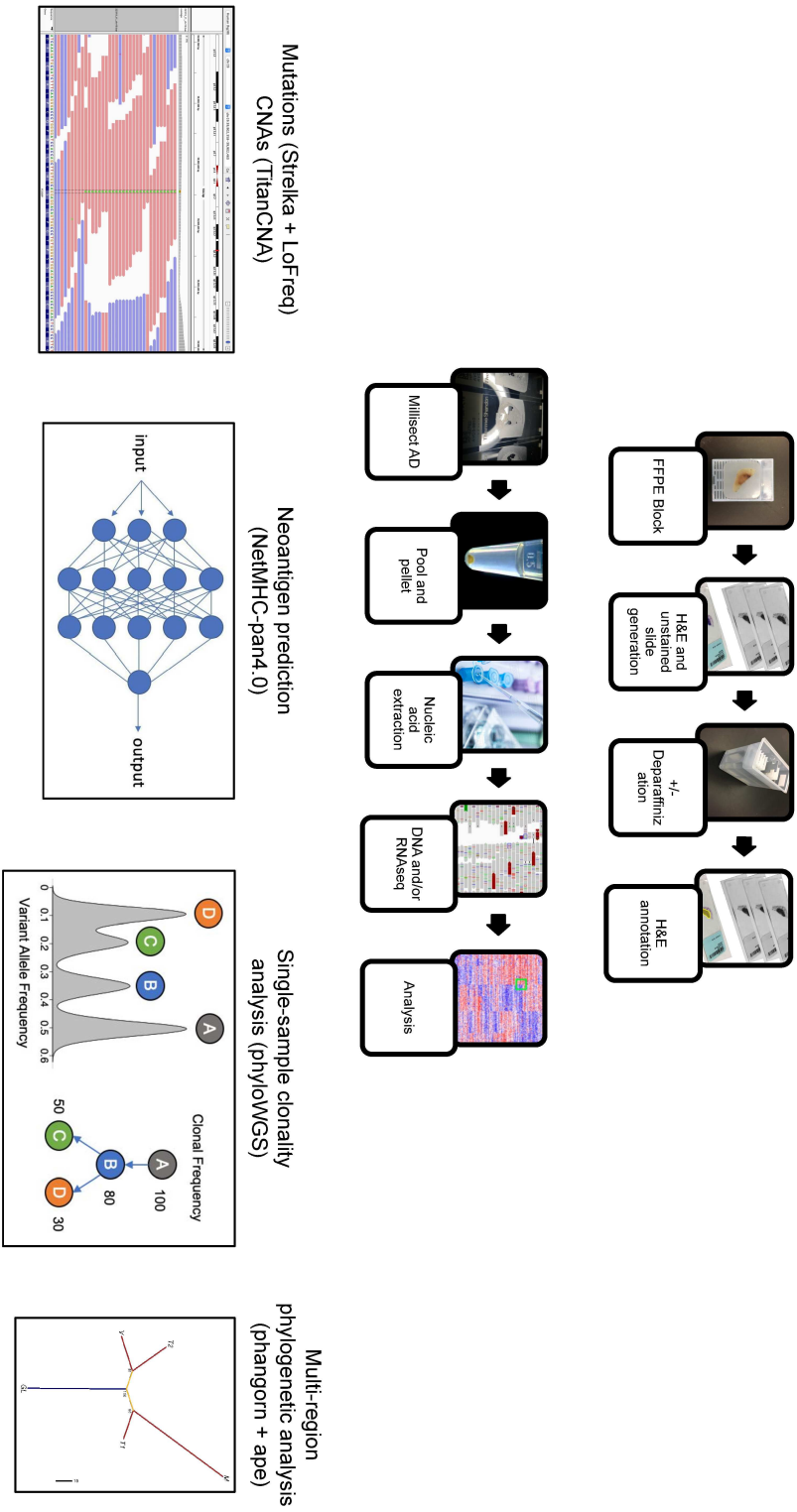
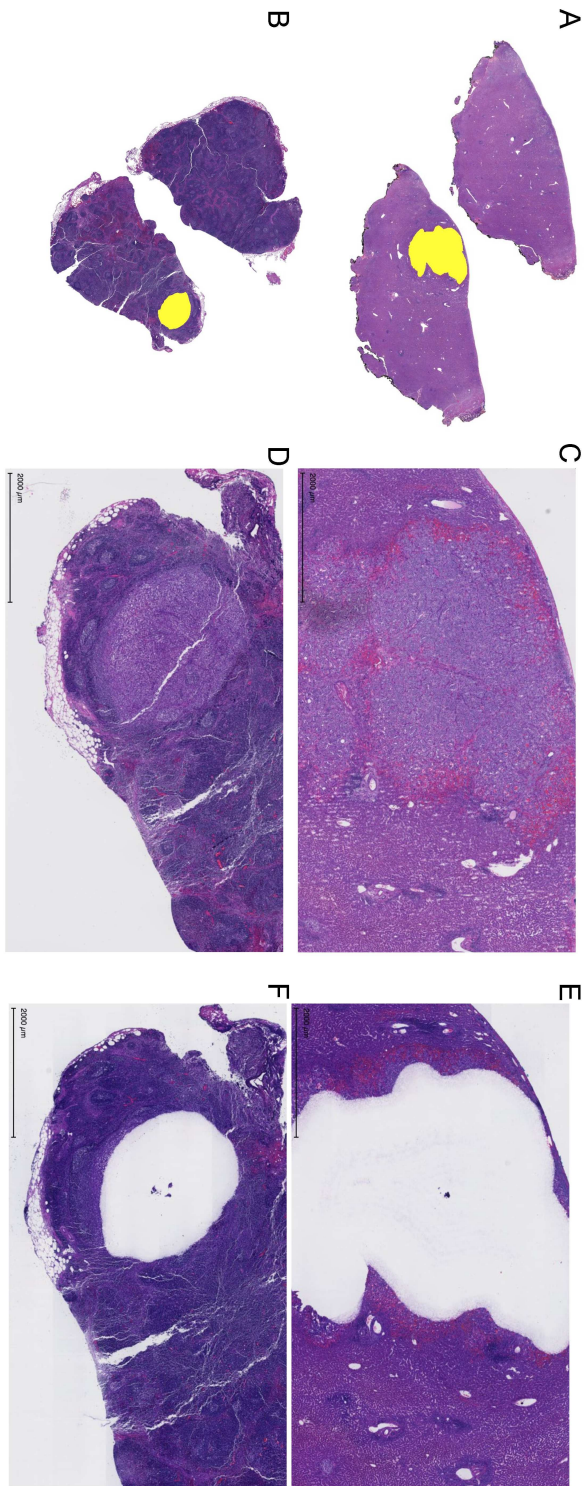


