compare outliers from different comparison cohorts 2023.11.27 11.25.57

hbeale

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version 2023.11.27_11.25.57 adds per-patient analysis

```
underscore_to_space <- function(x) str_replace_all(x, "_", " ")
```

```
outliers <- read_tsv("../input_data/druggable_outliers_from_treehouse_and_other_cohorts_2023_11_09-13_4
  mutate(high_level_cohort = ifelse(str_detect(comparison_cohort, "Treehouse"),
                                    "Treehouse",
                                    comparison_cohort))
```

```
## Rows: 287 Columns: 5
## -- Column specification --------------------------------------------------------
## Delimiter: "\t"
## chr (4): Sample_ID, comparison_cohort, gene, donor_ID
## lgl (1): pathway_support
##
## i Use `spec()` to retrieve the full column specification for this data.
## i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
n_distinct(outliers$Sample_ID)
```

```
## [1] 34
```

```
n_distinct(outliers$donor_ID)
```

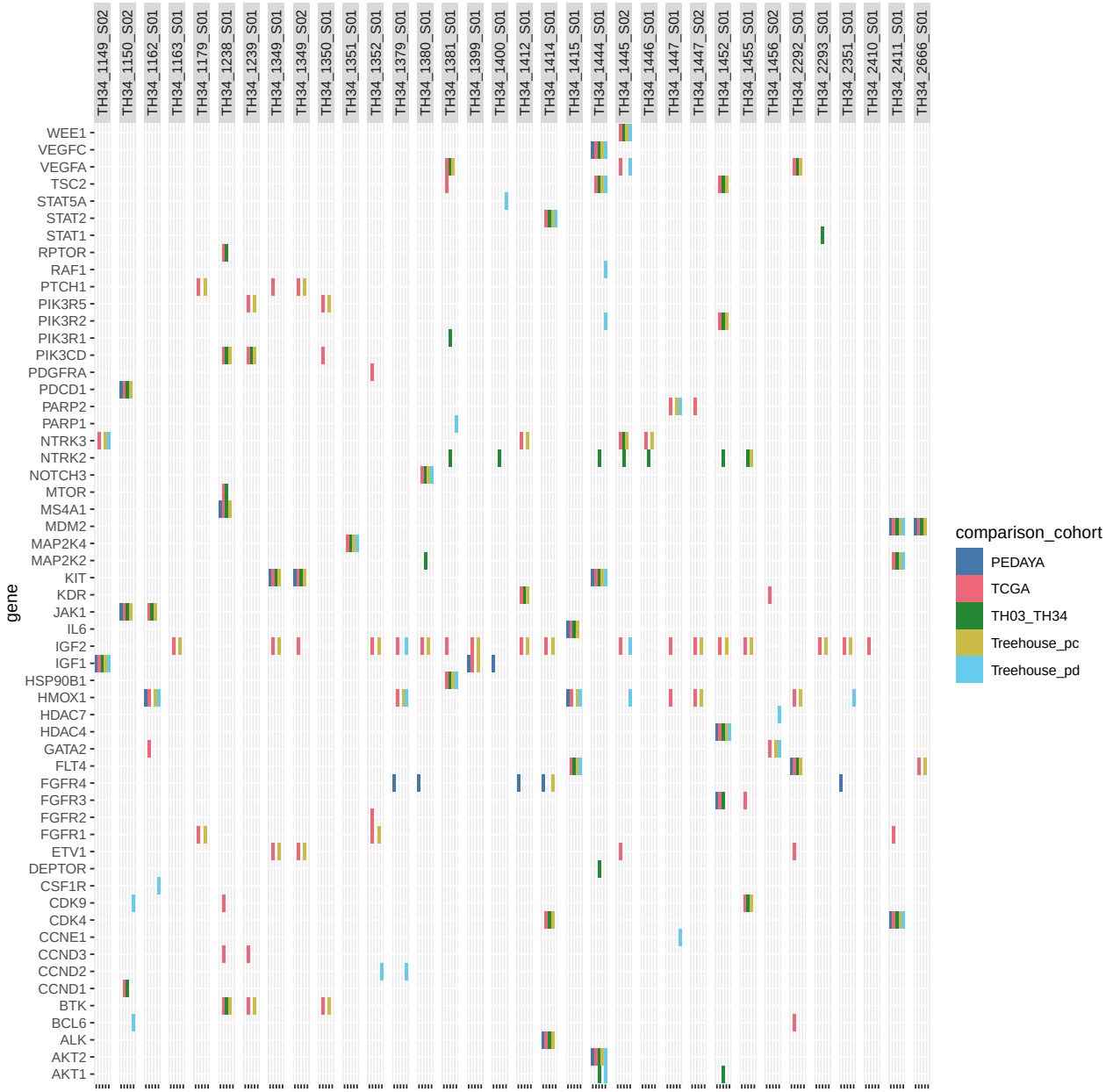
```
## [1] 32
```

Define cohort codes

```
cohort_codes <- tibble(
  cohort_name =
    c("PEDAYA", "TCGA", "TH03_TH34", "Treehouse_pc", "Treehouse_pd"),
  cohort_code =
    c("P", "T", "S", "C", "D"))
```

Tile plot of all outliers

```
ggplot(outliers) +
  geom_tile(aes(x=comparison_cohort,
                y=gene,
                fill = comparison_cohort)) +
  facet_wrap(~Sample_ID,
             nrow = 1) +
  theme(#axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5),
    axis.text.x = element_blank(),
    strip.text.x = element_text(angle = 90),
        ) +
  xlab("")  +
  scale_fill_bright()
```



Heatmap shows number of cohorts in which outlier were detected

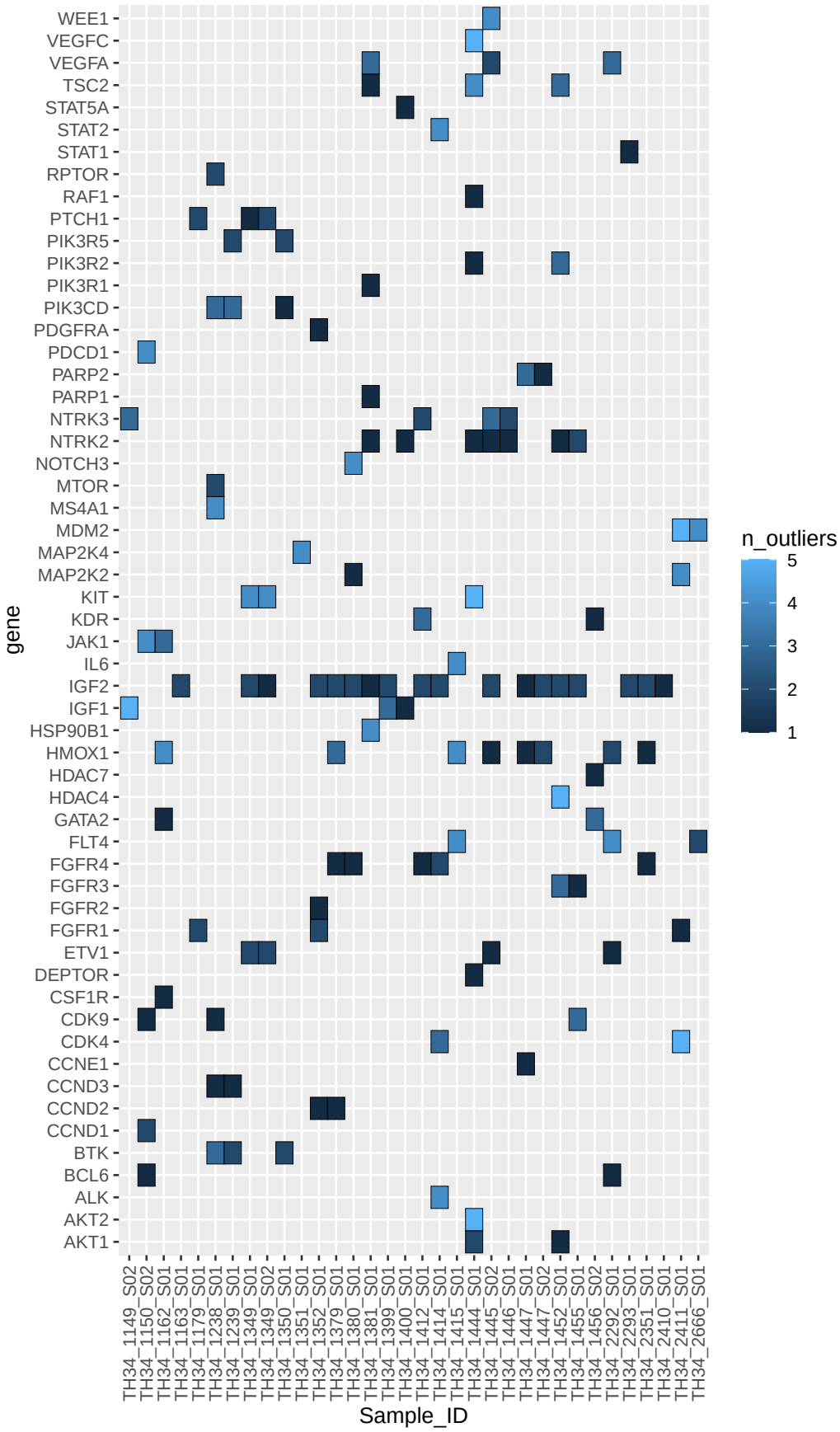
I can make this look better if we decide to use it, but it's non-trivial

```
outliers_heatmap_data <- outliers %>%
  group_by(Sample_ID, gene) %>%
  summarize(n_outliers = n())
```

```
## `summarise()` has grouped output by 'Sample_ID'. You can override using the
## `.groups` argument.
```

