

Supplementary Information

Expanding PROTACtable genome universe of E3 ligases

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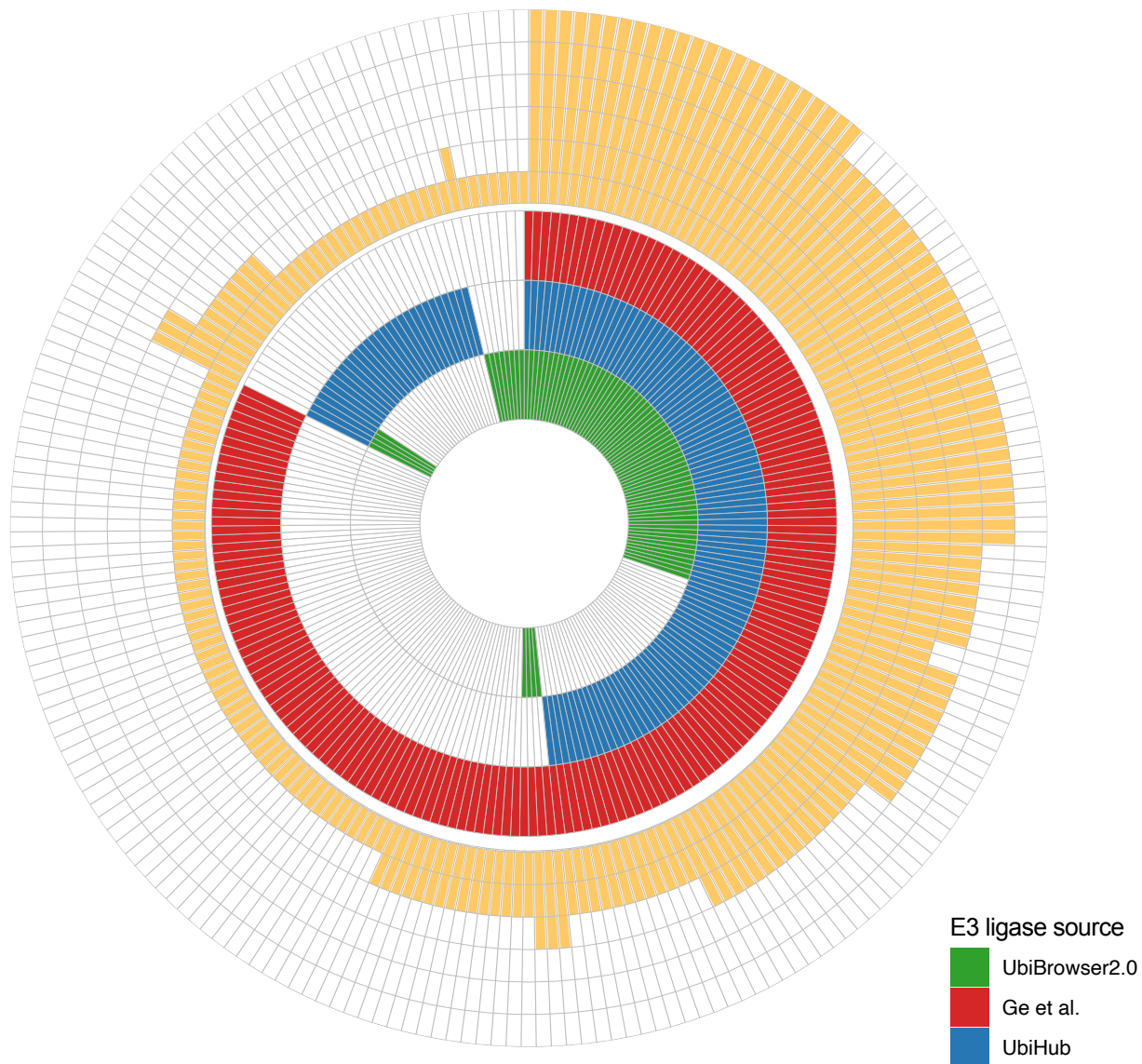
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Supplementary Fig. 14 Panels of E3Atlas web portal. (a) E3 ligase profile module: directly going into a specific gene's profile. (b) comprehensive profile page of E3 ligase: showing the profile of a specific E3 ligase. (c) General E3 ligase search module: offering users the to create a set of criteria and define their own threshold. (d) Search by target module: offering users to search for E3 ligases against a specific target. (e) Search results as a table.

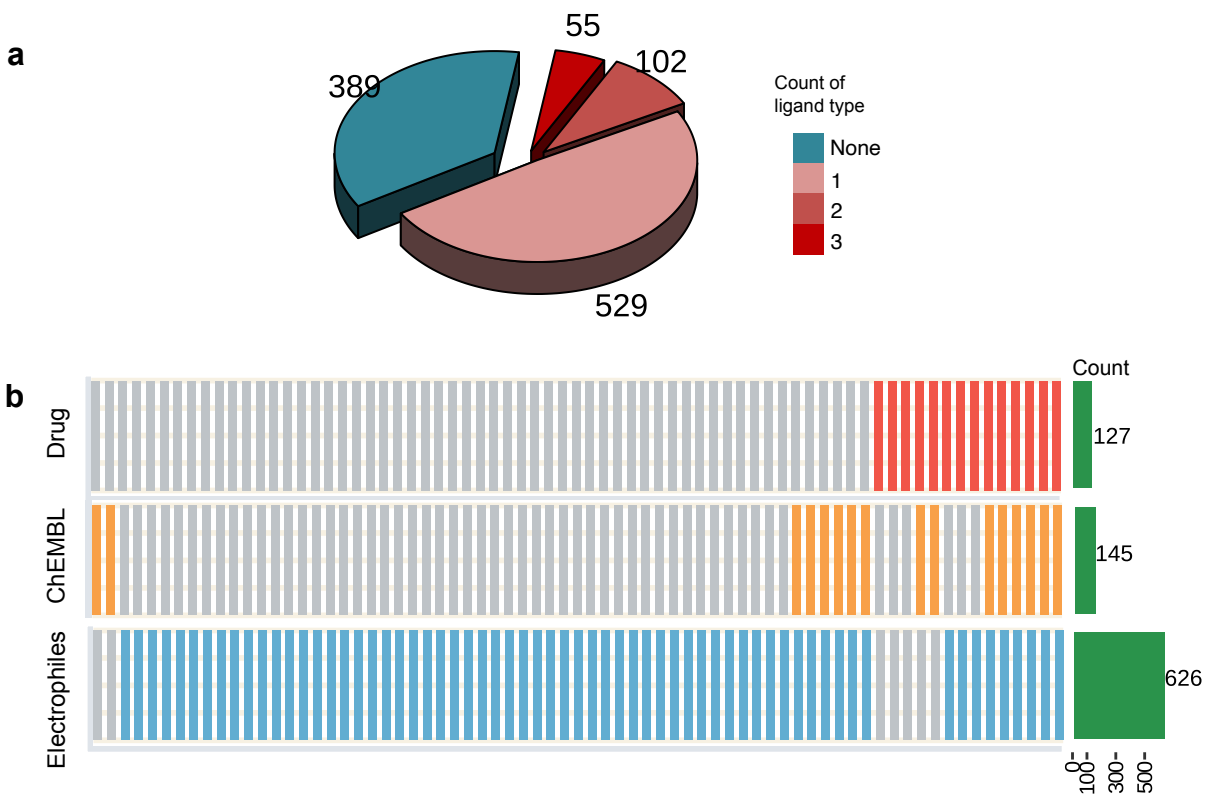
Supplementary Fig. 15 Use case: Integration of ligandability, PPI, expression pattern, confidence score, and cellular location of E3 ligases. From outer to inner ring, PPI, ligandability, E3 ligases, the number of high expression of cancer types in TCGA, the number of high expression of normal tissues in GTEx, confidence score, and cellular localization. E3 ligases in red were proceeded to PROTAC clinical trials. E3 ligases in blue were experimentally explored in PROTAC experiment. E3 ligases in bold were mentioned in context.