Supplementary Fig. 1.



Supplementary Fig. 2.





Supplementary Table 1.

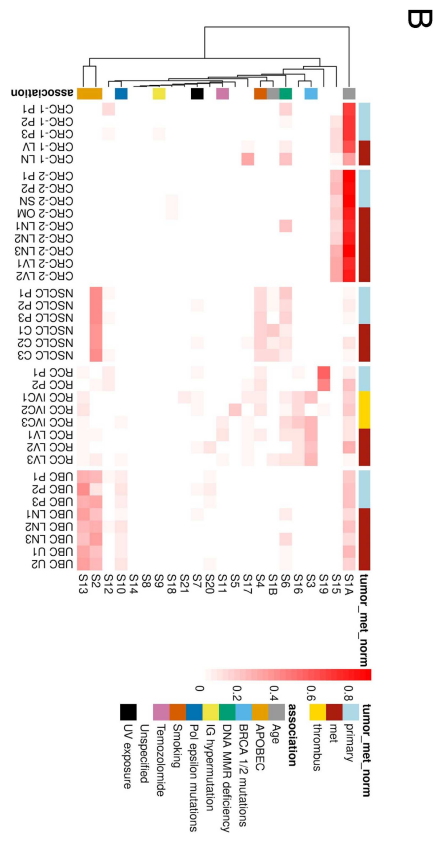
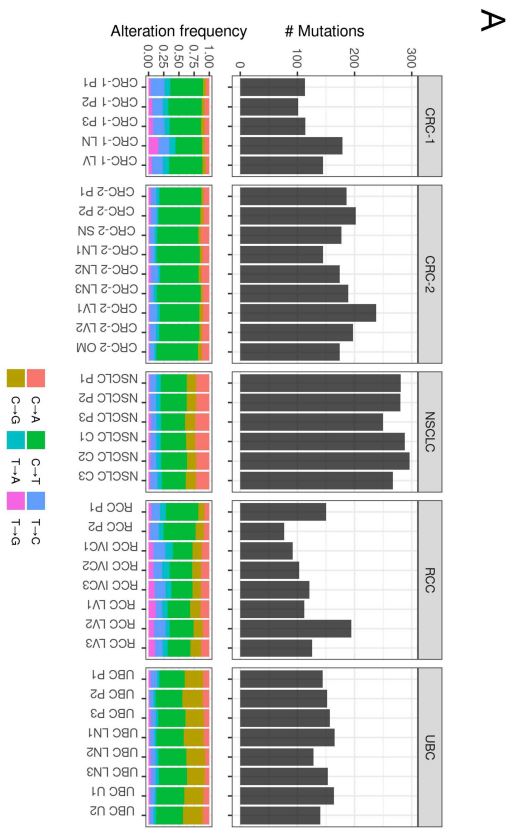
| Case  | Tissue Regions | Primary (P)/Metastatic (M) or Normal (N) | %Tumor Area | %Tumor Nuclei | %Tumor necrosis | Harvested Area (mm <sup>2</sup> ) | Rationale for cases excluded             | RNA (µg)          | DNA (µg) |
|-------|----------------|--|-------------|---------------|-----------------|-----------------------------------|--|-------------------|----------|
| CRC1  | IV             | M  | 20          | 10            | 80              | 1612.5                            |  | 2.800             | 2.170    |
|       | CD             | P  | 5           | 3             | 1               | 369                               |  | 1.378             | 0.763    |
|       | CD             | P  | 1           | 0.1           | 1               | 563.1                             |  | 2.332             | 0.998    |
|       | CD             | P  | 5           | 25            | 0               | 652                               |  | 3.72 <sup>a</sup> | 1.478    |
|       | LN             | N  | N/A         | N/A           | N/A             | 291.7                             |  | 0.52 <sup>a</sup> | 0.610    |
|       | LN             | M  | 2           | 0.5           | 50              | 91.8                              |  | 0.286             | 0.183    |
| CRC2  | CD             | P  | 25          | 10            | 1               | 440.5                             |  | 2.79 <sup>a</sup> | 2.86     |
|       | CD             | P  | 20          | 15            | 10              | 791                               |  | 5.51 <sup>a</sup> | 3.40     |
|       | CD             | P  | 5           | 0.1           | 0               | 571                               | VAF distribution, low copy number signal | 4.02              | 3.70     |
|       | OM             | M  | 20          | 60            | 0               | 520                               |  | 2.01 <sup>a</sup> | 0.936    |
|       | LN             | M  | 1           | 0.01          | 20              | 308.1                             |  | 2.555             | 1.867    |
|       | LN             | M  | 2           | 0.01          | 10              | 45.1                              |  | 0.137             | 0.179    |
|       | LN             | M  | 60          | 50            | 60              | 569.5                             |  | 2.033             | 1.502    |
|       | IV             | M  | 45          | 10            | 15              | 530.5                             |  | 3.152             | 2.064    |
|       | IV             | M  | 25          | 20            | 50              | 491.5                             |  | 1.775             | 0.808    |
|       | IV             | N  | N/A         | N/A           | N/A             | 1307.5                            |  | 9.438             | 0.562    |
| CD    | P              | 5  | 3           | 5             | 926.5           |                                   | 6.440                                    | 3.706             |          |
| UBC   | LN             | M  | 5           | 1             | 0               | 20.5                              |  | 0.286             | 0.122    |
|       | LN             | M  | 25          | 10            | 30              | 497                               |  | 4.508             | 3.074    |
|       | LN             | M  | 10          | 1             | 2               | 295.5                             |  | 1.086             | 2.094    |
|       | UR             | M  | 20          | 50            | 5               | 700                               |  | 4.816             | 2.083    |
|       | UR             | M  | 30          | 30            | 1               | 500                               |  | 7.117             | 4.790    |
|       | UD             | P  | 15          | 50            | 2               | 391.5                             |  | 5.262             | 2.251    |
|       | UD             | P  | 60          | 30            | 35              | 1025                              |  | 4.172             | 3.062    |