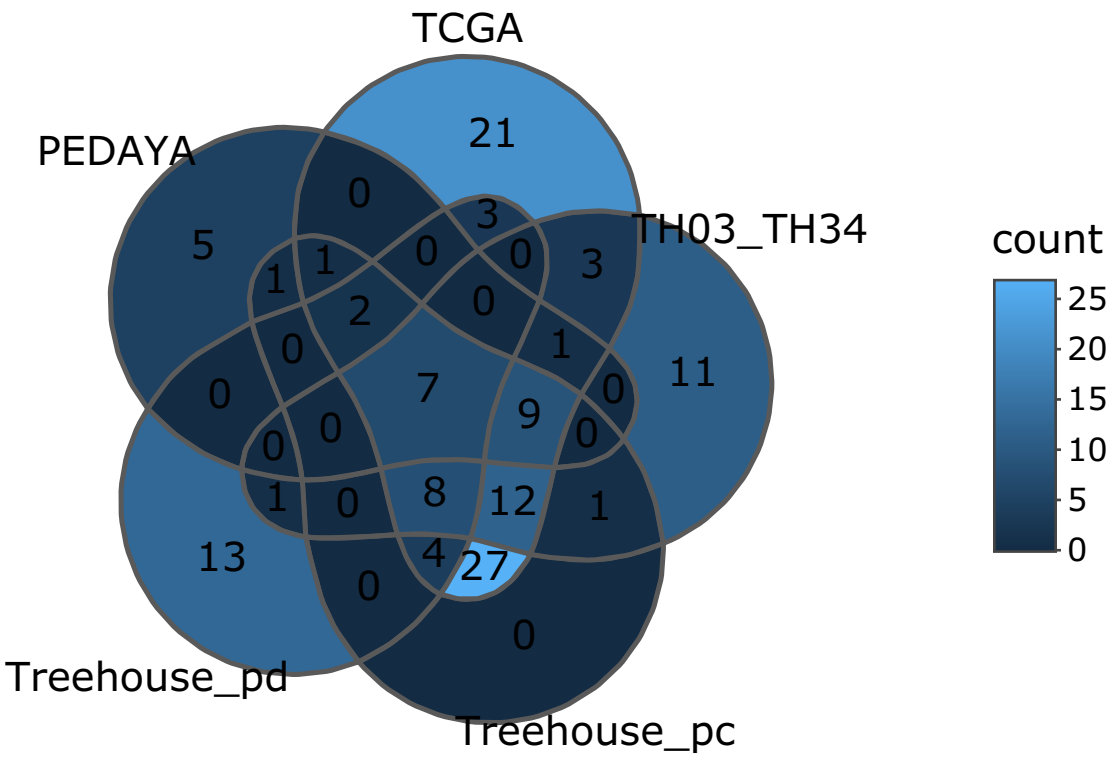
```
ggplot(outliers_heatmap_data) +
  geom_tile(aes(x=Sample_ID,
                y=gene,
```

```
              fill = n_outliers),
          color = "black")  +
#theme_bw() +
theme(axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5))
```

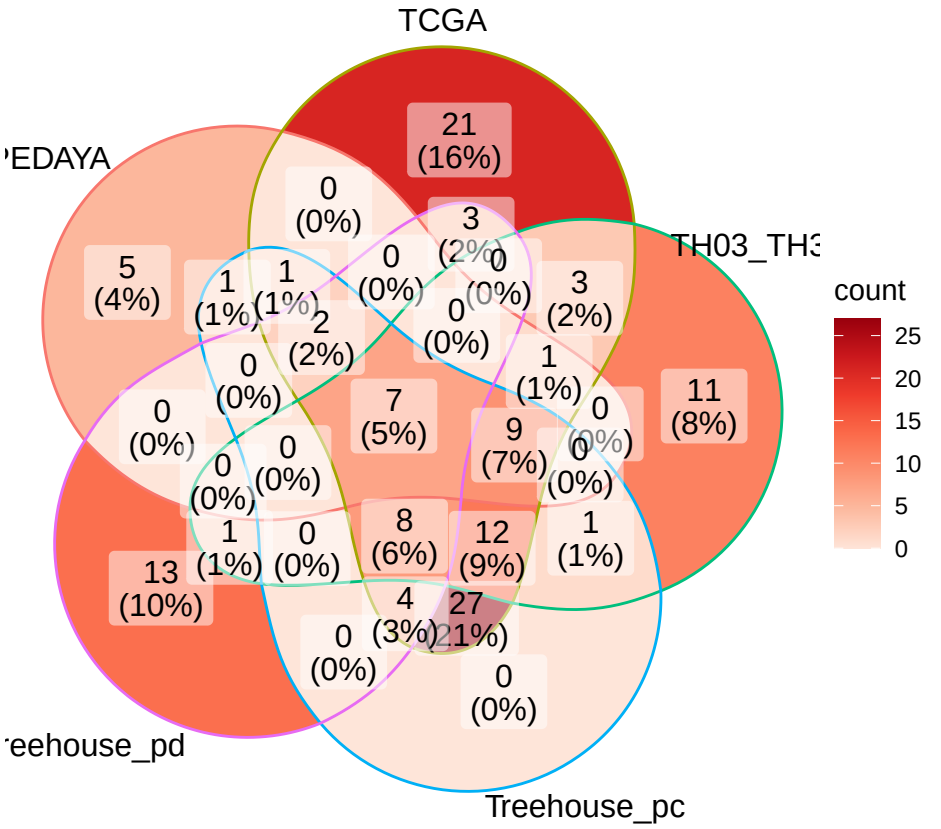

gene
WEE1
VEGFC
VEGFA
TSC2
STAT5A
STAT2
STAT1
RPTOR
RAF1
PTCH1
PIK3R5
PIK3R2
PIK3R1
PIK3CD
PDGFRA
PDCD1
PARP2
PARP1
NTRK3
NTRK2
NOTCH3
MTOR
MS4A1
MDM2
MAP2K4
MAP2K2
KIT
KDR
JAK1
IL6
IGF2
IGF1
HSP90B1
HMOX1
HDAC7
HDAC4
GATA2
FLT4
FGFR4
FGFR3
FGFR2
FGFR1
ETV1
DEPTOR
CSF1R
CDK9
CDK4
CCNE1
CCND3
CCND2
CCND1
BTK
BCL6
ALK
AKT2
AKT1
TH34_1149_S02
TH34_1150_S02
TH34_1162_S01
TH34_1163_S01
TH34_1179_S01
TH34_1238_S01
TH34_1239_S01
TH34_1349_S01
TH34_1349_S02
TH34_1350_S01
TH34_1351_S01
TH34_1352_S01
TH34_1379_S01
TH34_1380_S01
TH34_1381_S01
TH34_1399_S01
TH34_1400_S01
TH34_1412_S01
TH34_1414_S01
TH34_1415_S01
TH34_1444_S01
TH34_1445_S02
TH34_1446_S01
TH34_1447_S01
TH34_1447_S02
TH34_1452_S01
TH34_1455_S01
TH34_1456_S02
TH34_2292_S01
TH34_2293_S01
TH34_2351_S01
TH34_2410_S01
TH34_2411_S01
TH34_2666_S01
Sample_ID
n_outliers
5
4
3
2
1

```
library(ggVennDiagram)
raw_outliers_for_venn <- outliers %>%
  mutate(sample_gene = paste(Sample_ID, gene, sep = "_")) %>%
  arrange(comparison_cohort) %>%
  select(sample_gene, comparison_cohort) %>%
  group_split(comparison_cohort)


list_of_outliers_for_venn <-  lapply(raw_outliers_for_venn, function(x) x %>% pull(sample_gene))
names(list_of_outliers_for_venn) <- unique(outliers$comparison_cohort) %>% sort

ggVennDiagram(list_of_outliers_for_venn,
              show_intersect = TRUE)
```

```
## Warning in geom_text(aes_string(label = "count", text = "text"), x =
## label_coord[, : Ignoring unknown aesthetics: text
```




```
ggVennDiagram(list_of_outliers_for_venn) +
  scale_fill_distiller(palette = "Reds", direction = 1)
```



export list of genes found only by TCGA

```
outliers %>%
  group_by(Sample_ID, gene) %>%
  filter(length(comparison_cohort) == 1,
         "TCGA" %in% comparison_cohort) %>%
  ungroup %>%
  select(gene) %>% write_tsv("../gather_input_data/genes found only by TCGA in at least one sample.txt")
```

