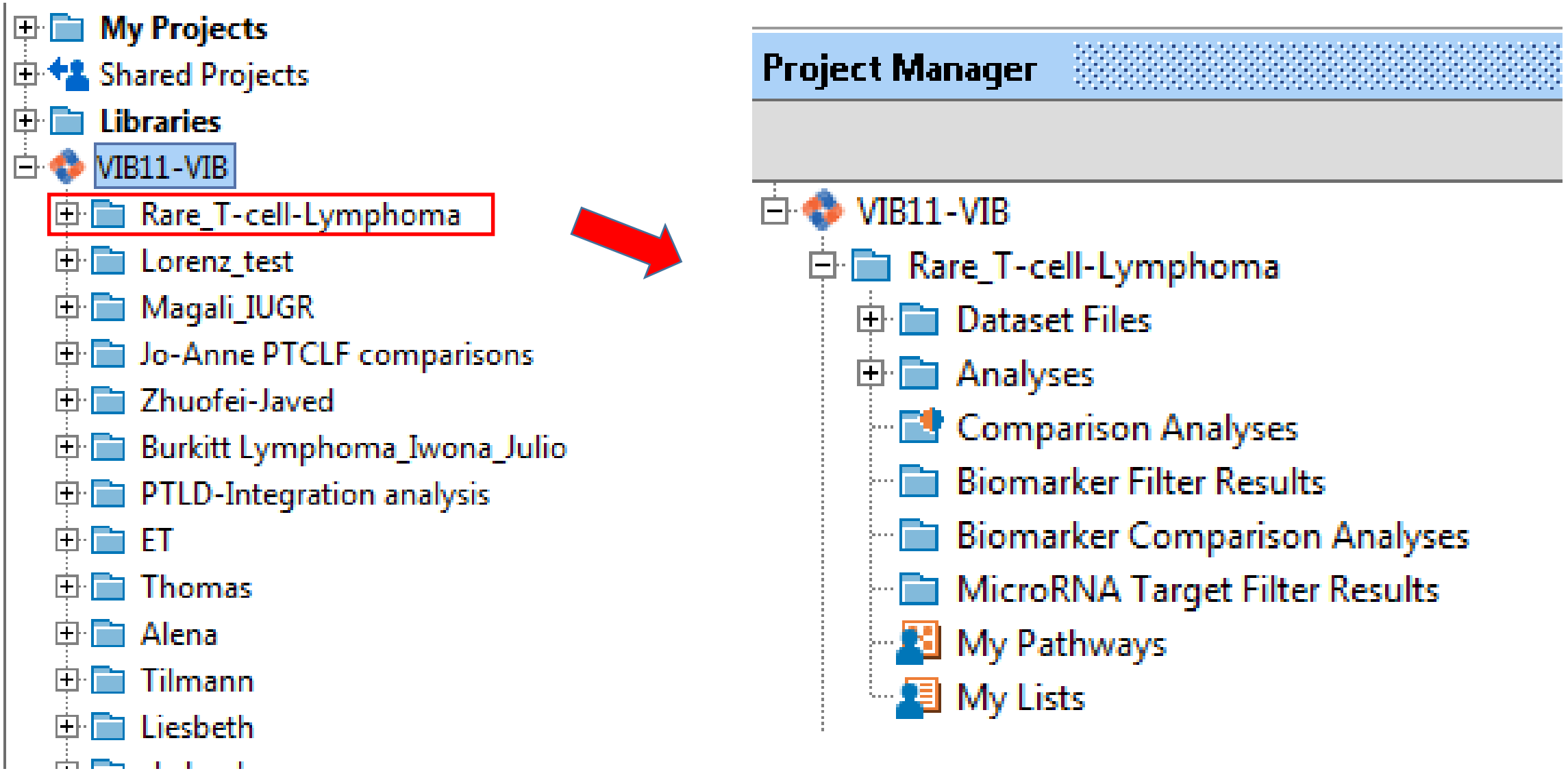
Creation of a new project



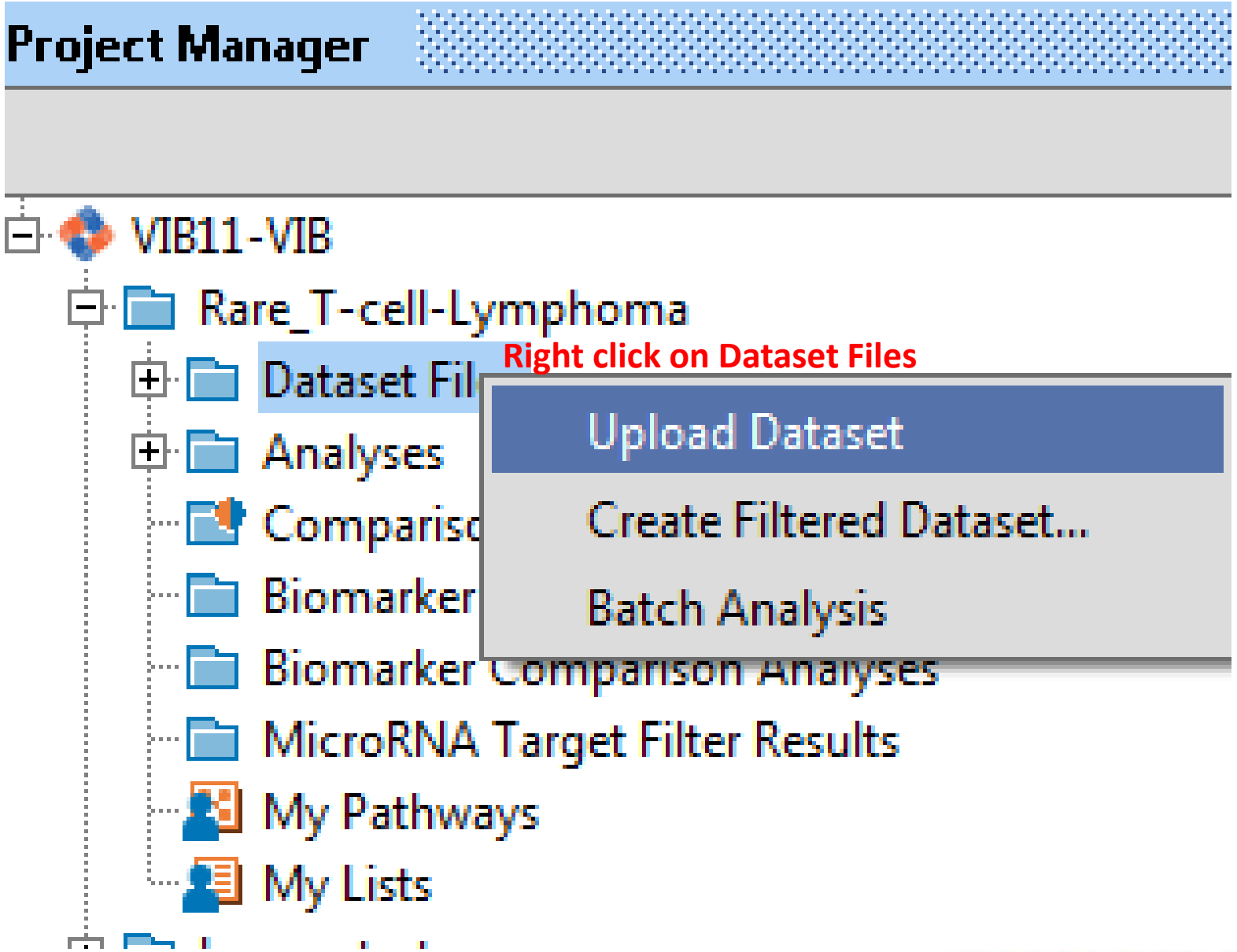
Creation of a new project, alternative