Supplementary Fig. 16 Use Case: Searching for E3 ligases against a critical oncogene, KRAS. From top to bottom: cellular location, ligandability, real structure availability, number of PPIs, expression level in PAAD, COAD, LUAD, LUSC, CHOL, UCEC, TGCT, and CESC, percentage of highly expressed cancer type in TCGA, and percentage of highly expressed normal tissues in GTEx. E3 ligases in bold were mentioned in context.

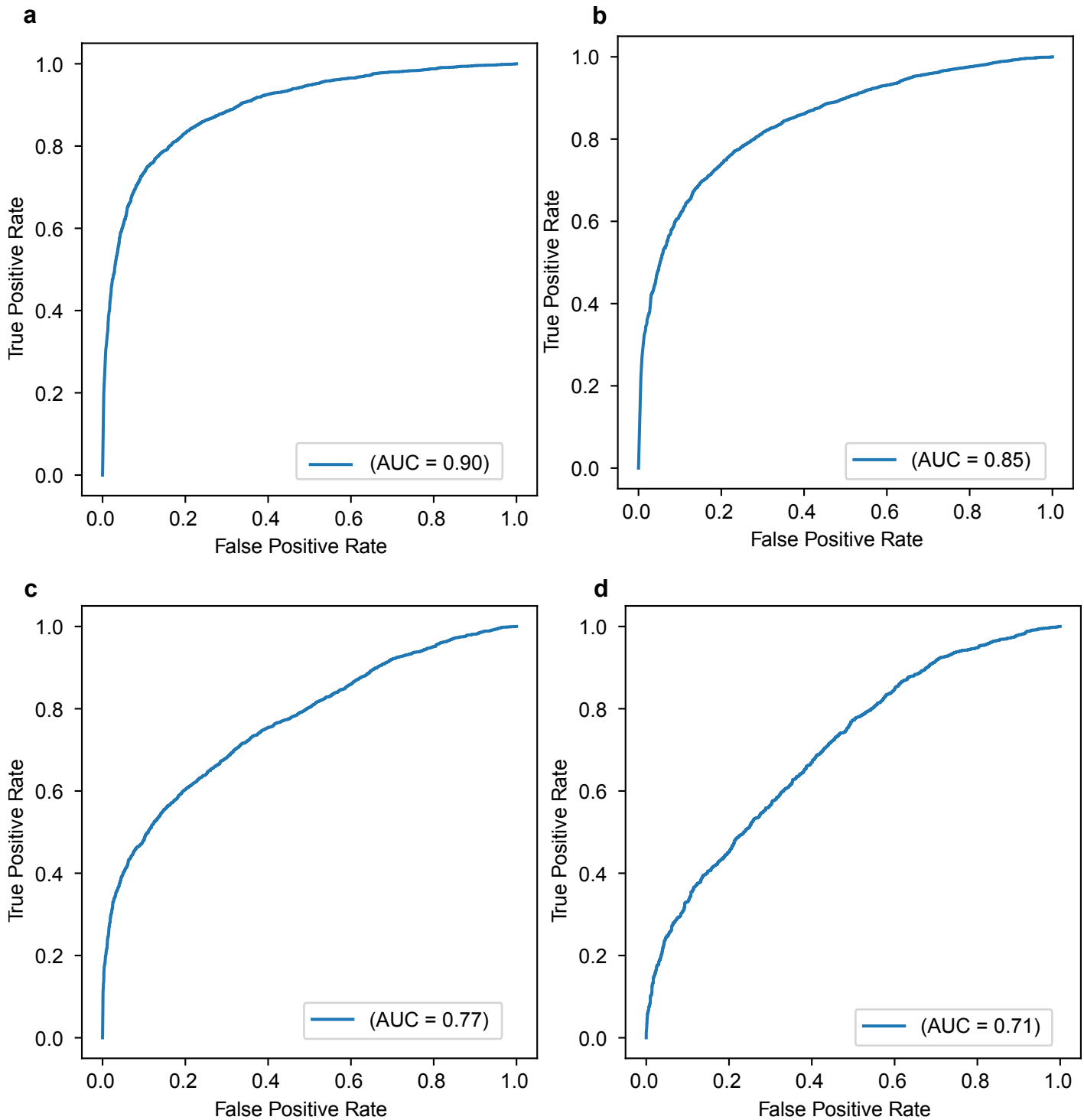
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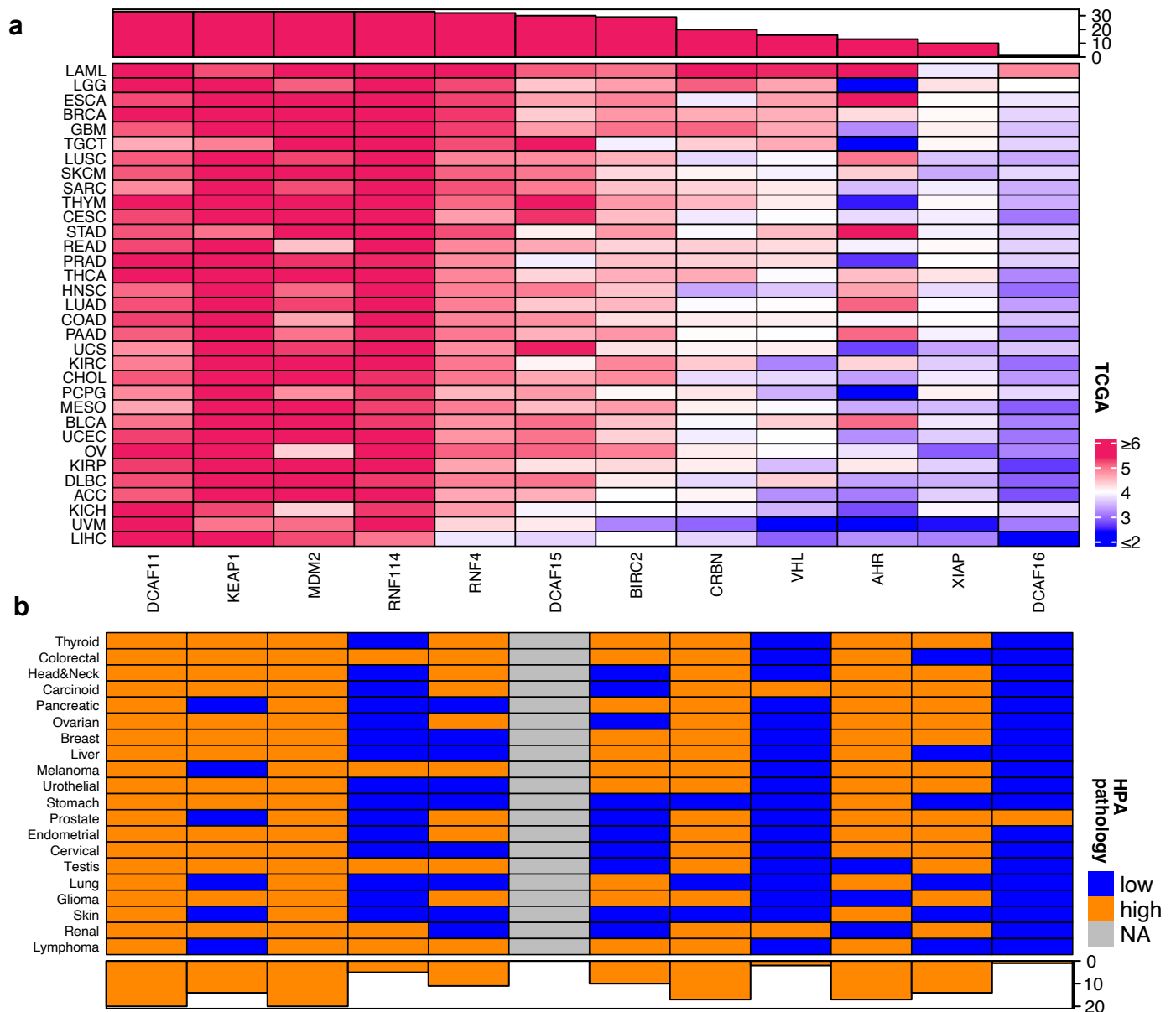