Annotate with combined full low level cohort names

```
collapse_fun <- function(x){ paste(x,collapse = ", ") }

all_outliers_combined_wide <- outliers %>%
  select(-pathway_support, -donor_ID, -high_level_cohort) %>%
  pivot_wider(names_from = Sample_ID,
              values_from = comparison_cohort,
              values_fn = collapse_fun)

n_distinct(outliers$Sample_ID)
```

```
## [1] 34
```

comparison_cohorts	n	percent
TCGA, Treehouse_pc	27	20.8%
TCGA	21	16.2%
Treehouse_pd	13	10.0%
TCGA, TH03_TH34, Treehouse_pc	12	9.2%
TH03_TH34	11	8.5%
PEDAYA, TCGA, TH03_TH34, Treehouse_pc	9	6.9%
TCGA, TH03_TH34, Treehouse_pc, Treehouse_pd	8	6.2%
PEDAYA, TCGA, TH03_TH34, Treehouse_pc, Treehouse_pd	7	5.4%
PEDAYA	5	3.8%
TCGA, Treehouse_pc, Treehouse_pd	4	3.1%
TCGA, TH03_TH34	3	2.3%
TCGA, Treehouse_pd	3	2.3%
PEDAYA, TCGA, Treehouse_pc, Treehouse_pd	2	1.5%
PEDAYA, TCGA, TH03_TH34	1	0.8%
PEDAYA, TCGA, Treehouse_pc	1	0.8%
PEDAYA, Treehouse_pc	1	0.8%
TH03_TH34, Treehouse_pc	1	0.8%
TH03_TH34, Treehouse_pd	1	0.8%
Total	130	-

```
n_distinct(outliers$gene)
```

```
## [1] 56
```

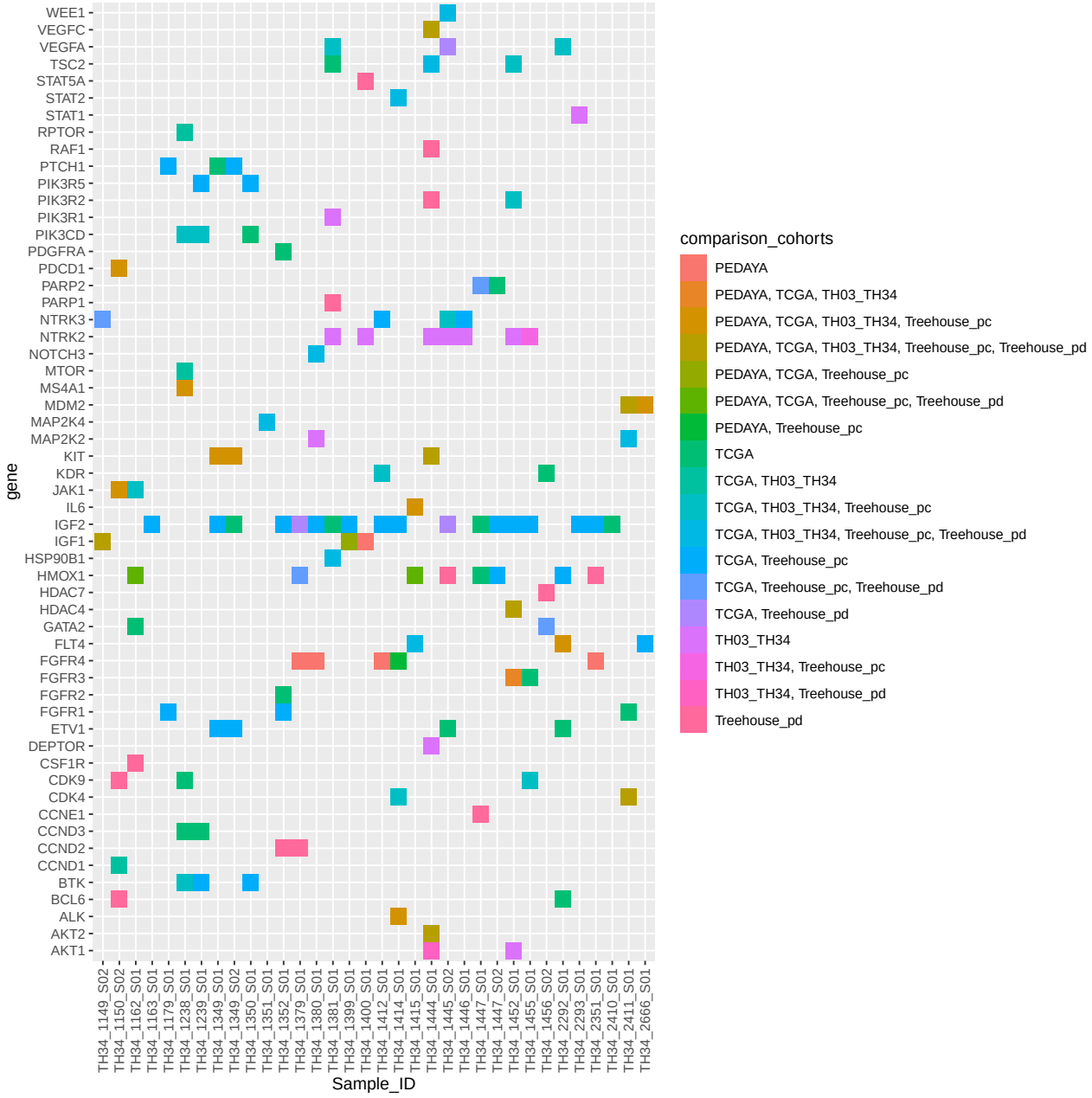
```
all_outliers_combined_long <- all_outliers_combined_wide %>%
  pivot_longer(-gene,
               names_to = "Sample_ID",
               values_to = "comparison_cohorts") %>%
  na.omit()
```

How many outliers are present in each combination of cohorts?

```
tabyl(all_outliers_combined_long,
      comparison_cohorts) %>%
  arrange(desc(n)) %>%
  adorn_pct_formatting() %>%
  adorn_totals() %>%
  kbl() %>%
  kable_styling(full_width = F)
```

Tile plot of combination of outliers

```
ggplot(all_outliers_combined_long) +
  geom_tile(aes(x=Sample_ID,
                y=gene,
                fill = comparison_cohorts))  +
  theme(axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5))
```




```
n_distinct(all_outliers_combined_long$Sample_ID)
```

```
## [1] 34
```

Annotate with combined full high level cohort names

```
high_level_all_outliers_combined_wide <- outliers %>%
  select(-pathway_support, -donor_ID, -comparison_cohort) %>%
  distinct() %>%
  pivot_wider(names_from = Sample_ID,
              values_from = high_level_cohort,
              values_fn = collapse_fun)
```

comparison_cohorts	n	percent
TCGA, Treehouse	34	26.2%
TCGA	21	16.2%
TCGA, TH03_TH34, Treehouse	20	15.4%
PEDAYA, TCGA, TH03_TH34, Treehouse	16	12.3%
Treehouse	13	10.0%
TH03_TH34	11	8.5%
PEDAYA	5	3.8%
PEDAYA, TCGA, Treehouse	3	2.3%
TCGA, TH03_TH34	3	2.3%
TH03_TH34, Treehouse	2	1.5%
PEDAYA, TCGA, TH03_TH34	1	0.8%
PEDAYA, Treehouse	1	0.8%
Total	130	-

```
n_distinct(outliers$Sample_ID)
```

```
## [1] 34
```

```
n_distinct(outliers$gene)
```

```
## [1] 56
```

```
high_level_all_outliers_combined_long <- high_level_all_outliers_combined_wide %>%
  pivot_longer(-gene,
               names_to = "Sample_ID",
               values_to = "comparison_cohorts") %>%
  na.omit()
```