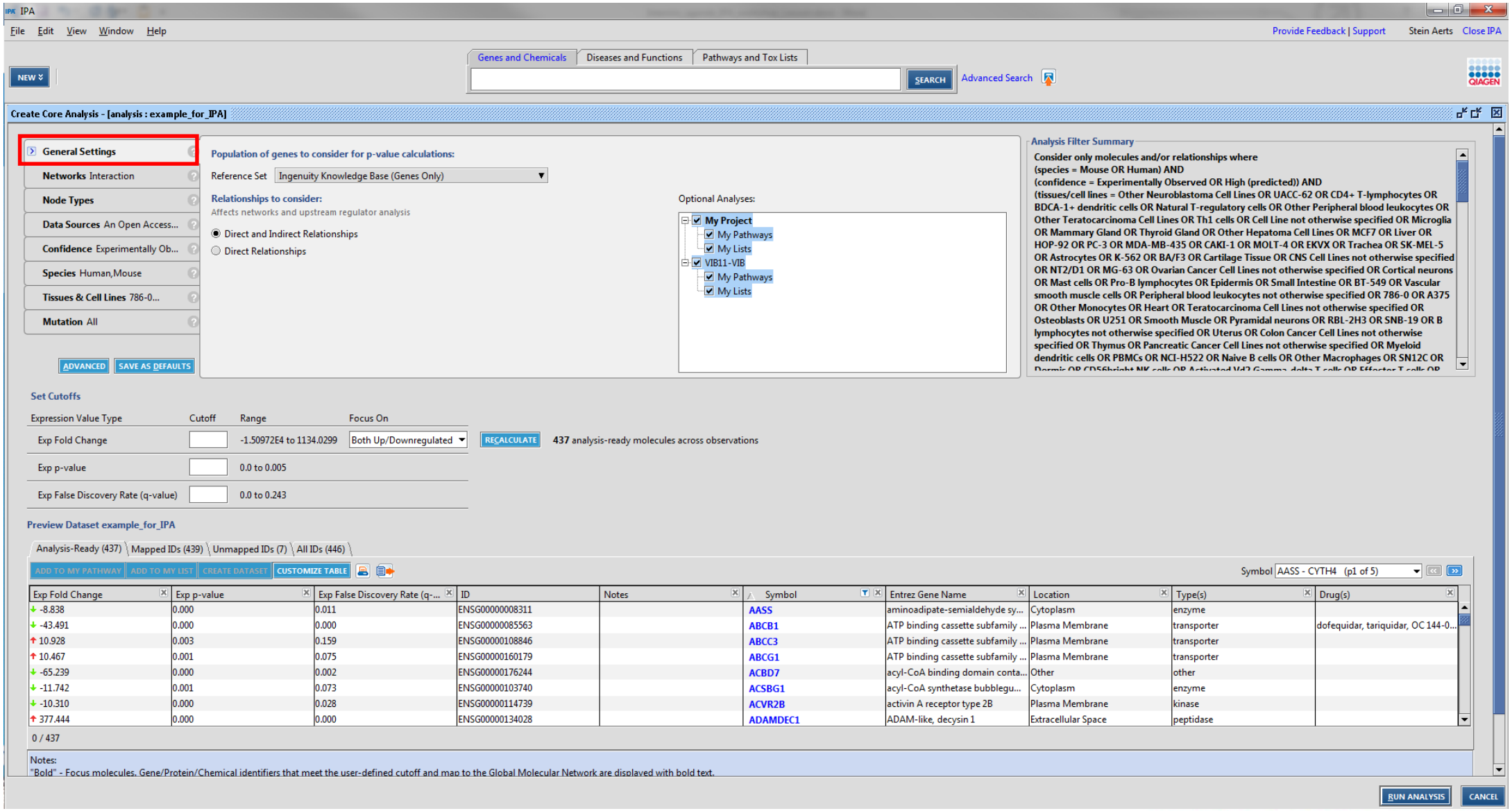
Items in a project



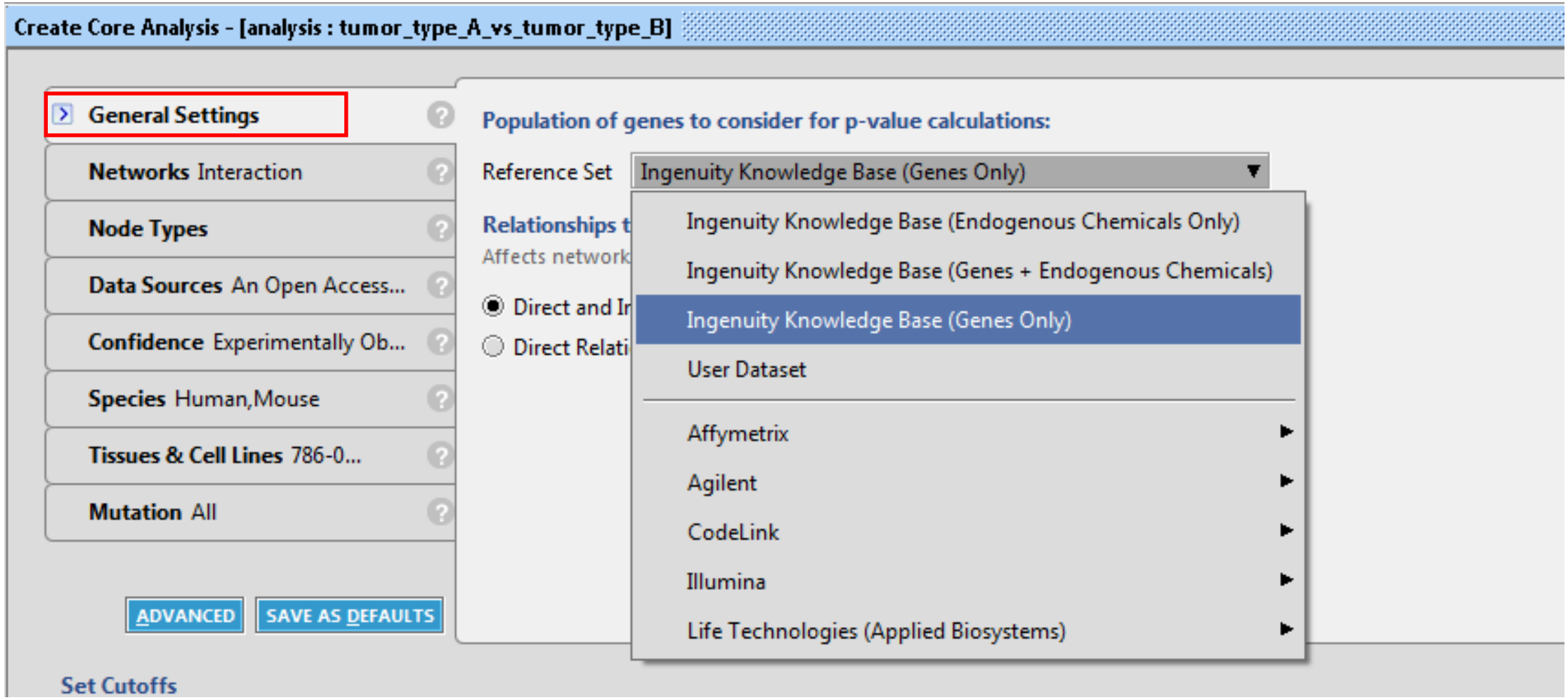
Data upload


Project Manager
VIB11-VIB
Rare_T-cell-Lymphoma
Dataset Fil
Analyses
Biomarker
MicroRNA Target Filter Results
My Pathways
My Lists
Right click on Dataset Files
Upload Dataset
Create Filtered Dataset...