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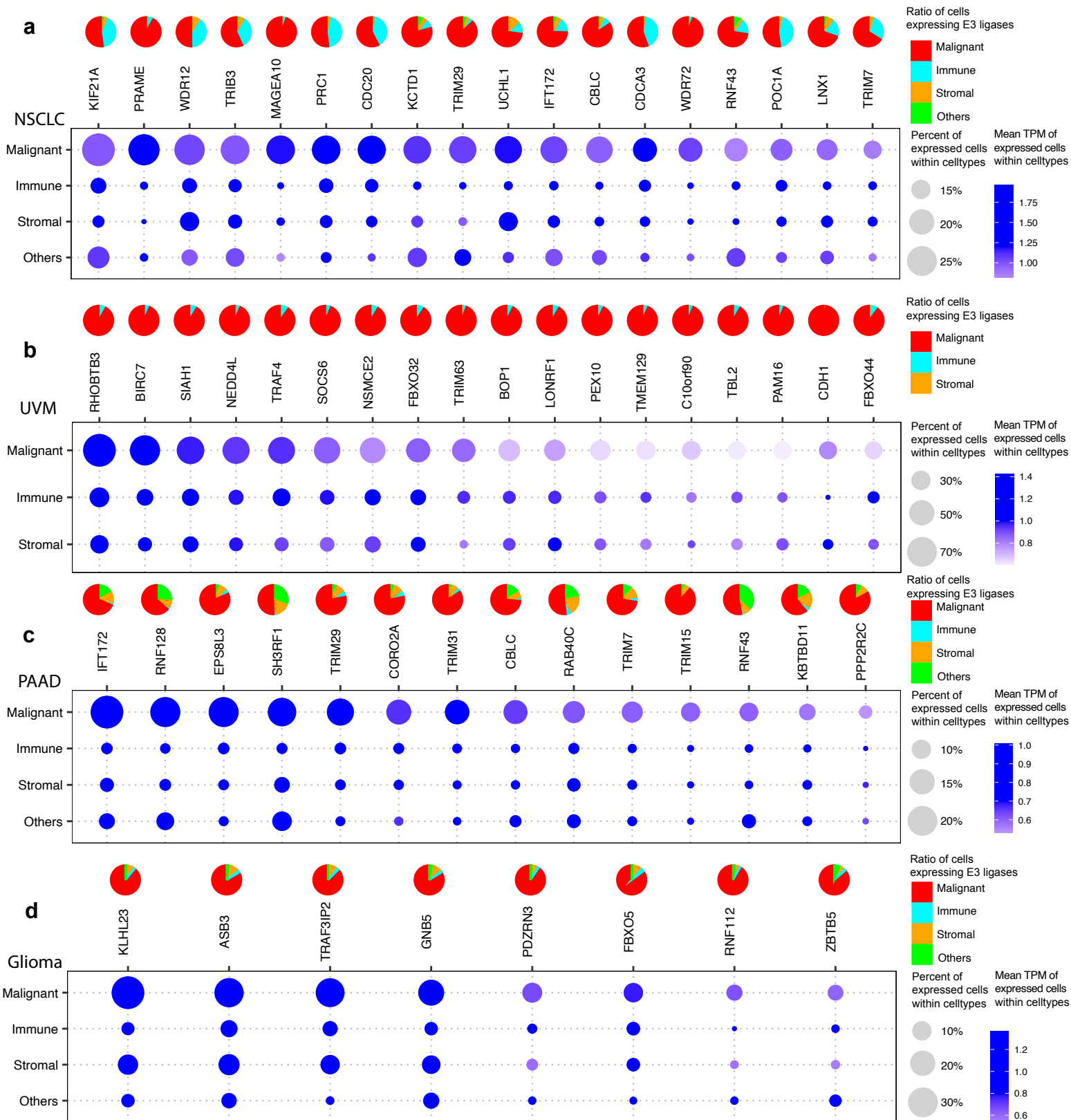
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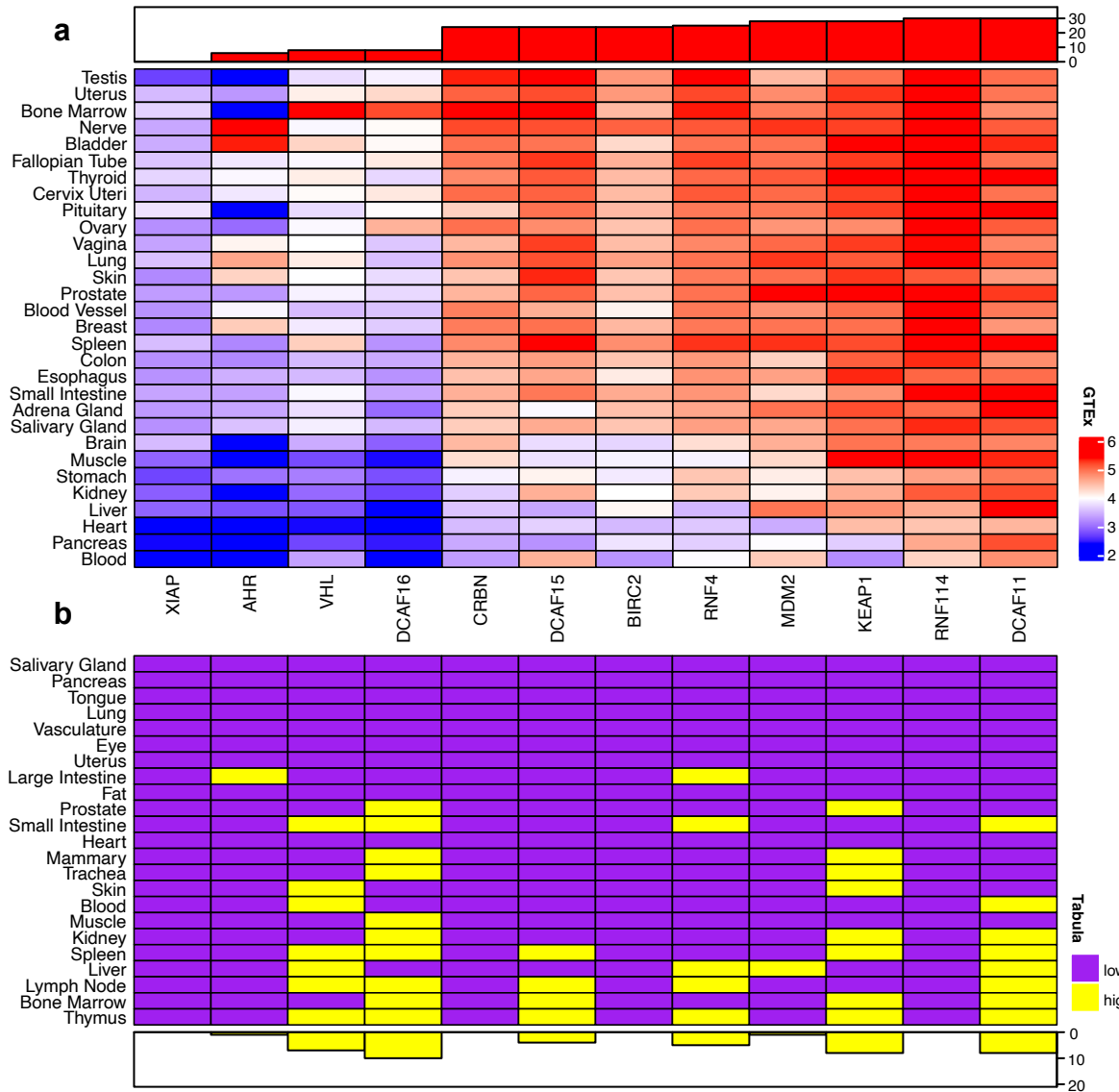
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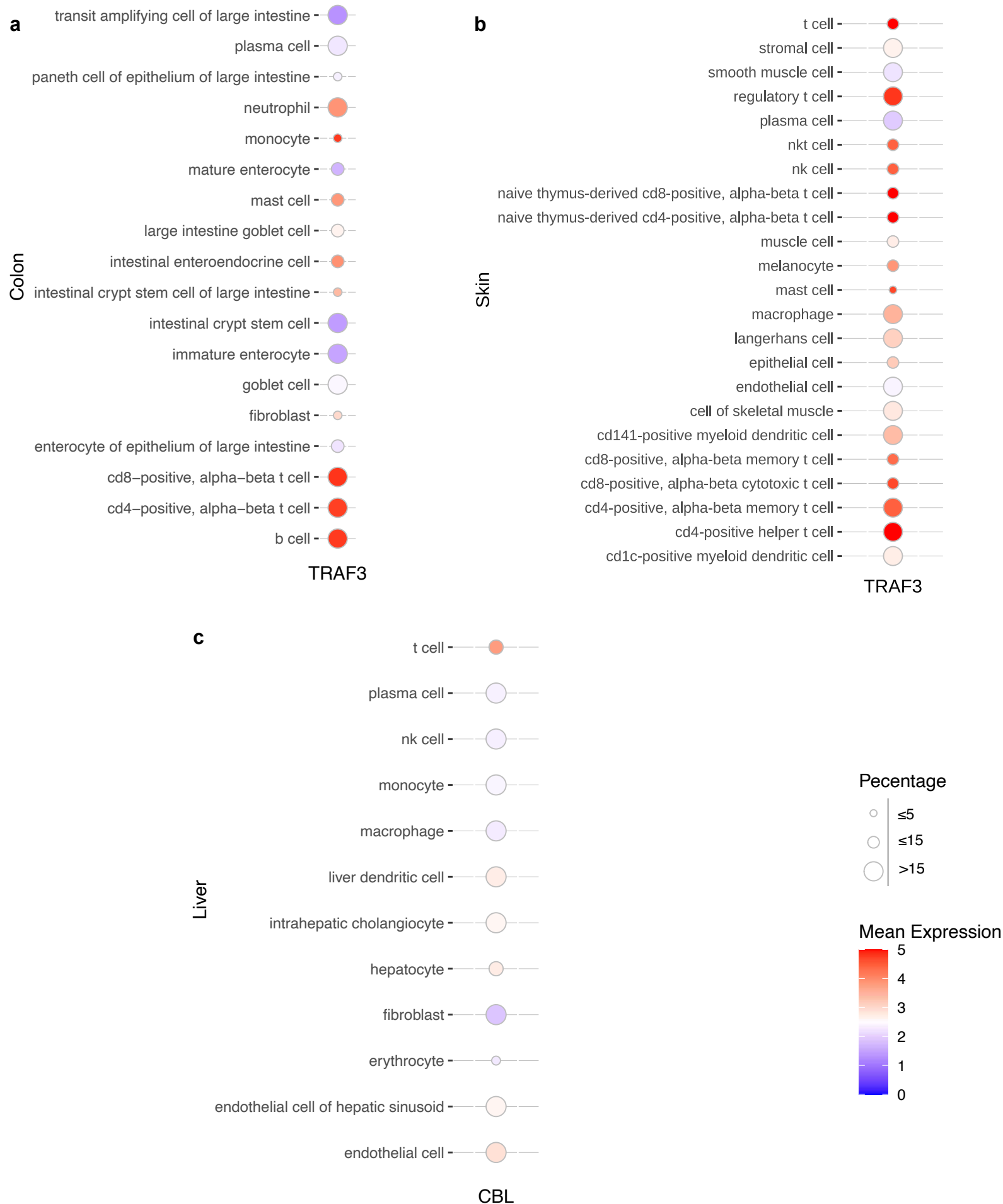
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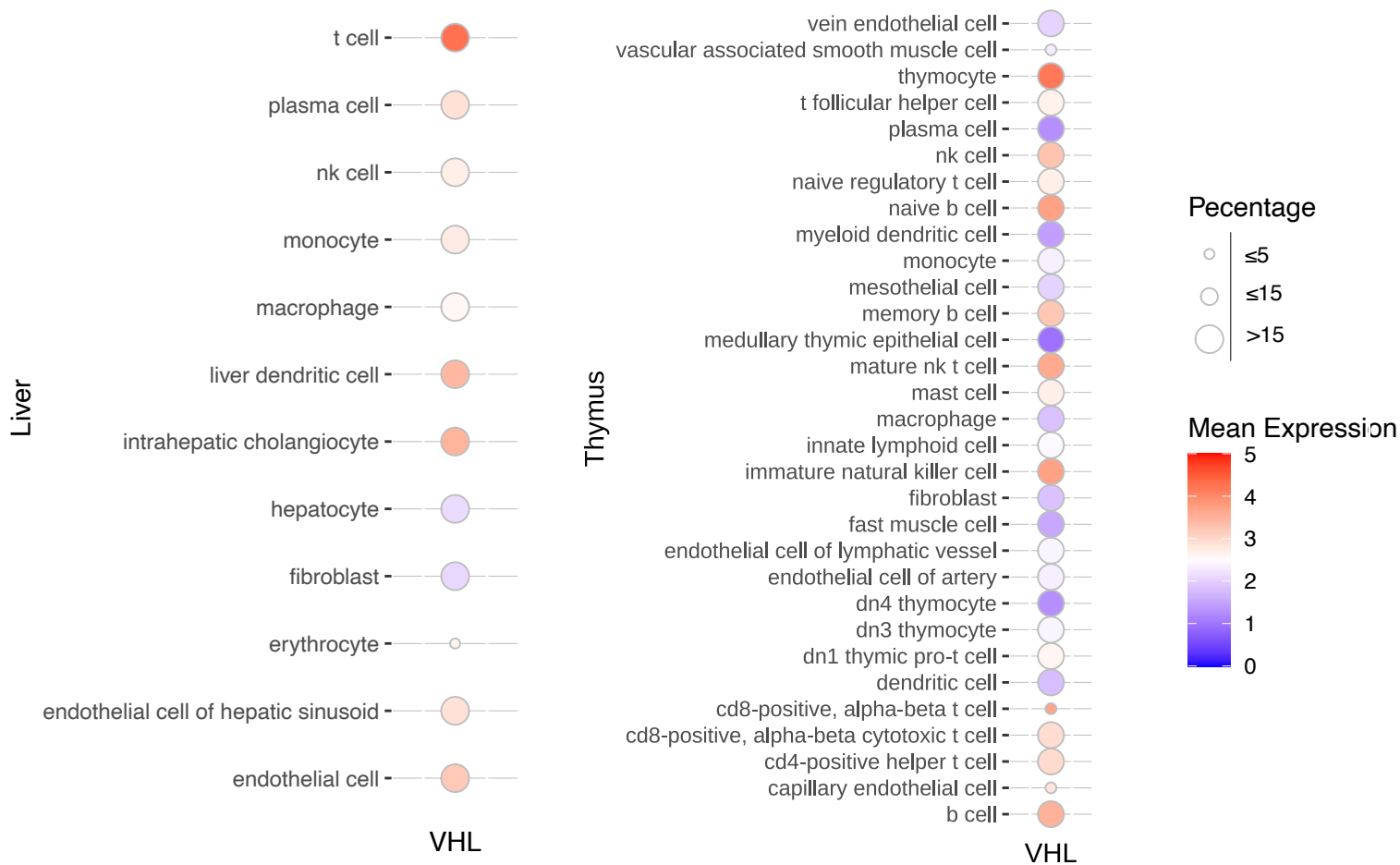
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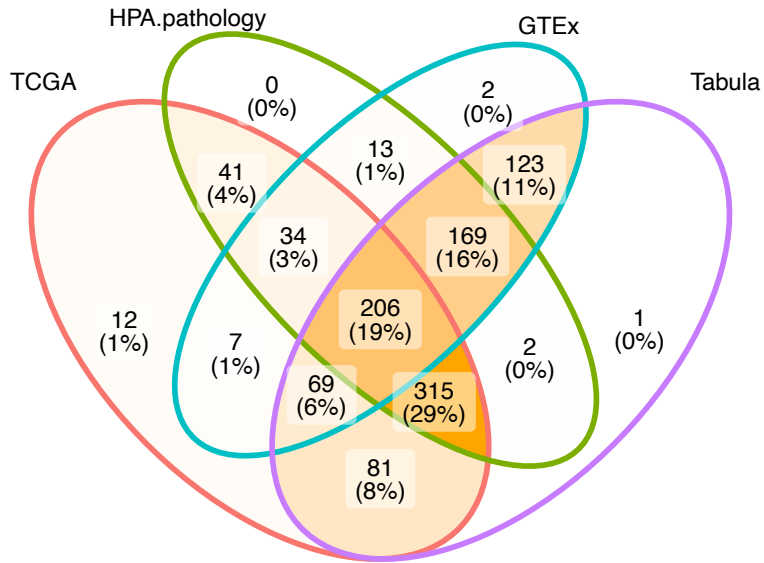
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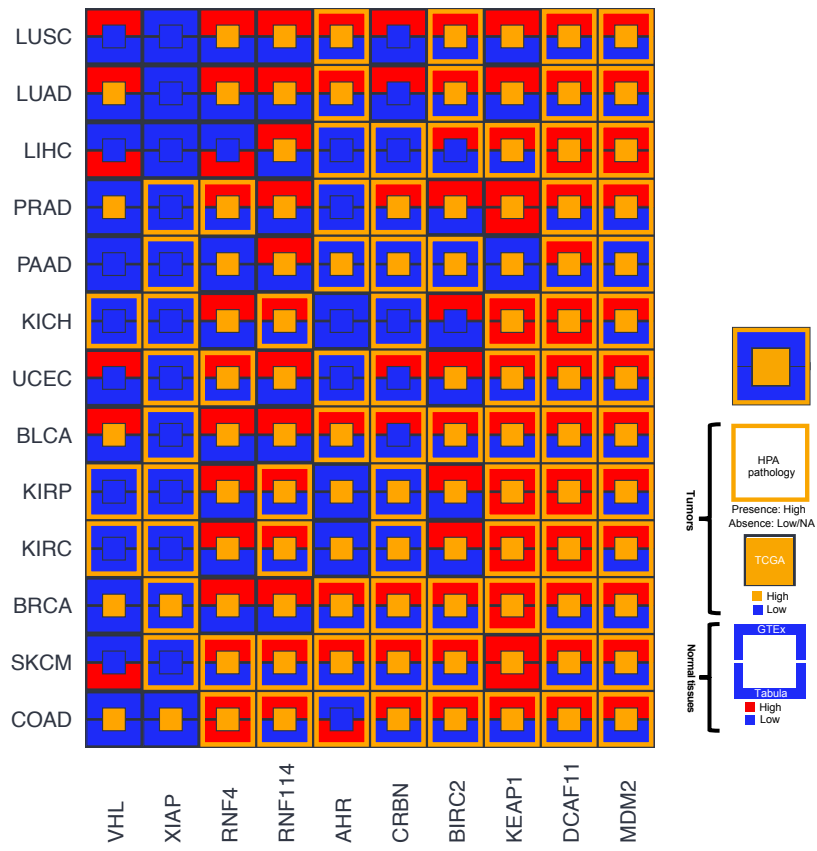