How many outliers are present in each high level combination of cohorts?

```
tabyl(high_level_all_outliers_combined_long,
      comparison_cohorts) %>%
  arrange(desc(n)) %>%
  adorn_pct_formatting() %>%
  adorn_totals() %>%
  kbl() %>%
  kable_styling(full_width = F)
```

Annotate with minimal combined cohort abbreviations

```
collapse_fun_no_coma <- function(x){ paste(x,collapse = "") }

# backslashes prevent asterisks from being interpreted as italics in the kbl table

all_outliers_min_abbrev_combined_wide <- outliers %>%
  left_join(cohort_codes,
```

```
            by=c("comparison_cohort"="cohort_name")) %>%
  mutate(cohort_code_pathway = ifelse(pathway_support,
                                      paste0(cohort_code, "\\*"),
                                      cohort_code)) %>%
  select(-pathway_support, -donor_ID,
         -comparison_cohort,
         -cohort_code) %>%
  pivot_wider(names_from = Sample_ID,
              values_from = cohort_code_pathway,
              values_fn = collapse_fun_no_coma,
              values_fill = "")


all_outliers_min_abbrev_combined_wide %>%
  arrange(gene) %>%
  rename_all(underscore_to_space) %>%
  kbl() %>%
  kable_styling(full_width = F,
                bootstrap_options = "bordered")
```

Annotate with combined cohort abbreviations

```
all_outliers_abbrev_combined_wide <- outliers %>%
  left_join(cohort_codes,
            by=c("comparison_cohort"="cohort_name")) %>%
  select(-pathway_support, -donor_ID,
         -comparison_cohort) %>%
  pivot_wider(names_from = Sample_ID,
              values_from = cohort_code,
              values_fn = collapse_fun,
              values_fill = "")
```

```
all_outliers_abbrev_combined_wide %>%
  arrange(gene) %>%
  rename_all(underscore_to_space) %>%
  kbl() %>%
  kable_styling(full_width = F,
                bootstrap_options = "bordered")
```

Summary table for all outliers and low level cohorts

```
n_outliers_detected_by_any_method <- outliers %>%
  select(Sample_ID, gene) %>%
  distinct %>%
  nrow()

n_outliers_with_pathway_support_detected_by_any_method <- outliers %>%
  filter(pathway_support) %>%
  select(Sample_ID, gene) %>%
```

gene	high level cohort	TH34 1162 S01	TH34 1149 S02	TH34 1238 S01	TH34 1349 S01	TH34 1349 S02
AKT1	TH03_TH34					
AKT1	Treehouse					
AKT2	PEDAYA					
AKT2	TCGA					
AKT2	TH03_TH34					
AKT2	Treehouse					
ALK	PEDAYA					
ALK	TCGA					
ALK	TH03_TH34					
ALK	Treehouse					
BCL6	TCGA					
BCL6	Treehouse					
BTK	TCGA			T*		
BTK	TH03_TH34			S*		
BTK	Treehouse			C*		
CCND1	TCGA					
CCND1	TH03_TH34					
CCND2	Treehouse					
CCND3	TCGA			T*		
CCNE1	Treehouse					
CDK4	PEDAYA					
CDK4	TCGA					
CDK4	TH03_TH34					
CDK4	Treehouse					
CDK9	TCGA			T*		
CDK9	TH03_TH34					
CDK9	Treehouse					
CSF1R	Treehouse	D*				
DEPTOR	TH03_TH34					
ETV1	TCGA				T	T*
ETV1	Treehouse				C*	C*
FGFR1	TCGA					
FGFR1	Treehouse					
FGFR2	TCGA					
FGFR3	PEDAYA					
FGFR3	TCGA					
FGFR3	TH03_TH34					
FGFR4	PEDAYA					
FGFR4	Treehouse					
FLT4	PEDAYA					
FLT4	TCGA					
FLT4	TH03_TH34					
FLT4	Treehouse					
GATA2	TCGA	T				
GATA2	Treehouse					
HDAC4	PEDAYA					
HDAC4	TCGA					
HDAC4	TH03_TH34					
HDAC4	Treehouse					
HDAC7	Treehouse					
HMOX1	PEDAYA	P				
HMOX1	TCGA	T				
HMOX1	Treehouse	CD*				
HSP90B1	TCGA		12			
HSP90B1	TH03_TH34					
HSP90B1	Treehouse					
IGF1	PEDAYA		P*			
IGF1	TCGA		T*			

gene	high level cohort	TH34 1162 S01	TH34 1149 S02	TH34 1238 S01	TH34 1349 S01	TH34 1349 S02
AKT1	TH03_TH34					
AKT1	Treehouse					
AKT2	PEDAYA					
AKT2	TCGA					
AKT2	TH03_TH34					
AKT2	Treehouse					
ALK	PEDAYA					
ALK	TCGA					
ALK	TH03_TH34					
ALK	Treehouse					
BCL6	TCGA					
BCL6	Treehouse					
BTK	TCGA			T		
BTK	TH03_TH34			S		
BTK	Treehouse			C		
CCND1	TCGA					
CCND1	TH03_TH34					
CCND2	Treehouse					
CCND3	TCGA			T		
CCNE1	Treehouse					
CDK4	PEDAYA					
CDK4	TCGA					
CDK4	TH03_TH34					
CDK4	Treehouse					
CDK9	TCGA			T		
CDK9	TH03_TH34					
CDK9	Treehouse					
CSF1R	Treehouse	D				
DEPTOR	TH03_TH34					
ETV1	TCGA				T	T
ETV1	Treehouse				C	C
FGFR1	TCGA					
FGFR1	Treehouse					
FGFR2	TCGA					
FGFR3	PEDAYA					
FGFR3	TCGA					
FGFR3	TH03_TH34					
FGFR4	PEDAYA					
FGFR4	Treehouse					
FLT4	PEDAYA					
FLT4	TCGA					
FLT4	TH03_TH34					
FLT4	Treehouse					
GATA2	TCGA	T				
GATA2	Treehouse					
HDAC4	PEDAYA					
HDAC4	TCGA					
HDAC4	TH03_TH34					
HDAC4	Treehouse					
HDAC7	Treehouse					
HMOX1	PEDAYA	P				
HMOX1	TCGA	T				
HMOX1	Treehouse	C, D				
HSP90B1	TCGA		13			
HSP90B1	TH03_TH34					
HSP90B1	Treehouse					
IGF1	PEDAYA		P			

comparison cohort	n outliers detected	n outliers with pathway support	pct outliers detected	pct outliers with path
PEDAYA	26	12	20	
TCGA	98	74	75	
TH03_TH34	53	39	41	
Treehouse_pc	72	47	55	
Treehouse_pd	38	29	29	
Total	130	101	NA	

```
  distinct %>%
  nrow()
# these have pathway support in at least one cohort

totals_tibble <-  tibble(high_level_cohort= " Total",
                         comparison_cohort = " Total",
                  n_outliers_detected = n_outliers_detected_by_any_method,
                  n_outliers_with_pathway_support = n_outliers_with_pathway_support_detected_by_any_metho
                  pct_outliers_with_pathway_support = 100*n_outliers_with_pathway_support_detected_by_any

outlier_summary <- outliers %>%
  group_by(comparison_cohort) %>%
  summarize(n_outliers_detected = n(),
         n_outliers_with_pathway_support = sum(pathway_support)) %>%
  ungroup() %>%
  mutate(pct_outliers_detected = 100*n_outliers_detected/n_outliers_detected_by_any_method,
         pct_outliers_with_pathway_support_detected =
           100*n_outliers_with_pathway_support/n_outliers_with_pathway_support_detected_by_any_method,
         pct_outliers_with_pathway_support = 100*n_outliers_with_pathway_support/n_outliers_detected)

outlier_summary_with_totals <-
  bind_rows(outlier_summary,
            totals_tibble %>% select(-high_level_cohort))



outlier_summary_with_totals %>%
  rename_all(underscore_to_space) %>%
  kbl(digits = c(NA, 0, 0, 0, 0)) %>%
  kable_styling(full_width = F)
```