Batch Analysis

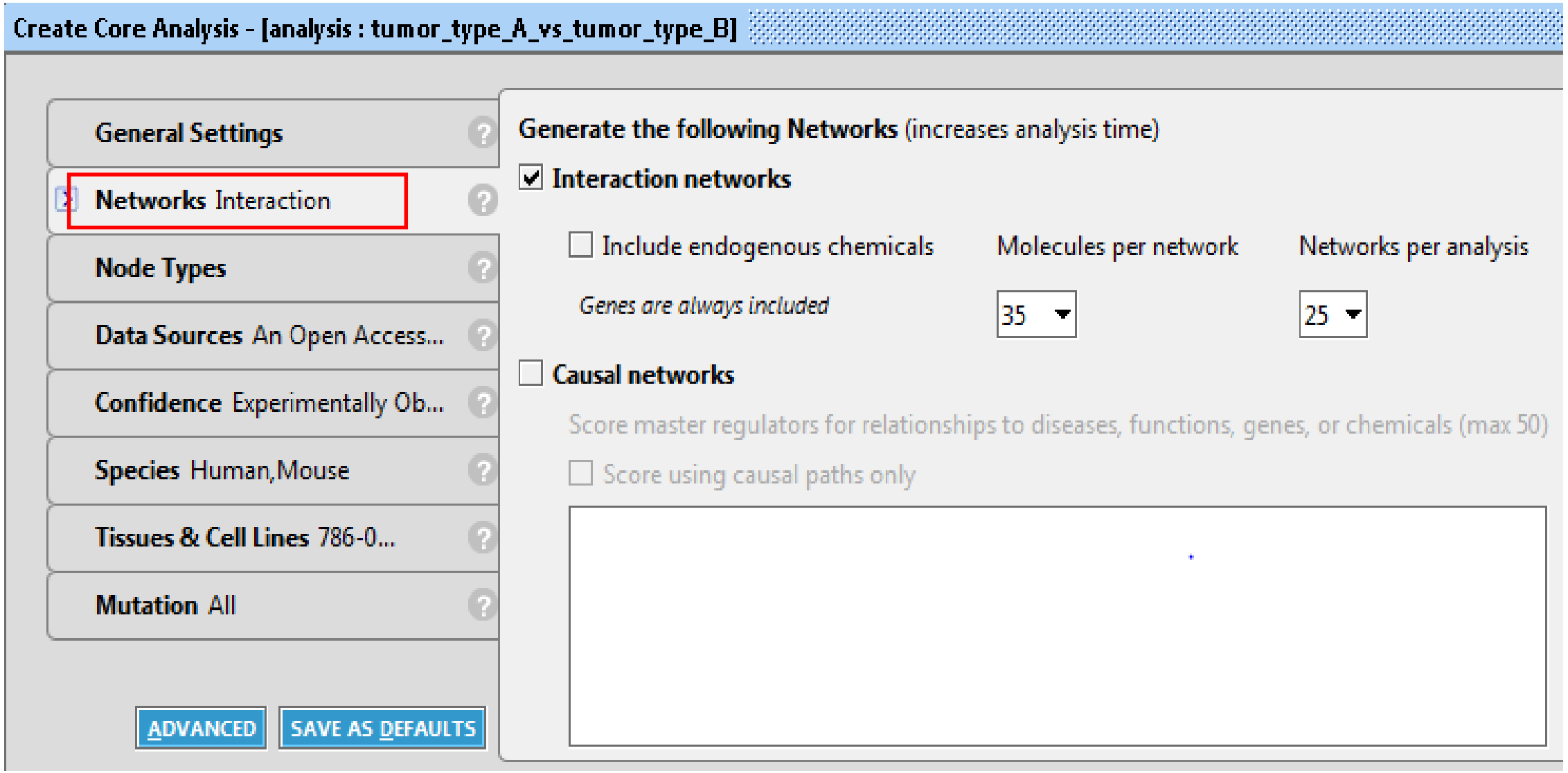
Setting up a Core Analysis: General Settings



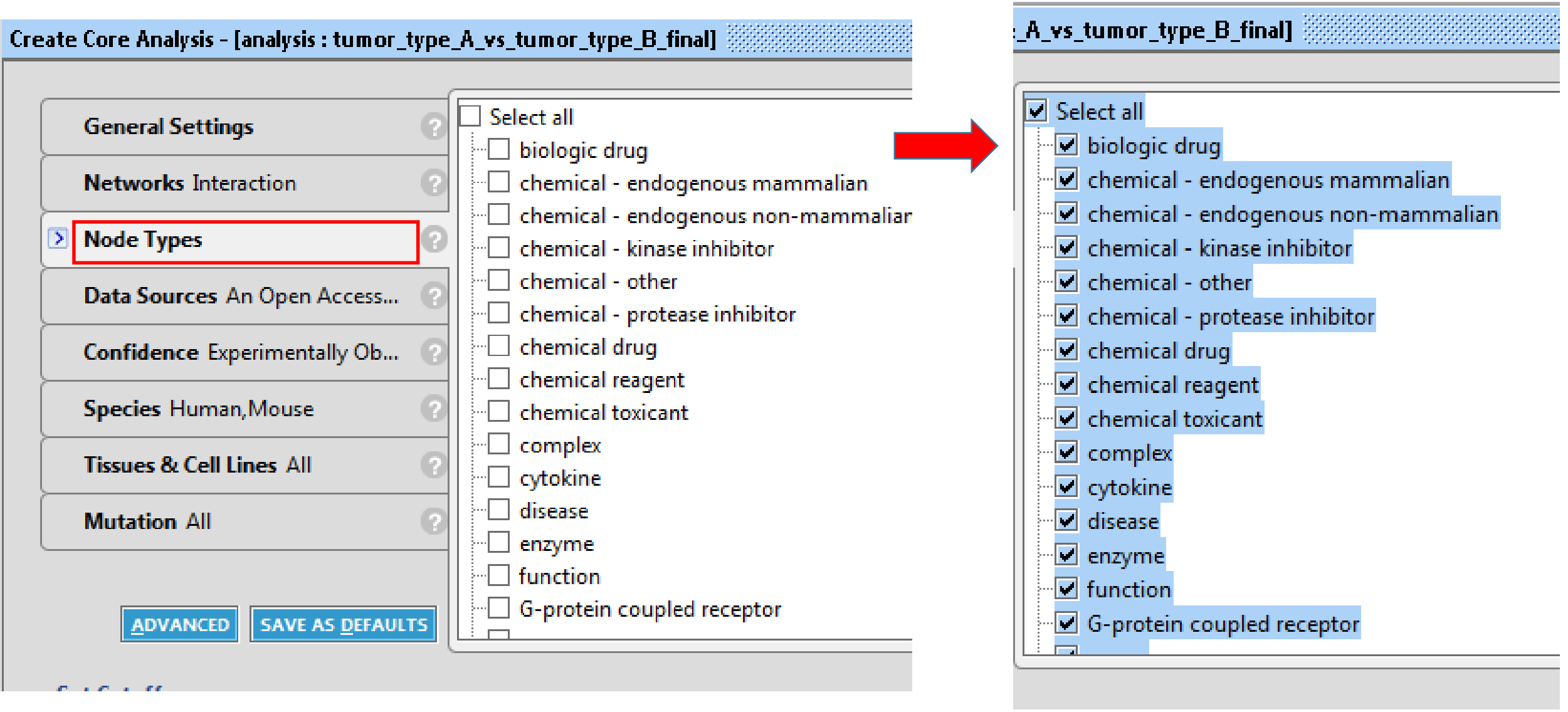
Setting up a Core Analysis: General Settings > select Genes Only



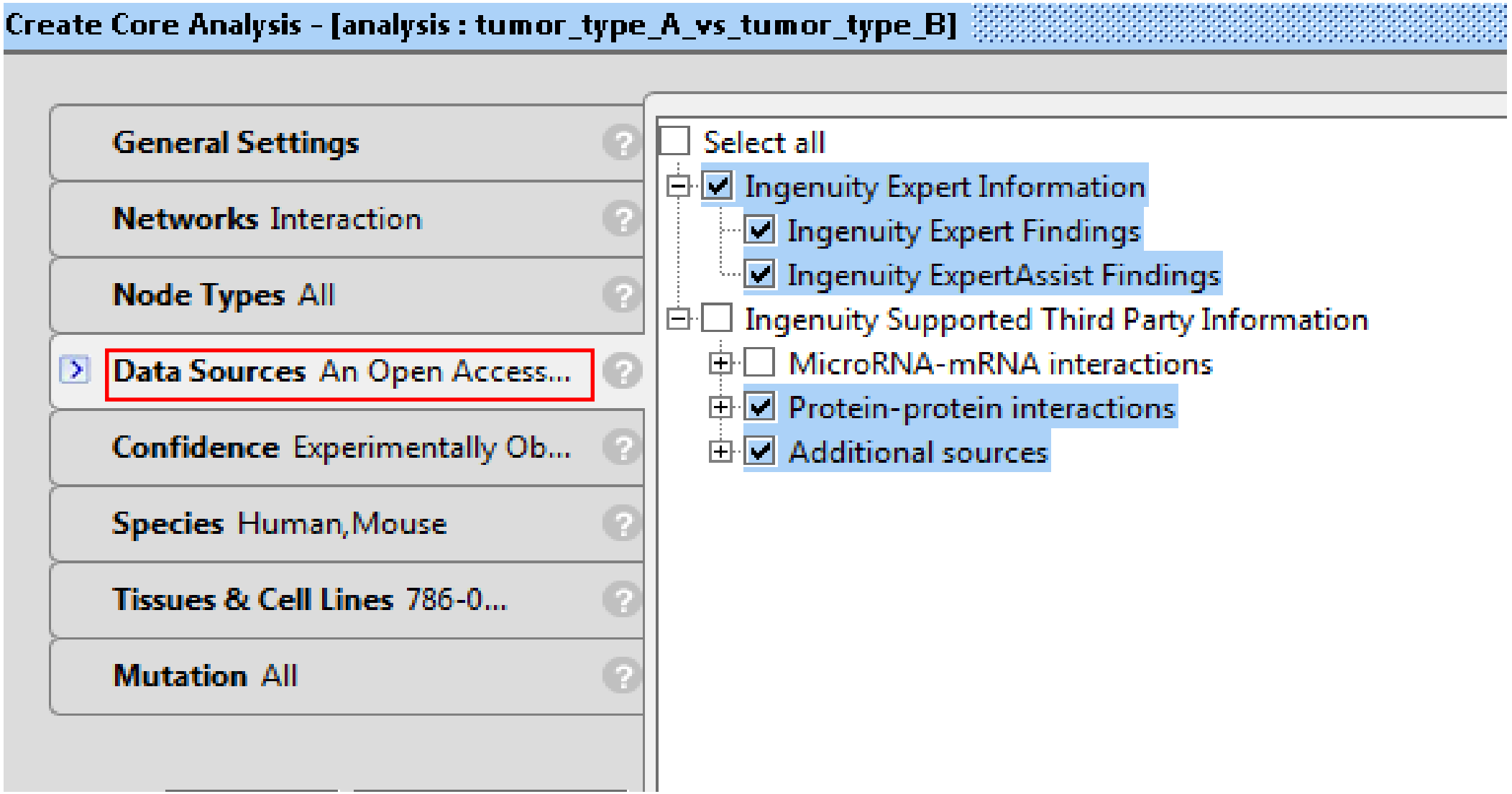
Setting up a Core Analysis: Networks