|       | UD             | P  | 10          | 5             | 30              | 271                               |  | 1.014             | 0.528    |
| UD    | N              | N/A                                      | N/A         | N/A           | 1088.5          |                                   | 1.193                                    | 1.364             |          |
| RCC   | UD             | P  | 50          | 30            | 60              | 516                               |  | <LOD              | 0.105    |
|       | UD             | P  | 40          | 5             | 75              | 433                               |  | <LOD              | 0.085    |
|       | UD             | P  | 1           | 0.1           | 98              | 941                               | VAF distribution, low copy number signal | <LOD              | 0.115    |
|       | IV             | M  | 10          | 8             | 0               | 79                                |  | 0.52 <sup>a</sup> | 0.282    |
|       | IV             | M  | 25          | 15            | 0               | 201                               |  | 2.542             | 0.931    |
|       | IV             | M  | 15          | 25            | 0               | 101                               |  | 1.182             | 0.479    |
|       | BW             | M  | 20          | 40            | 25              | 397                               |  | 1.182             | 0.789    |
|       | BW             | M  | 85          | 85            | 0               | 861.5                             |  | 1.338             | 1.531    |
|       | BW             | M  | 30          | 80            | 0               | 212                               |  | 0.812             | 0.231    |
|       | IV             | N  | N/A         | N/A           | N/A             | 556.5                             |  | 5.310             | 0.878    |
| NSCLC | LU             | P  | 95          | 90            | 2               | 1472                              |  | 12.432            | 4.445    |
|       | LU             | P  | 40          | 20            | 8               | 721                               |  | 5.748             | 1.982    |
|       | LU             | P  | 90          | 40            | 10              | 1950                              |  | 1.49 <sup>a</sup> | 2.040    |
|       | LN             | M  | 25          | 2             | 0               | 62.5                              | VAF distribution, low copy number signal | 0.711             | 0.40272  |
|       | LN             | M  | 5           | 1             | 0               | 22.5                              | Low input material                       | <LOD              | 0.048    |
|       | SDF            | M  | 20          | 50            | 5               | 511                               |  | 4.582             | 2.040    |
|       | SDF            | M  | 25          | 40            | 5               | 315.5                             |  | 5.656             | 1.802    |
|       | SDF            | M  | 30          | 20            | 2               | 271                               |  | 2.587             | 0.630    |
|       | LN             | M  | 25          | 5             | 0               | 24.5                              | Low input material                       | 1.333             | 0.931    |
|       | LN             | M  | 15          | 0.1           | 5               | 19                                | Low input material                       | 0.655             | 0.442    |
|       | LN             | M  | 2           | 0.01          | 0               | 2.5                               | Low input material, not sequenced        | <LOD              | 0.015    |
|       | LN             | M  | 5           | 0.5           | 0               | 9.9                               | Low input material, not sequenced        | <LOD              | 0.049    |
|       | LU             | N  | N/A         | N/A           | N/A             | 1505                              |  | 0.857             | 2.813    |