Summary table for all outliers and high level cohorts

```
high_level_outlier_summary <- outliers %>%
  group_by(high_level_cohort, Sample_ID, gene) %>%
  summarize(pathway_support = any(pathway_support)) %>%
  group_by(high_level_cohort) %>%
  summarize(n_outliers_detected = n(),
         n_outliers_with_pathway_support = sum(pathway_support),
         pct_outliers_with_pathway_support = 100*n_outliers_with_pathway_support/n_outliers_detected,
         pct_outliers_detected = 100*n_outliers_detected/n_outliers_detected_by_any_method)
```

high level cohort	n outliers detected	n outliers with pathway support	pct outliers with pathway support	pct outlie
Treehouse	89	64	72	
TH03_TH34	53	39	74	
TCGA	98	74	76	
PEDAYA	26	12	46	
Total	130	101	78	

```
## `summarise()` has grouped output by 'high_level_cohort', 'Sample_ID'. You can
## override using the `.groups` argument.
```

```
high_level_outlier_summary_with_totals <-
  bind_rows(high_level_outlier_summary %>%
              arrange(desc(high_level_cohort)),
            totals_tibble %>% select(-comparison_cohort))



high_level_outlier_summary_with_totals %>%
  rename_all(underscore_to_space) %>%
  kbl(format.args = list(big.mark = ","), digits = c(NA, 0, 0, 0, 0)) %>%
  kable_styling(full_width = F)
```

Combined high and low level tables

```
high_low <- bind_rows(
  high_level_outlier_summary_with_totals %>%
    rename(comparison_cohort=high_level_cohort) %>%
    mutate(index = c(1, 4:7)),
  outlier_summary_with_totals %>%
    filter(str_detect(comparison_cohort, "Treehouse")) %>%
    mutate(index = 2:3)
) %>%
  arrange(index) %>%
  select(-index)


high_low_outlier_summary <- high_low %>%
  filter(! str_detect(comparison_cohort, "Total")) %>%
  mutate(pct_outliers_with_pathway_support_detected =
           100*n_outliers_with_pathway_support/n_outliers_with_pathway_support_detected_by_any_method,
         `Druggable outliers detected` =
           paste0(n_outliers_detected, "/", n_outliers_detected_by_any_method, " (",
                  round(pct_outliers_detected), "%)"),
         `Druggable outliers with pathway support` =
           paste0(n_outliers_with_pathway_support, "/",
                  n_outliers_with_pathway_support_detected_by_any_method, " (",
                  round(pct_outliers_with_pathway_support_detected), "%)"),
         `Fraction of druggable outliers with pathway support` =
           paste0(n_outliers_with_pathway_support, "/",
                  n_outliers_detected, " (",
                  round(100*n_outliers_with_pathway_support/n_outliers_detected), "%)")
         ) %>%
```

comparison cohort	Druggable outliers detected	Druggable outliers with pathway support	Fraction of druggable outli
Treehouse	89/130 (68%)	64/101 (63%)	64/89 (72%)
Treehouse_pc	72/130 (55%)	47/101 (47%)	47/72 (65%)
Treehouse_pd	38/130 (29%)	29/101 (29%)	29/38 (76%)
TH03_TH34	53/130 (41%)	39/101 (39%)	39/53 (74%)
TCGA	98/130 (75%)	74/101 (73%)	74/98 (76%)
PEDAYA	26/130 (20%)	12/101 (12%)	12/26 (46%)
Total	130	101	101/130 (78%)

```
  select(comparison_cohort,
         `Druggable outliers detected`,
         `Druggable outliers with pathway support`,
         `Fraction of druggable outliers with pathway support`) %>%
  bind_rows(totals_tibble %>%
              mutate(`Fraction of druggable outliers with pathway support` =
                       paste0(n_outliers_with_pathway_support, "/",
                     n_outliers_detected, " (",
                    round(100*n_outliers_with_pathway_support/n_outliers_detected), "%)"),
                    `Druggable outliers detected` = as.character(n_outliers_detected),
                    `Druggable outliers with pathway support` = as.character(n_outliers_with_pathway_suppo
              ) %>%
             select(comparison_cohort,
         `Druggable outliers detected`,
         `Druggable outliers with pathway support`,
         `Fraction of druggable outliers with pathway support`)
  )
```

```
high_low_outlier_summary %>%
  rename_all(underscore_to_space) %>%
  kbl(format.args = list(big.mark = ","), digits = c(NA, 0, 0, 0, 0)) %>%
  kable_styling(full_width = F) %>%
  add_indent(c(2, 3), level_of_indent = 1)
```

Patient level summary table for all outliers

```
outliers %>%
  group_by(donor_ID) %>%
  summarize(any_PEDAYA = "PEDAYA" %in% comparison_cohort,
            any_TH03_TH34 = "TH03_TH34" %in% comparison_cohort,
            any_TCGA = "TCGA" %in% comparison_cohort,
            any_Treehouse_pc = "Treehouse_pc" %in% comparison_cohort,
            any_Treehouse_pd = "Treehouse_pd" %in% comparison_cohort,
            any_Treehouse = any_Treehouse_pc | any_Treehouse_pd) %>%
  pivot_longer(starts_with("any")) %>%
  mutate(name = str_remove(name, "any_")) %>%
```

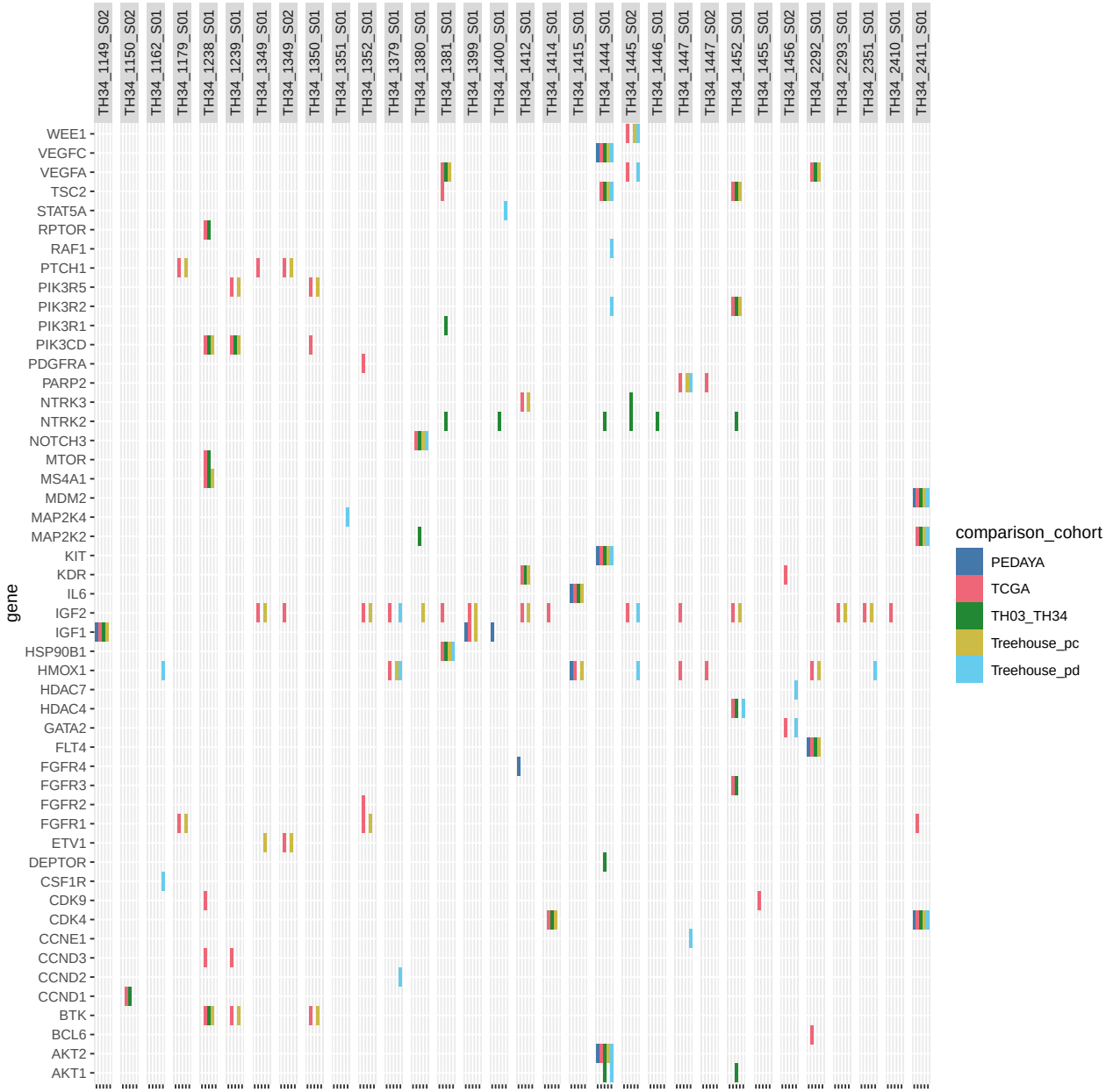
name	n_patients_with_druggable_outliers
PEDAYA	18
TCGA	31
TH03_TH34	22
Treehouse	31
Treehouse_pc	30
Treehouse_pd	18

```
  group_by(name) %>%
  summarize(n_patients_with_druggable_outliers = sum(value)) %>%
  kbl() %>%
  kable_styling(full_width = F)
```