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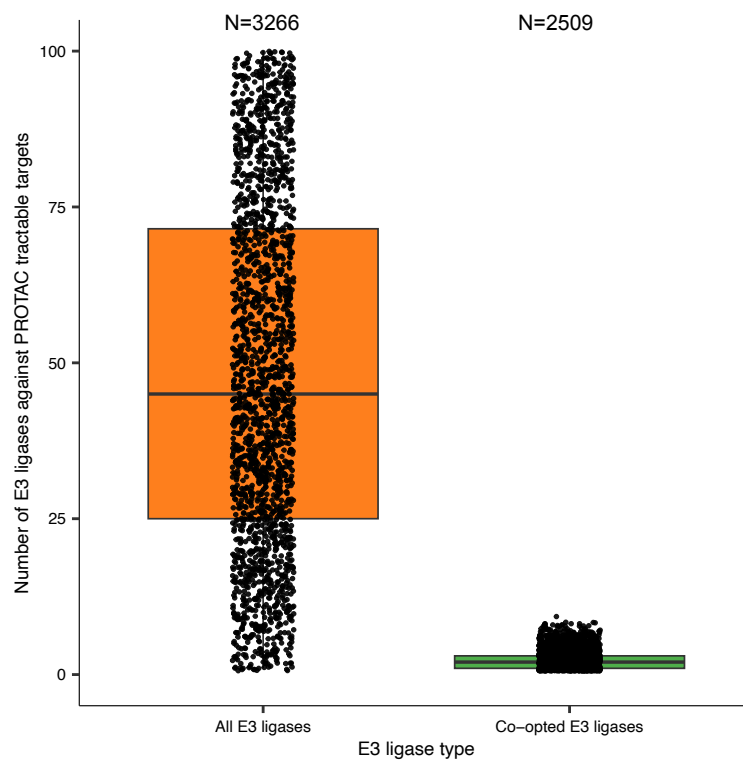