Supplementary Table 2

|                | All coding mutations |        |                 | Nonsynonymous mutations (missense or frameshift) |        |                 | Expressed mutations |        |                 | Expressed nonsynonymous mutations |        |                 | Neoantigenic mutations |        |                 | Expressed neoantigenic mutations |        |                 |
|----------------|----------------------|--------|-----------------|--|--------|-----------------|---------------------|--------|-----------------|-----------------------------------|--------|-----------------|------------------------|--------|-----------------|----------------------------------|--------|-----------------|
|                | total                | global | global fraction | total  | global | global fraction | total               | global | global fraction | total                             | global | global fraction | total                  | global | global fraction | total                            | global | global fraction |
| <i>patient</i> |                      |        |                 |  |        |                 |                     |        |                 |                                   |        |                 |                        |        |                 |                                  |        |                 |
| CRC1           | 262                  | 74     | 0.28            | 131  | 44     | 0.34            | 57                  | 34     | 0.60            | 35                                | 26     | 0.74            | 107                    | 39     | 0.36            | 31                               | 23     | 0.74            |
| CRC2           | 425                  | 78     | 0.18            | 201  | 36     | 0.18            | 113                 | 39     | 0.35            | 63                                | 20     | 0.32            | 160                    | 28     | 0.18            | 52                               | 15     | 0.29            |
| NSCLC          | 397                  | 201    | 0.51            | 166  | 101    | 0.61            | 153                 | 100    | 0.65            | 84                                | 59     | 0.70            | 134                    | 84     | 0.63            | 69                               | 51     | 0.74            |
| RCC            | 375                  | 31     | 0.08            | 153  | 16     | 0.10            | 89                  | 19     | 0.21            | 52                                | 10     | 0.19            | 129                    | 15     | 0.12            | 47                               | 9      | 0.19            |
| UBC            | 259                  | 88     | 0.34            | 117  | 50     | 0.43            | 111                 | 62     | 0.56            | 60                                | 35     | 0.58            | 91                     | 34     | 0.37            | 44                               | 23     | 0.52            |
| <i>total</i>   | 1718                 | 472    | 0.27            | 768  | 247    | 0.32            | 523                 | 254    | 0.49            | 294                               | 150    | 0.51            | 621                    | 200    | 0.32            | 243                              | 121    | 0.50            |

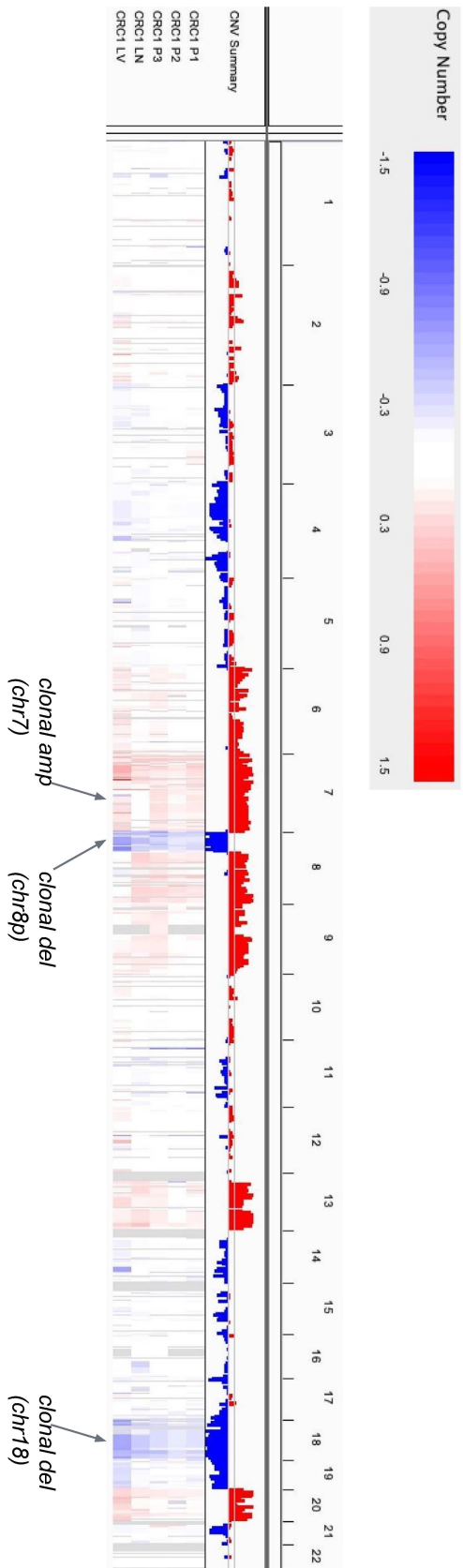
$$\text{global fraction} = \frac{\text{\# muts present in all regions}}{\text{\# unique muts across all regions}} \text{ (per tumor)}$$

Supplementary Fig. 3.