REPEAT ANALYSIS USING ONLY OUTLIERS WITH PATHWAY SUPPORT

Tile plot of outliers with pathway support

```
ggplot(outliers %>%
         filter(pathway_support)) +
  geom_tile(aes(x=comparison_cohort,
                y=gene,
                fill = comparison_cohort)) +
  facet_wrap(~Sample_ID,
             nrow = 1) +
  theme(#axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5),
    axis.text.x = element_blank(),
    strip.text.x = element_text(angle = 90),
        ) +
  xlab("")  +
  scale_fill_bright()
```



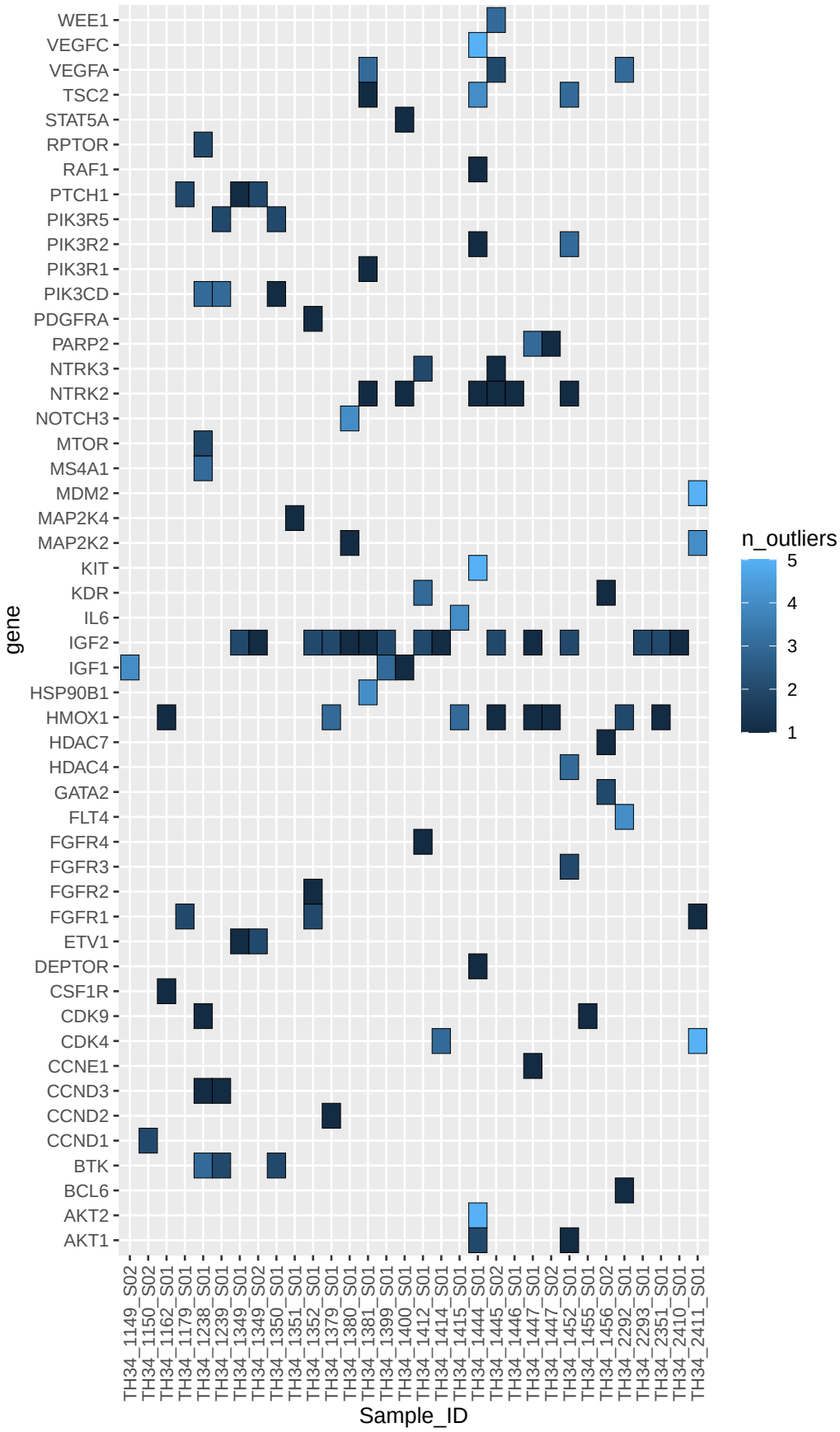
Heatmap shows number of cohorts in which outlier were detected

I can make this look better if we decide to use it, but it's non-trivial

```
pathway_outliers_heatmap_data <- outliers %>%
  filter(pathway_support) %>%
  group_by(Sample_ID, gene) %>%
  summarize(n_outliers = n())
```

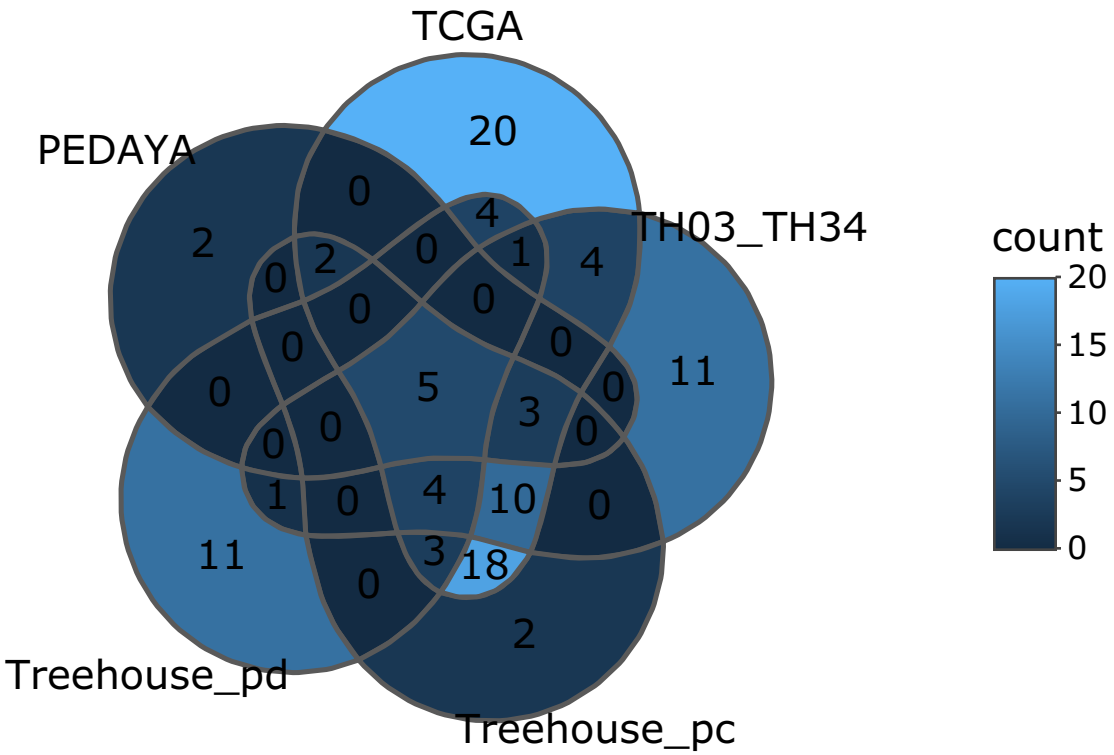
```
## `summarise()` has grouped output by 'Sample_ID'. You can override using the
## `.groups` argument.
```

```r
ggplot(pathway_outliers_heatmap_data) +
  geom_tile(aes(x=Sample_ID,
                y=gene,
                fill = n_outliers),
            color = "black")  +
  #theme_bw() +
  theme(axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5))
```