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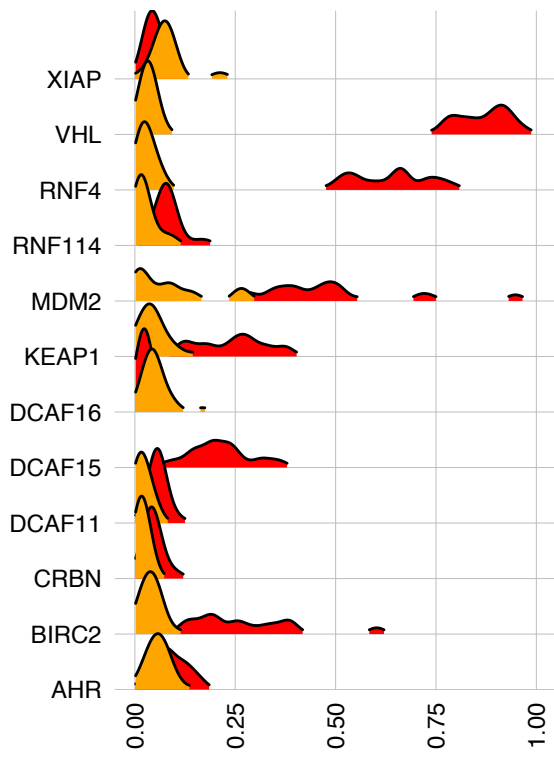
Venn plot of E3 ligases that were highly expressed in at least one cancer type in TCGA and HPA pathology and lowly expressed in the majority number of normal tissues in GTEx and Tabula.