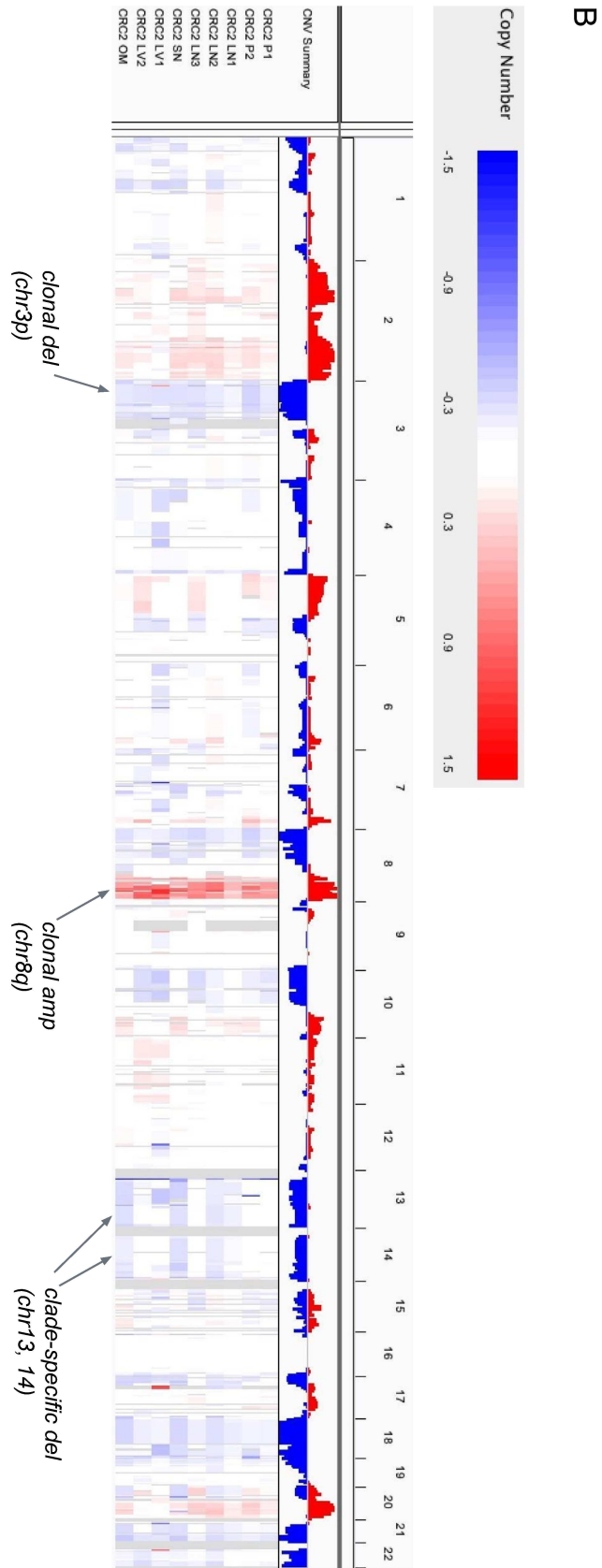


Supplementary Fig. 4A.