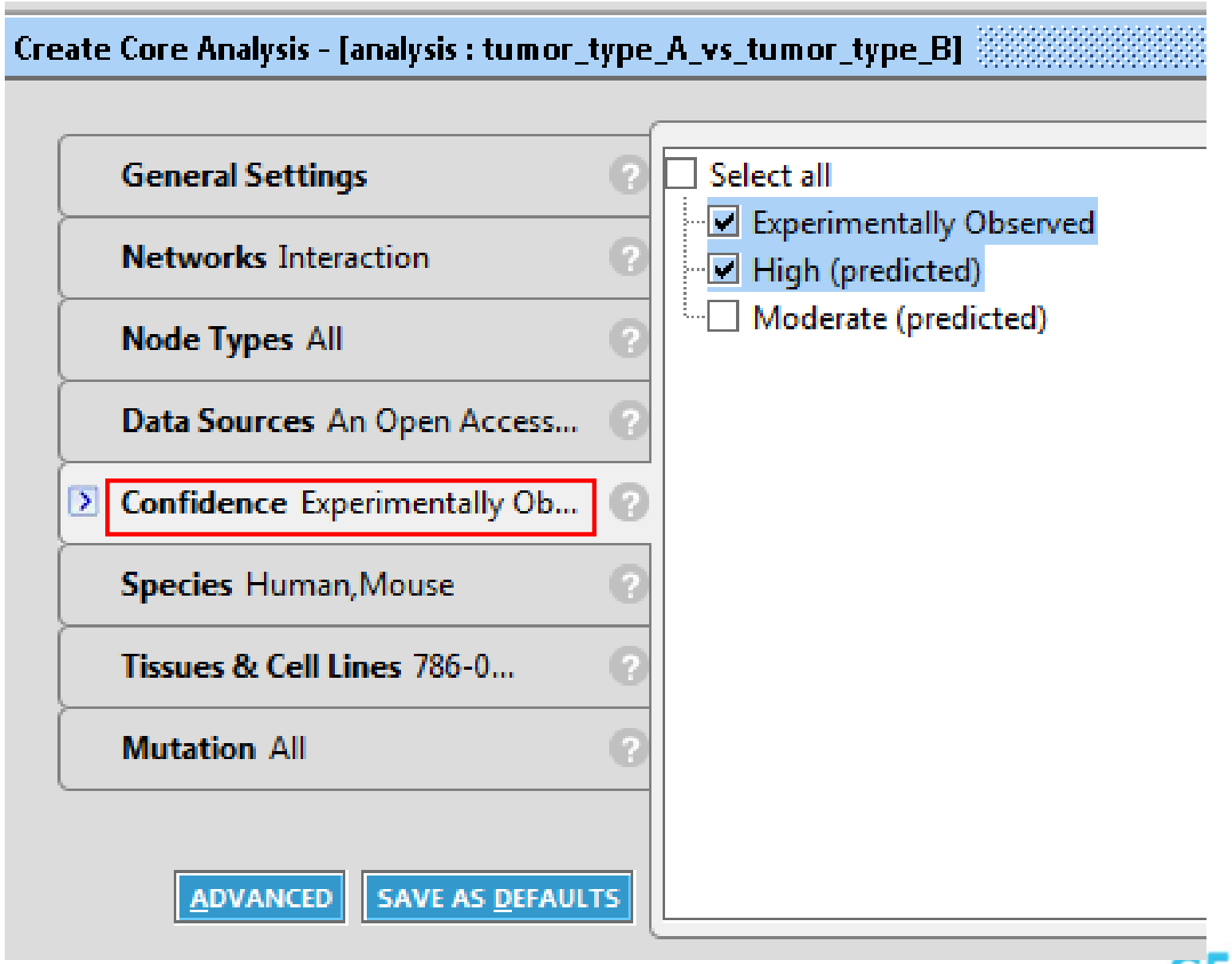
Setting up a Core Analysis: Nodes types, select all



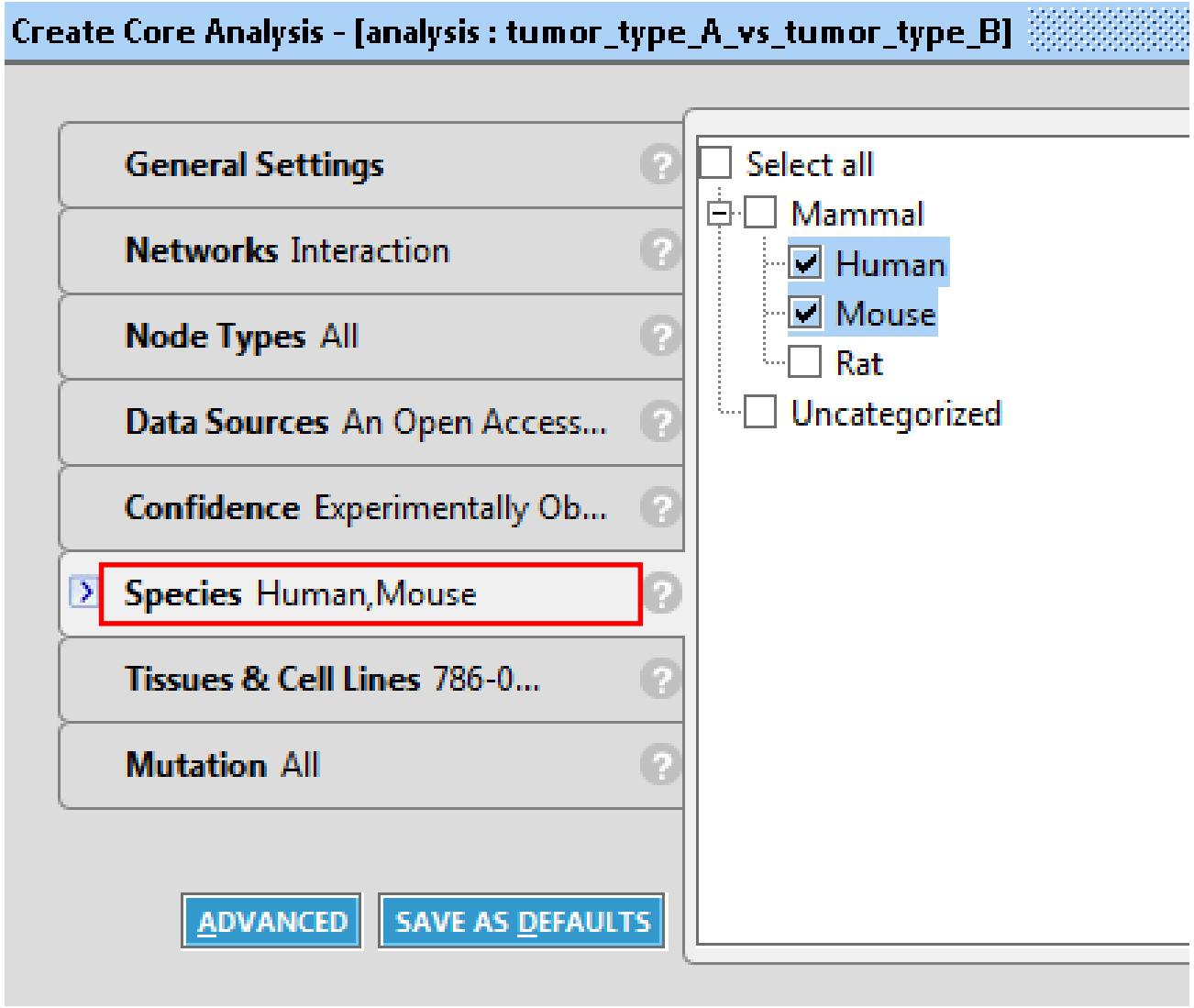
Setting up a Core Analysis: Data sources, select all



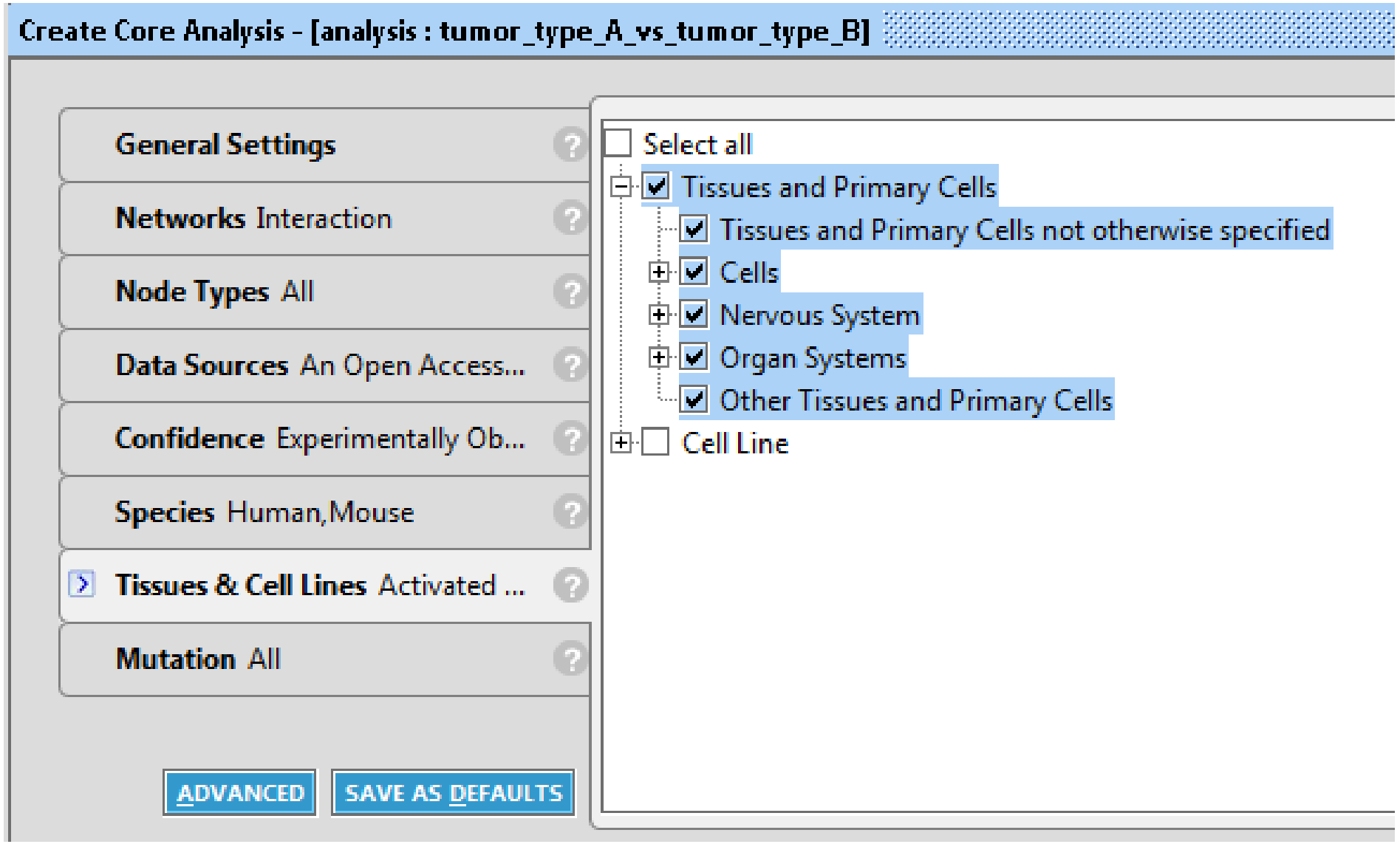
Setting up a Core Analysis: Confidence