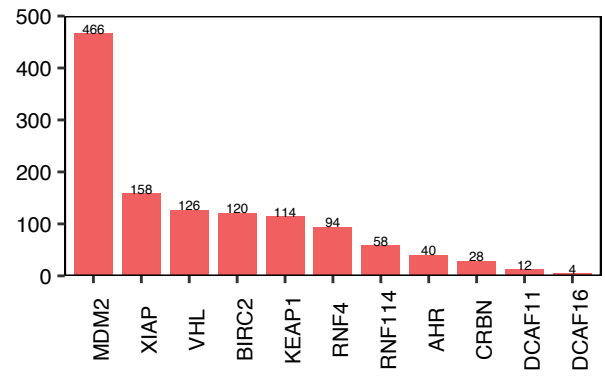
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Supplementary Fig. 13 Number of PPI interfaces associated with co-opted E3 ligases

a

Look for a specific E3

Get a full profile of each E3 ligase

CR

CRBN
CREBBP
NCRP1

b

Ligandability

Expression

TCGA High Expression Cancer Tumor: MPPC1, MPPC2, MPPC3, MPPC4, MPPC5, MPPC6, MPPC7, MPPC8, MPPC9, MPPC10, MPPC11, MPPC12, MPPC13, MPPC14, MPPC15, MPPC16, MPPC17, MPPC18, MPPC19, MPPC20, MPPC21, MPPC22, MPPC23, MPPC24, MPPC25, MPPC26, MPPC27, MPPC28, MPPC29, MPPC30, MPPC31, MPPC32, MPPC33, MPPC34, MPPC35, MPPC36, MPPC37, MPPC38, MPPC39, MPPC40, MPPC41, MPPC42, MPPC43, MPPC44, MPPC45, MPPC46, MPPC47, MPPC48, MPPC49, MPPC50, MPPC51, MPPC52, MPPC53, MPPC54, MPPC55, MPPC56, MPPC57, MPPC58, MPPC59, MPPC60, MPPC61, MPPC62, MPPC63, MPPC64, MPPC65, MPPC66, MPPC67, MPPC68, MPPC69, MPPC70, MPPC71, MPPC72, MPPC73, MPPC74, MPPC75, MPPC76, MPPC77, MPPC78, MPPC79, MPPC80, MPPC81, MPPC82, MPPC83, MPPC84, MPPC85, MPPC86, MPPC87, MPPC88, MPPC89, MPPC90, MPPC91, MPPC92, MPPC93, MPPC94, MPPC95, MPPC96, MPPC97, MPPC98, MPPC99, MPPC100, MPPC101, MPPC102, MPPC103, MPPC104, MPPC105, MPPC106, MPPC107, MPPC108, MPPC109, MPPC110, MPPC111, MPPC112, MPPC113, MPPC114, MPPC115, MPPC116, MPPC117, MPPC118, MPPC119, MPPC120, MPPC121, MPPC122, MPPC123, MPPC124, MPPC125, MPPC126, MPPC127, MPPC128, MPPC129, MPPC130, MPPC131, MPPC132, MPPC133, MPPC134, MPPC135, MPPC136, MPPC137, MPPC138, MPPC139, MPPC140, MPPC141, MPPC142, MPPC143, MPPC144, MPPC145, MPPC146, MPPC147, MPPC148, MPPC149, MPPC150, MPPC151, MPPC152, MPPC153, MPPC154, MPPC155, MPPC156, MPPC157, MPPC158, MPPC159, MPPC160, MPPC161, MPPC162, MPPC163, MPPC164, MPPC165