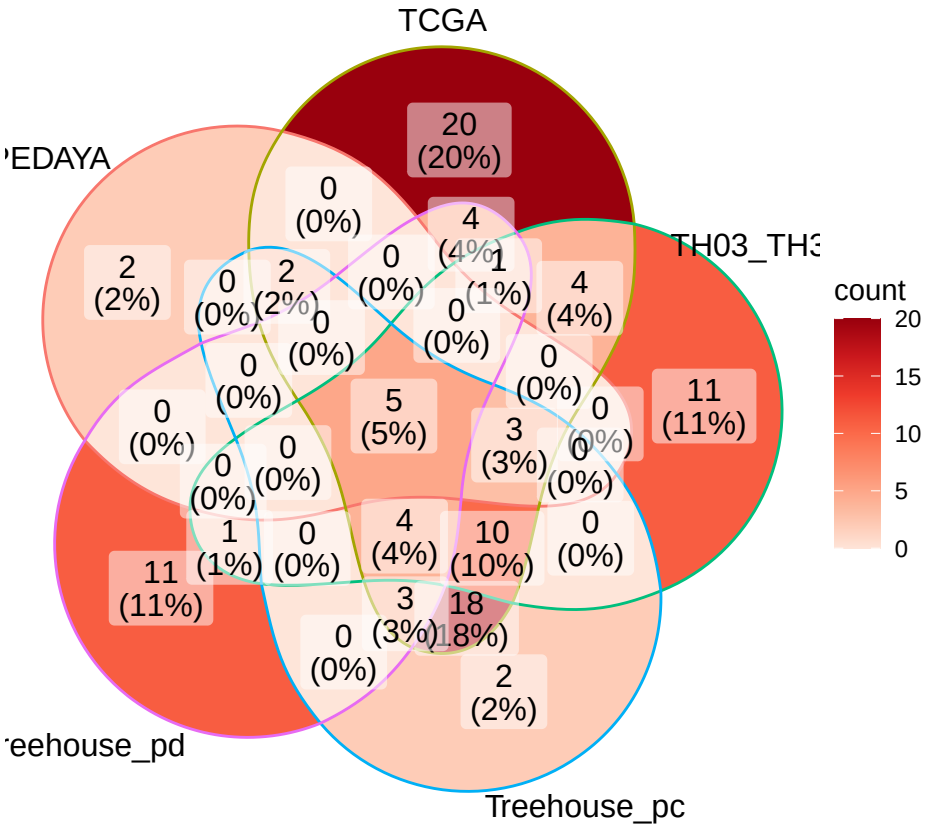

gene
WEE1
VEGFC
VEGFA
TSC2
STAT5A
RPTOR
RAF1
PTCH1
PIK3R5
PIK3R2
PIK3R1
PIK3CD
PDGFRA
PARP2
NTRK3
NTRK2
NOTCH3
MTOR
MS4A1
MDM2
MAP2K4
MAP2K2
KIT
KDR
IL6
IGF2
IGF1
HSP90B1
HMOX1
HDAC7
HDAC4
GATA2
FLT4
FGFR4
FGFR3
FGFR2
FGFR1
ETV1
DEPTOR
CSF1R
CDK9
CDK4
CCNE1
CCND3
CCND2
CCND1
BTK
BCL6
AKT2
AKT1
TH34_1149_S02
TH34_1150_S02
TH34_1162_S01
TH34_1179_S01
TH34_1238_S01
TH34_1239_S01
TH34_1349_S01
TH34_1349_S02
TH34_1350_S01
TH34_1351_S01
TH34_1352_S01
TH34_1379_S01
TH34_1380_S01
TH34_1381_S01
TH34_1399_S01
TH34_1400_S01
TH34_1412_S01
TH34_1414_S01
TH34_1415_S01
TH34_1444_S01
TH34_1445_S02
TH34_1446_S01
TH34_1447_S01
TH34_1447_S02
TH34_1452_S01
TH34_1455_S01
TH34_1456_S02
TH34_2292_S01
TH34_2293_S01
TH34_2351_S01
TH34_2410_S01
TH34_2411_S01
Sample_ID
n_outliers
5
4
3
2
1

```
raw_pathway_support_outliers_for_venn <- outliers %>%
  filter(pathway_support)  %>%
  mutate(sample_gene = paste(Sample_ID, gene, sep = "_")) %>%
  arrange(comparison_cohort) %>%
  select(sample_gene, comparison_cohort) %>%
  group_split(comparison_cohort)


list_of_pathway_support_outliers_for_venn <-  lapply(raw_pathway_support_outliers_for_venn, function(x)
names(list_of_pathway_support_outliers_for_venn) <- outliers %>%
  filter(pathway_support) %>%
  arrange(comparison_cohort) %>%
  select(comparison_cohort) %>%
  distinct() %>%
  pull(comparison_cohort)

ggVennDiagram(list_of_pathway_support_outliers_for_venn,
              show_intersect = TRUE)
```

```
## Warning in geom_text(aes_string(label = "count", text = "text"), x =
## label_coord[, : Ignoring unknown aesthetics: text
```




```
ggVennDiagram(list_of_pathway_support_outliers_for_venn) +
  scale_fill_distiller(palette = "Reds", direction = 1)
```



Annotate with combined full cohort names

```
outliers_with_pathway_support_combined_wide <- outliers %>%
  filter(pathway_support) %>%
  select(-pathway_support, -donor_ID) %>%
  pivot_wider(names_from = Sample_ID,
              values_from = comparison_cohort,
              values_fn = collapse_fun)

outliers_with_pathway_support_combined_long <- outliers_with_pathway_support_combined_wide %>%
  pivot_longer(-gene,
               names_to = "Sample_ID",
               values_to = "comparison_cohorts") %>%
  na.omit()
```

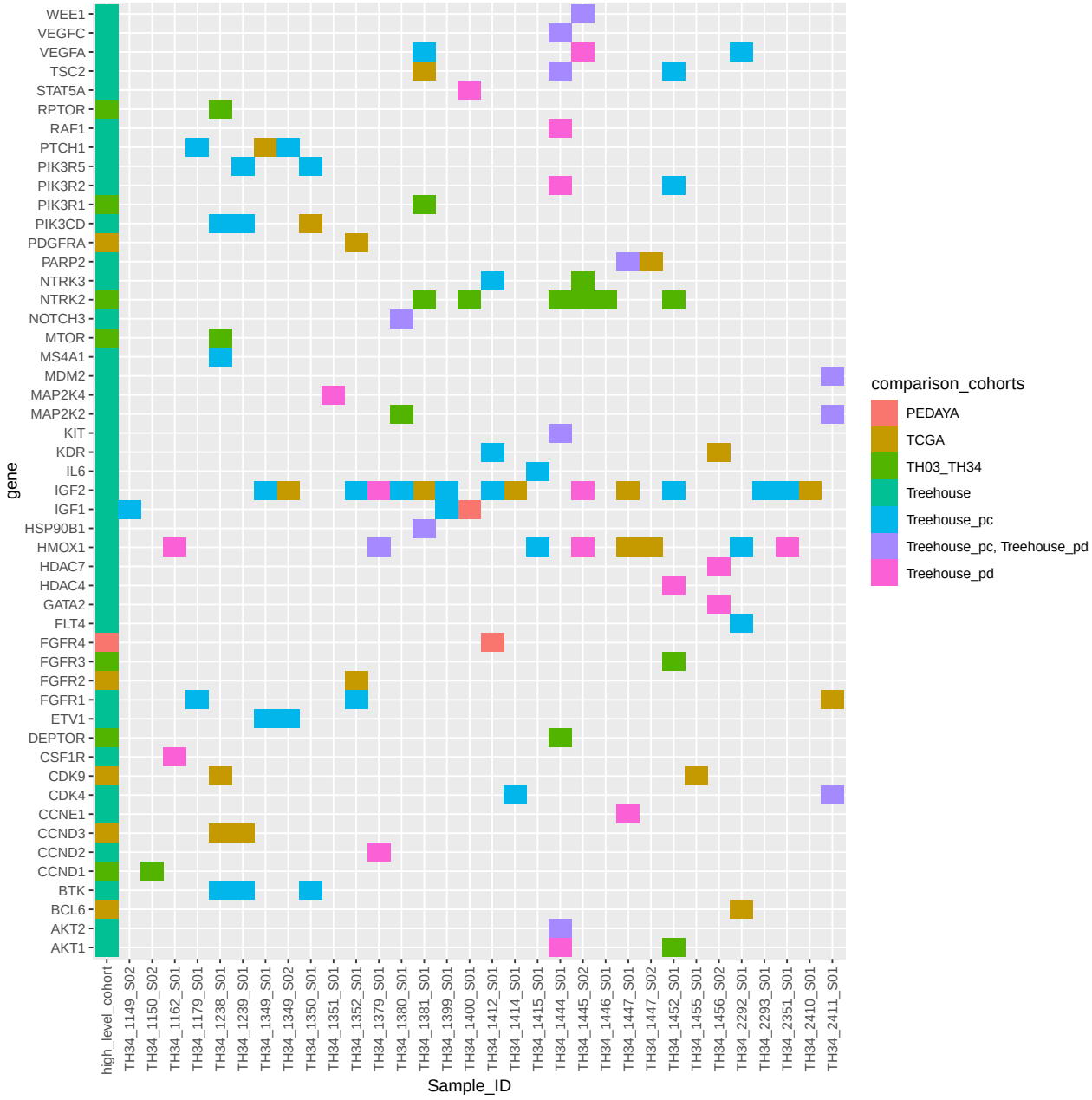
How many outliers with pathway support are present in each combination of cohorts?

```
tabyl(outliers_with_pathway_support_combined_long,
      comparison_cohorts) %>%
  arrange(desc(n)) %>%
  adorn_pct_formatting() %>%
```