A

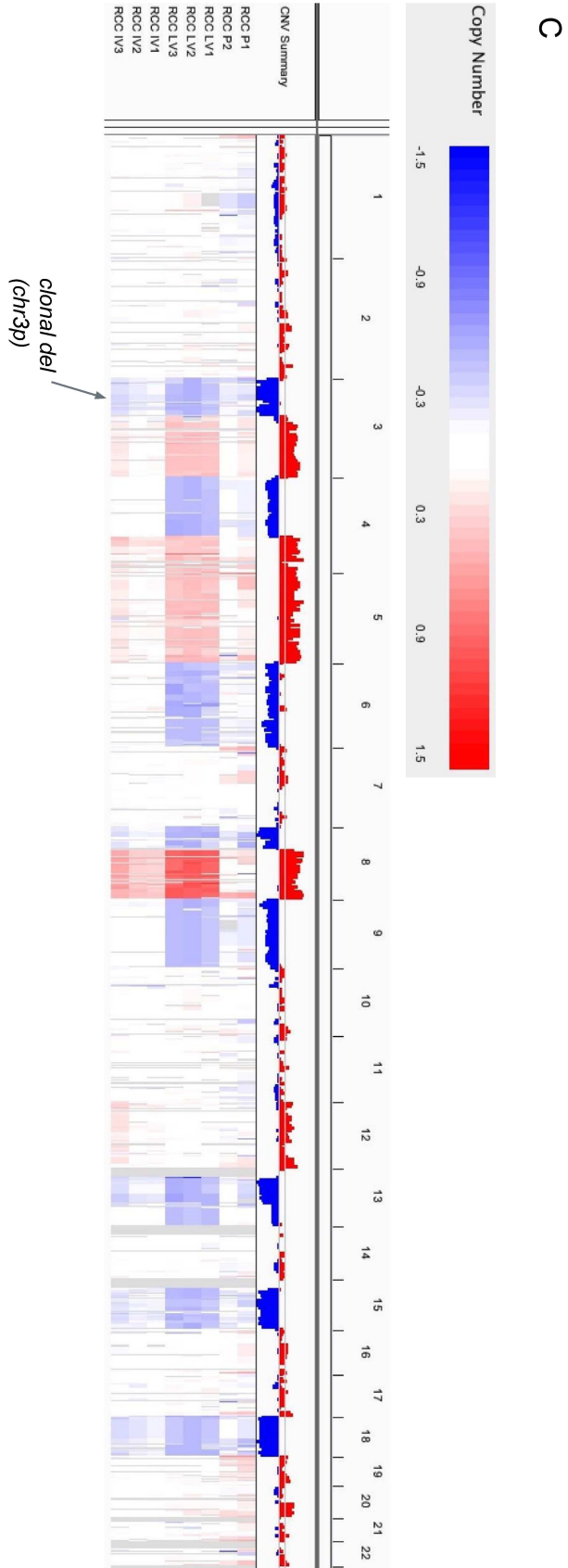


Supplementary Fig. 4B.



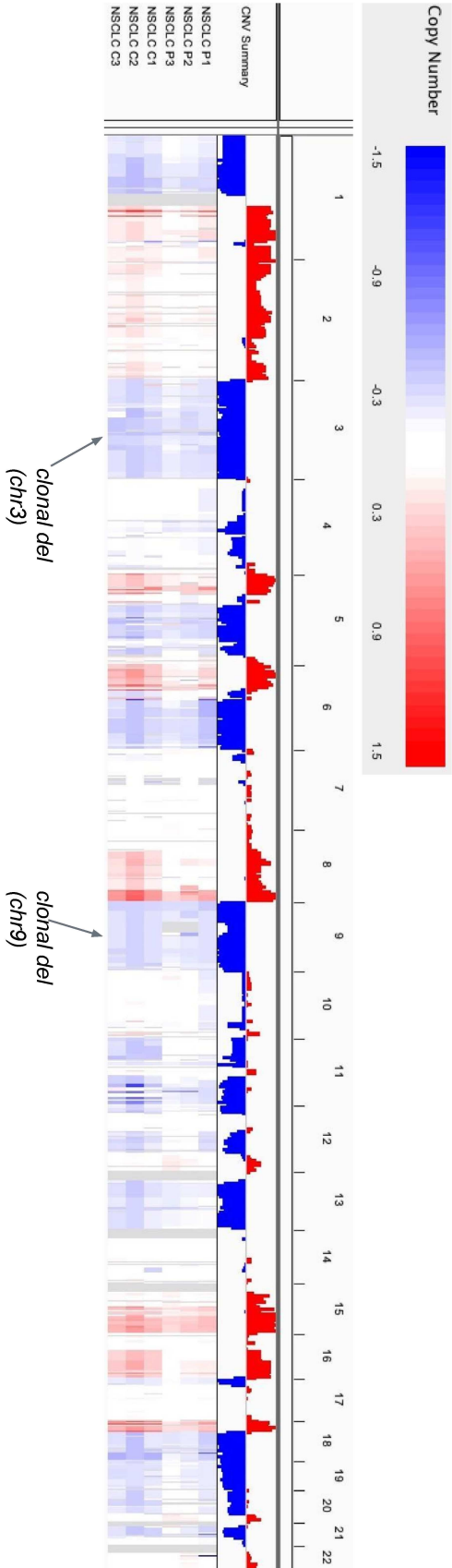


Supplementary Fig. 4C.



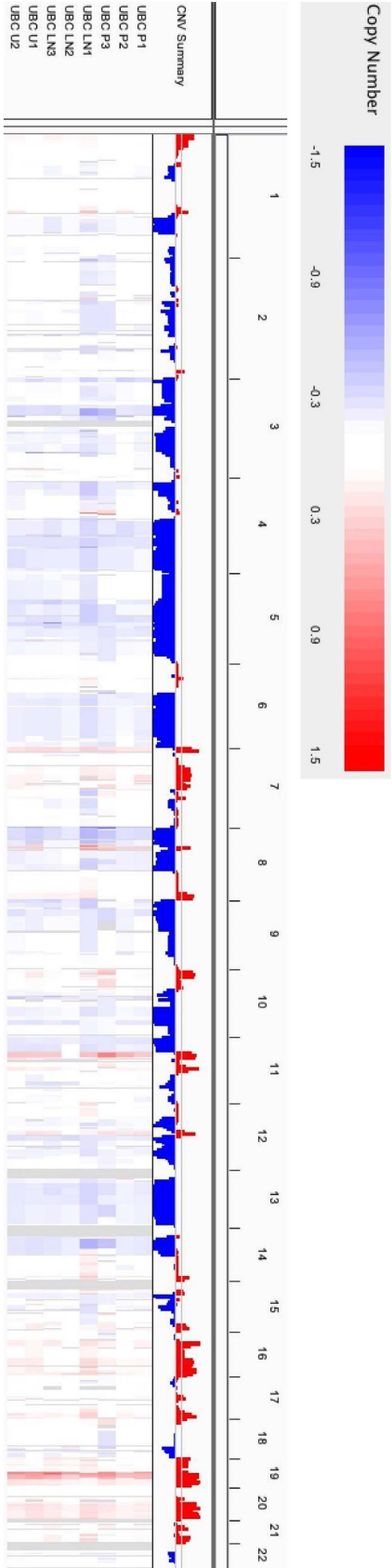
Supplementary Fig. 4D.