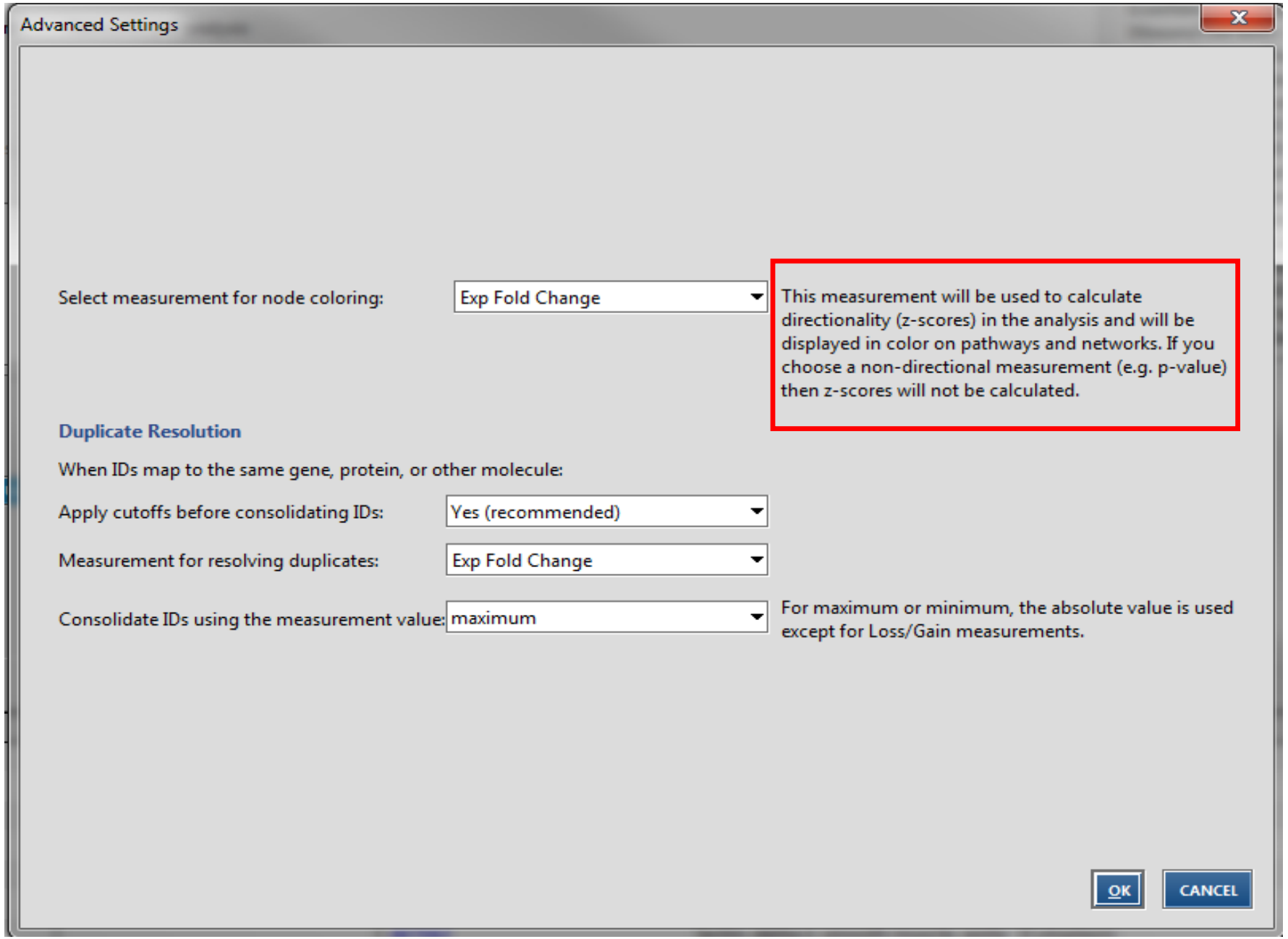


Setting up a Core Analysis: Species, select human and mouse



Setting up a Core Analysis: Tissue and cell lines; select all




Advanced Settings
Select measurement for node coloring:
Exp Fold Change
This measurement will be used to calculate directionality (z-scores) in the analysis and will be displayed in color on pathways and networks. If you choose a non-directional measurement (e.g. p-value) then z-scores will not be calculated.
Duplicate Resolution
When IDs map to the same gene, protein, or other molecule:
Apply cutoffs before consolidating IDs:
Yes (recommended)
Measurement for resolving duplicates:
Exp Fold Change
Consolidate IDs using the measurement value:
maximum
For maximum or minimum, the absolute value is used except for Loss/Gain measurements.
OK
CANCEL