comparison_cohorts	n	percent
TCGA	112	37.1%
TH03_TH34	67	22.2%
Treehouse	37	12.3%
Treehouse_pc	35	11.6%
PEDAYA	22	7.3%
Treehouse_pd	17	5.6%
Treehouse_pc, Treehouse_pd	12	4.0%
Total	302	-

```
  adorn_totals() %>%
  kbl() %>%
  kable_styling(full_width = F)
```

```
ggplot(outliers_with_pathway_support_combined_long) +
  geom_tile(aes(x=Sample_ID,
                y=gene,
                fill = comparison_cohorts))  +
  theme(axis.text.x = element_text(angle = 90, hjust = 1, vjust = 0.5))
```




```
n_distinct(outliers_with_pathway_support_combined_long$Sample_ID)
```

```
## [1] 33
```

Patient level summary table for outliers with pathway support

```
outliers %>%
  filter(pathway_support) %>%
  group_by(donor_ID) %>%
  summarize(any_PEDAYA = "PEDAYA" %in% comparison_cohort,
            any_TH03_TH34 = "TH03_TH34" %in% comparison_cohort,
            any_TCGA = "TCGA" %in% comparison_cohort,
```

name	n_patients_with_druggable_outliers
PEDAYA	8
TCGA	26
TH03_TH34	16
Treehouse	26
Treehouse_pc	22
Treehouse_pd	13

```
            any_Treehouse_pc = "Treehouse_pc" %in% comparison_cohort,
            any_Treehouse_pd = "Treehouse_pd" %in% comparison_cohort,
            any_Treehouse = any_Treehouse_pc | any_Treehouse_pd) %>%
  pivot_longer(starts_with("any")) %>%
  mutate(name = str_remove(name, "any_")) %>%
  group_by(name) %>%
  summarize(n_patients_with_druggable_outliers = sum(value)) %>%
  kbl() %>%
  kable_styling(full_width = F)
```

Annotate with combined cohort abbreviations

```
outliers_with_pathway_support_abbrev_combined_wide <- outliers %>%
  filter(pathway_support) %>%
  left_join(cohort_codes,
            by=c("comparison_cohort"="cohort_name")) %>%
  select(-pathway_support, -donor_ID,
         -comparison_cohort) %>%
  pivot_wider(names_from = Sample_ID,
              values_from = cohort_code,
              values_fn = collapse_fun,
              values_fill = "")
```

Big table of outliers with pathway support

```
outliers_with_pathway_support_abbrev_combined_wide %>%
  arrange(gene) %>%
  rename_all(underscore_to_space) %>%
  kbl() %>%
  kable_styling(full_width = F,
                bootstrap_options = "bordered")
```

```
sessionInfo()
```

```
## R version 4.2.1 (2022-06-23)
## Platform: aarch64-apple-darwin20 (64-bit)
## Running under: macOS Monterey 12.2
##
## Matrix products: default
## BLAS:   /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/lib/libRblas.0.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/lib/libRlapack.dylib
```

gene	high level cohort	TH34 1149 S02	TH34 1238 S01	TH34 1399 S01	TH34 1400 S01	TH34 1412 S01
AKT1	TH03_TH34					
AKT1	Treehouse					
AKT2	PEDAYA					
AKT2	TCGA					
AKT2	TH03_TH34					
AKT2	Treehouse					
BCL6	TCGA					
BTK	TCGA		T			
BTK	TH03_TH34		S			
BTK	Treehouse		C			
CCND1	TCGA					
CCND1	TH03_TH34					
CCND2	Treehouse					
CCND3	TCGA		T			
CCNE1	Treehouse					
CDK4	PEDAYA					
CDK4	TCGA					
CDK4	TH03_TH34					
CDK4	Treehouse					
CDK9	TCGA		T			
CSF1R	Treehouse					
DEPTOR	TH03_TH34					
ETV1	TCGA					
ETV1	Treehouse					
FGFR1	TCGA					
FGFR1	Treehouse					
FGFR2	TCGA					
FGFR3	TCGA					
FGFR3	TH03_TH34					
FGFR4	PEDAYA					P
FLT4	PEDAYA					
FLT4	TCGA					
FLT4	TH03_TH34					
FLT4	Treehouse					
GATA2	TCGA					
GATA2	Treehouse					
HDAC4	TCGA					
HDAC4	TH03_TH34					
HDAC4	Treehouse					
HDAC7	Treehouse					
HMOX1	PEDAYA					
HMOX1	TCGA					
HMOX1	Treehouse					
HSP90B1	TCGA					
HSP90B1	TH03_TH34					
HSP90B1	Treehouse					
IGF1	PEDAYA	P		P	P	
IGF1	TCGA	T		T		
IGF1	TH03_TH34	S				
IGF1	Treehouse	C		C		
IGF2	TCGA			T		T
IGF2	Treehouse			C		C
IL6	PEDAYA					
IL6	TCGA		26			
IL6	TH03_TH34					
IL6	Treehouse					
KDR	TCGA					T

```
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
##  [1] ggVennDiagram_1.2.2 cowplot_1.1.1       gridExtra_2.3
##  [4] kableExtra_1.3.4    khroma_1.10.0       janitor_2.1.0
##  [7] forcats_0.5.2       stringr_1.5.0       dplyr_1.0.10
## [10] purrr_0.3.5         readr_2.1.3         tidyr_1.2.1
## [13] tibble_3.2.1        ggplot2_3.4.4       tidyverse_1.3.2
##
## loaded via a namespace (and not attached):
##  [1] fs_1.6.3            sf_1.0-9            lubridate_1.9.0
##  [4] bit64_4.0.5         RColorBrewer_1.1-3  webshot_0.5.4
##  [7] httr_1.4.4          tools_4.2.1         backports_1.4.1
## [10] utf8_1.2.3          R6_2.5.1            KernSmooth_2.23-20
## [13] DBI_1.1.3           lazyeval_0.2.2      colorspace_2.1-0
## [16] withr_2.5.0         tidyselect_1.2.0    processx_3.8.0
## [19] bit_4.0.5           compiler_4.2.1      cli_3.6.1
## [22] rvest_1.0.3         xml2_1.3.3          plotly_4.10.1
## [25] labeling_0.4.2      scales_1.2.1        classInt_0.4-9
## [28] callr_3.7.3         proxy_0.4-27        systemfonts_1.0.4
## [31] digest_0.6.33       yulab.utils_0.0.6   rmarkdown_2.23
## [34] svglite_2.1.0       pkgconfig_2.0.3     htmltools_0.5.5
## [37] dbplyr_2.2.1        fastmap_1.1.1       highr_0.10
## [40] htmlwidgets_1.6.2   rlang_1.1.1         readxl_1.4.1
## [43] rstudioapi_0.14     farver_2.1.1        generics_0.1.3
## [46] jsonlite_1.8.7      crosstalk_1.2.0     vroom_1.6.0
## [49] googlesheets4_1.0.1 magrittr_2.0.3      Rcpp_1.0.11
## [52] munsell_0.5.0       fansi_1.0.4         lifecycle_1.0.3
## [55] stringi_1.7.12      yaml_2.3.7          snakecase_0.11.0
## [58] grid_4.2.1          parallel_4.2.1      crayon_1.5.2
## [61] haven_2.5.1         hms_1.1.2           ps_1.7.2
## [64] knitr_1.43          pillar_1.9.0        reprex_2.0.2
## [67] glue_1.6.2          evaluate_0.21       data.table_1.14.6
## [70] modelr_0.1.10       vctrs_0.6.3         tzdb_0.3.0
## [73] cellranger_1.1.0    gtable_0.3.3        assertthat_0.2.1
## [76] xfun_0.39           broom_1.0.1         e1071_1.7-13
## [79] class_7.3-20        googledrive_2.0.0   RVenn_1.1.0
## [82] viridisLite_0.4.2   gargle_1.2.1        units_0.8-1
## [85] timechange_0.1.1    ellipsis_0.3.2
```