D

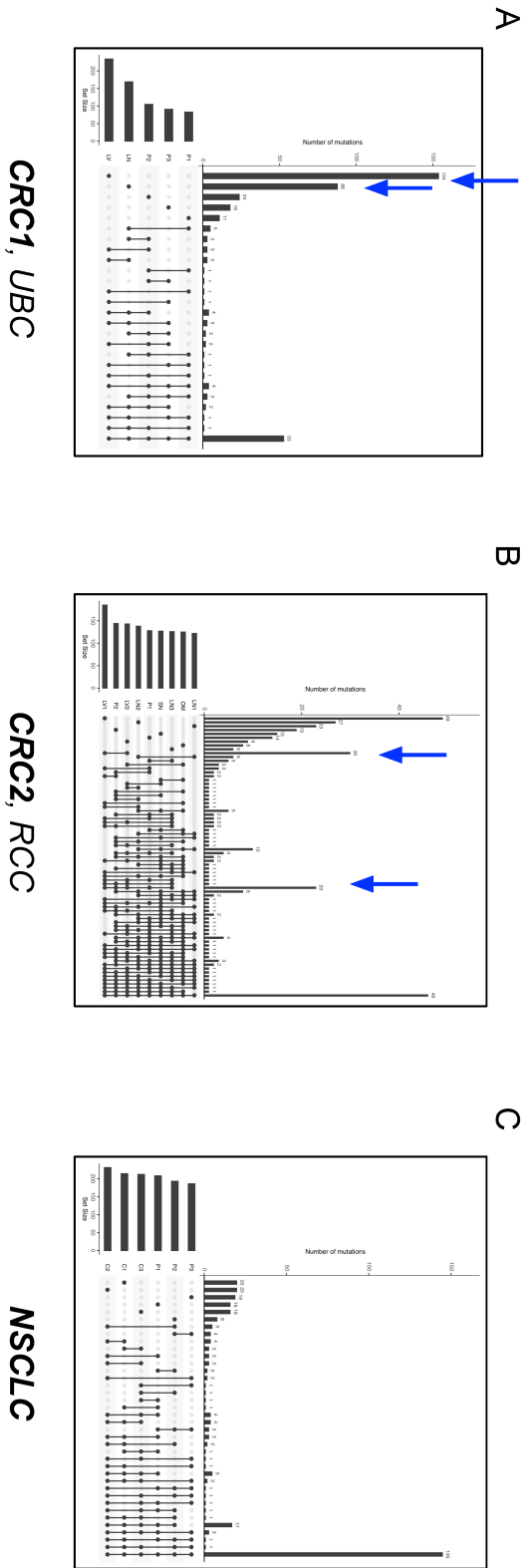


Supplementary Fig. 4E.

E



Supplementary Fig. 5



Supplementary Table 3A, B

**A**

| patient | n_neo_mutlex_loh | end_ref  | alt | n_non_neo_mutlex_loh | min_el_mut | regions_called | frac_mutlex_loh_muts_that_are_neo | frac_all_nonsyn_muts_that_are_neo |
|---------|------------------|----------|-----|----------------------|------------|----------------|-----------------------------------|-----------------------------------|
| CRC-1   | 9                | 78691263 | G   | 3                    | 4.3743     | LV,P1,P2,P3    | 0.75                              | 0.79                              |
| CRC-2   | 23               | 21703139 | A   | 7                    | 4.7622     | LV             | 0.77                              | 0.79                              |
| NSCLC   | 11               | 53267008 | T   | 5                    | 6.2988     | P1             | 0.69                              | 0.80                              |
| RCC     | 31               | 53353449 | G   | 7                    | 0.0519     | P3             | 0.82                              | 0.85                              |
| UBC     | 9                | 55541006 | T   | 1                    | 1.3357     | LN             | 0.90                              | 0.78                              |

**B**

| seqnames | start     | end       | ref | alt | neo_status | min_el_mut | regions_called | ena_status_in_called_region | loh_regions | ena_status_in_loh_regions |
|----------|-----------|-----------|-----|-----|------------|------------|----------------|-----------------------------|-------------|---------------------------|
| 16       | 78691263  | 78691263  | G   | A   | not_neo    | 4.3743     | LV,P1,P2,P3    | GAIN,HET                    | LN          | NLOH                      |
| 17       | 21703139  | 21703139  | A   | G   | not_neo    | 4.7622     | LV             | GAIN                        | LN          | NLOH                      |
| 19       | 53267008  | 53267008  | T   | C   | not_neo    | 6.2988     | P1             | HET                         | LV,LN       | NLOH                      |
| 19       | 53353449  | 53353449  | G   | A   | neo        | 0.0519     | P3             | HET                         | LV,LN       | NLOH                      |
| 19       | 55541006  | 55541006  | T   | C   | neo        | 1.3357     | LN             | HET                         | LV          | NLOH                      |
| 4        | 46041094  | 46041094  | C   | T   | neo        | 0.4303     | P3             | ASCNA                       | LV,LN       | NLOH                      |
| 6        | 31356262  | 31356262  | C   | T   | neo        | 0.0205     | P3             | GAIN                        | LN,P1,P2    | ALOH,NLOH                 |
| 6        | 31356284  | 31356284  | G   | T   | neo        | 1.3549     | LV             | HET                         | LN,P1,P2    | ALOH,NLOH                 |
| 7        | 21698167  | 21698167  | A   | C   | neo        | 0.1152     | LN             | GAIN                        | LV          | ALOH                      |
| 7        | 98628484  | 98628484  | G   | A   | neo        | 0.3080     | P1,P2,P3,LN    | GAIN                        | LV          | ALOH                      |
| 7        | 122054028 | 122054028 | G   | T   | neo        | 0.3947     | P1,P2,P3,LN    | no_call,GAIN,HET            | LV          | ALOH                      |
| 7        | 147108306 | 147108306 | C   | A   | neo        | 0.9224     | LN             | GAIN                        | LV          | ALOH                      |



