Supplementary plots to Figure 5

Below are some supplementary plots to Figure 5 of: Madeleine Darbyshire, Zachary du Toit, Mark F. Rogers, Tom Gaunt and Colin Campbell. Estimating the Frequency of Single Point Driver Mutations across Common Solid Tumours, *Scientific Reports* (Nature) 9, article number: 13452, (2019). In the plots below, a driver gene is labelled as such if it has at least one embedded high confidence SNV-driver. By *high confidence* we mean that we are using a false discovery rate of 5% which translates into a threshold cutoff on the $p$-score of 0.88 for *CScape*. Most of these genes are discussed in the text of the paper, and well studied in their respective contexts. Some comments are:

1-4 **TP53, KRAS, PIK3CA** and **CTC-297N7.11** are examples of genes with an important influence across multiple cancer types.

5,6 **SPOP** and **IDH1** are examples of genes with more restricted influence by cancer type: **SPOP** is relevant to prostate cancer (PRAD) but less so to early onset prostate cancer (EOPC), while also relevant to Uterine Corpus Endometrial Carcinoma (UCEC). **IDH1** has a more restricted role in brain lower grade glioma (LGG), among the cancers we consider.

7 **BRAF** as a driver gives a pointer towards drug repurposing: melanoma and thyroid cancer are obviously relevant. However, **BRAF** mutations are given as relevant to more than 10% of colon cancers (COAD). This is documented in the cancer literature. Currently two BRAF inhibitors are approved for clinical use: vemurafenib and dabrafenib, principally targeted at melanoma, but can be repurposed for other contexts. This gives support for the further development of predictors such as *CScape*, since they can highlight rare targets, infrequent for the given cancer type, but nonetheless a driver for the given tumour.

8 An unexpected result was for **TTN** and **TTN-AS1**, the latter transcribed from the opposite strand to **TTN** (*Titin*). Though commonly dismissed as a driver due to function and expression profile in the cell cycle, **TTN** may be conferring driver status through association with the long non-coding RNA gene **TTN-AS1**. The latter appears with a frequency, equal to, or slightly lower, than that for **TTN**.

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1. TP53

```
Percentage  Cancer Type
BLCA       |
BRCA       |
CESC       |
COAD       |
COCA       |
EOPC       |
ESCA       |
GACA       |
KIRC       |
KIRP       |
LGG        |
LIHC       |
LICA       |
MALY       |
NBL        |
ORCA       |
OV         |
PACA       |
PRAD       |
READ       |
RECA       |
SKCM       |
STAD       |
THCA       |
UCEC       |
```

![TP53 Bar Chart]

2. KRAS

```
Percentage  Cancer Type
BLCA       |
BRCA       |
CESC       |
COAD       |
COCA       |
EOPC       |
ESCA       |
GACA       |
KIRC       |
KIRP       |
LGG        |
LIHC       |
LICA       |
MALY       |
NBL        |
ORCA       |
OV         |
PACA       |
PRAD       |
READ       |
RECA       |
SKCM       |
STAD       |
THCA       |
UCEC       |
```

![KRAS Bar Chart]
3. PIK3CA

![PIK3CA Graph]

4. CTC-297N7.11

![CTC-287N7.11 Graph]
5. SPOP

![SPOP Graph]

6. IDH1

![IDH1 Graph]
7. BRAF

8. TTN and TTN-AS1