TCGA High Expression Tissue: Adipose, Adipose & soft tissue, Intestine (Large Intestine), Intestine (Small Intestine), Muscle, Skin, Skin (Not Sun Exposed) Lower Extremity, Skin (Sun Exposed) Lower Extremity, Skin (Sun Exposed) Upper Extremity, Stomach, Testis, Uterus

TCGA High Expression Tissue: (All Tissues) (All Tissues)

Target Disease Interface Target Interface E3 Interface Target

c

Property

Conf Score 0 6 Cutoff: 3

Cellular Location - Nucleus

Cellular Location - Cytoplasm

Ligandability

Expression in Tumors

TCGA 0% 100% Cutoff: \geq 70%

HPA pathology 0% 100% Cutoff: \geq 30%

Expression in Normal Tissues

GTEX 0% 100% Cutoff: \leq 53%

Tabula 0% 100% Cutoff: \leq 75%

d

Specify a target, e.g. KRAS

KRAS

Which Cancer Type (TCGA) E3 ligases High

BRCA

Property

Conf Score 0 6 Cutoff: 3

Cellular Location - Nucleus

Cellular Location - Cytoplasm

Ligandability

Drug

ChEMBL

Electrophile

e

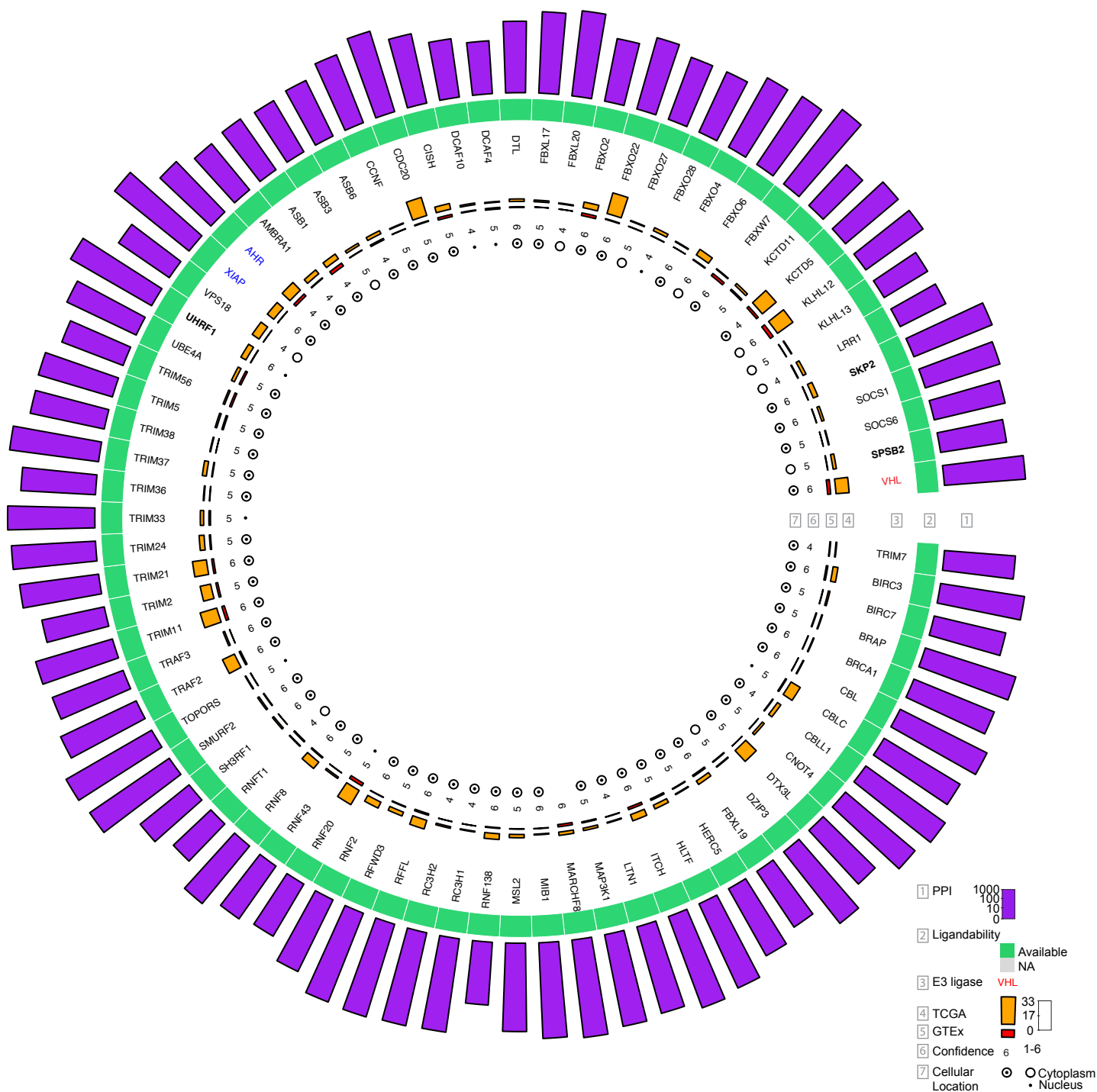
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ATG5
BACH1
BAZ1A
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BMI1
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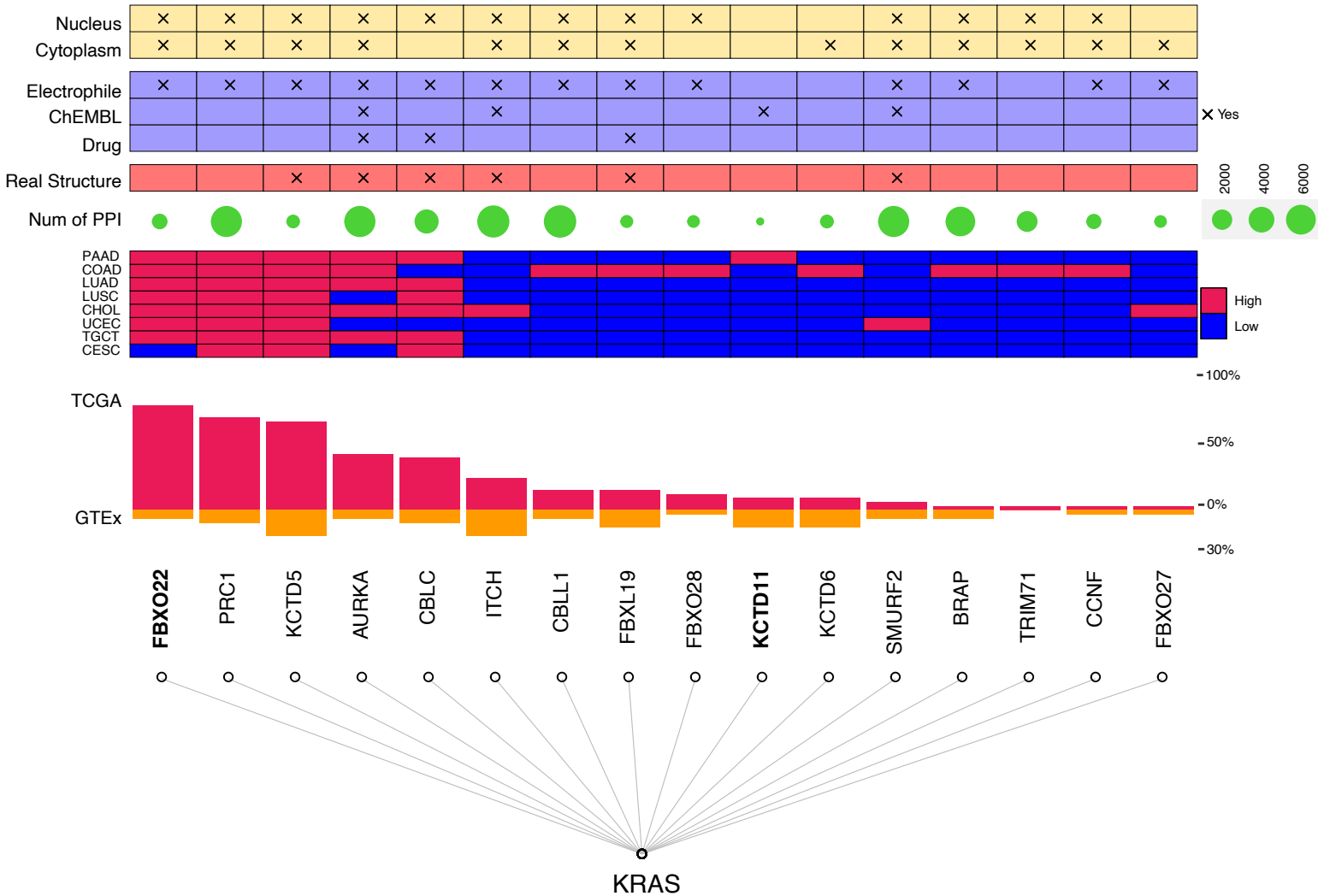
Showing 1 to 10 of 165 entries

Showing 11 to 20 of 165 entries

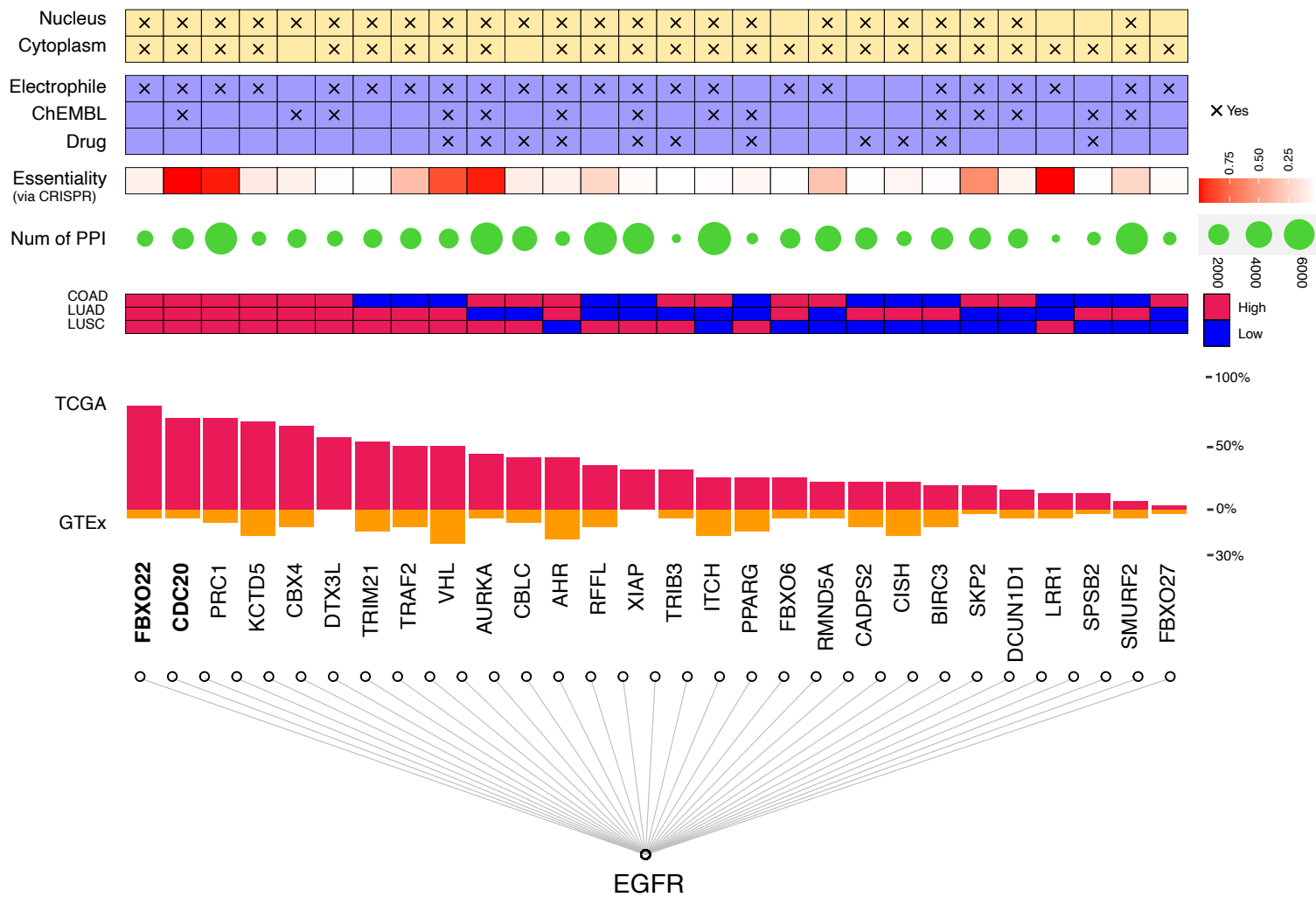
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