Supplementary Table 3C

C

| sequen | start     | end       | ref     | alt | neo_status | min_el  | mut | regions_called    | cna_status  | in_called | region | loh_regions                 | cna_status | in_loh | regions |
|--------|-----------|-----------|---------|-----|------------|---------|-----|-------------------|-------------|-----------|--------|-----------------------------|------------|--------|---------|
| 1      | 88983615  | 88983615  | C       | G   | neo        | 0.4898  |     | LV1               | HET         |           |        | SN                          | DLOH       |        |         |
| 1      | 113980336 | 113980336 | G       | A   | neo        | 1.5584  |     | P2,LN3,LV2        | no_call     |           |        | SN                          | DLOH       |        |         |
| 11     | 1244642   | 1244642   | G       | A   | neo        | 1.3105  |     | LV1               | ASCNA       |           |        | LN3,SN                      | NLOH       |        |         |
| 11     | 1244809   | 1244809   | A       | T   | neo        | 0.3378  |     | LV1               | ASCNA       |           |        | LN3,SN                      | NLOH       |        |         |
| 11     | 1249596   | 1249596   | T       | C   | neo        | 0.8063  |     | LV1               | no_call     |           |        | LN3,SN,OM,LV2               | NLOH       |        |         |
| 13     | 41193155  | 41193155  | G       | A   | neo        | 0.0111  |     | P1,P2,LN3,LV1,LV2 | HET         |           |        | SN                          | DLOH       |        |         |
| 13     | 109784443 | 109784449 | ACCGCCG | A   | not_neo    | 2.0874  |     | P1,P2,LN3,LV1,LV2 | HET         |           |        | SN                          | DLOH       |        |         |
| 13     | 113636697 | 113636697 | A       | G   | neo        | 0.4878  |     | LV1,LV2           | HET         |           |        | SN                          | DLOH       |        |         |
| 14     | 104152430 | 104152430 | G       | A   | neo        | 0.3514  |     | P2,LV1            | HET         |           |        | SN                          | DLOH       |        |         |
| 14     | 105588349 | 105588349 | G       | T   | neo        | 0.2842  |     | LV1,LV2           | no_call,HET |           |        | SN                          | DLOH       |        |         |
| 17     | 17816293  | 17816293  | C       | T   | neo        | 0.0406  |     | P2                | HET         |           |        | SN                          | DLOH       |        |         |
| 17     | 41226775  | 41226775  | G       | T   | not_neo    | 23.2973 |     | LV1               | no_call     |           |        | LN2                         | NLOH       |        |         |
| 18     | 10691247  | 10691247  | C       | T   | neo        | 0.0406  |     | P1,P2,LN3,LV2     | HET         |           |        | SN                          | DLOH       |        |         |
| 19     | 549168    | 549168    | G       | T   | not_neo    | 2.8992  |     | P2                | HET         |           |        | SN                          | DLOH       |        |         |
| 19     | 54595864  | 54595864  | G       | C   | neo        | 0.5174  |     | LV1               | ASCNA       |           |        | OM,LN2,P1,LV2,P2,LN3,LN1,SN | ALOH,NLOH  |        |         |
| 2      | 53700454  | 53700454  | C       | T   | neo        | 0.0092  |     | LV1,LV2           | HET         |           |        | SN                          | NLOH       |        |         |
| 20     | 17600864  | 17600864  | A       | G   | neo        | 0.8347  |     | LV1               | HET         |           |        | SN                          | DLOH       |        |         |
| 20     | 51004487  | 51004487  | G       | A   | not_neo    | 2.1646  |     | P1,P2,LN3,LV1,LV2 | BCNA,HET    |           |        | SN                          | ALOH       |        |         |
| 20     | 5919131   | 5919131   | G       | A   | neo        | 0.7026  |     | P2                | BCNA        |           |        | SN                          | ALOH       |        |         |
| 21     | 14219725  | 14219725  | G       | T   | neo        | 1.6107  |     | P1                | HET         |           |        | SN                          | DLOH       |        |         |
| 21     | 44424892  | 44424892  | C       | T   | neo        | 0.9374  |     | P1,LV1            | HET         |           |        | SN                          | DLOH       |        |         |
| 21     | 44551226  | 44551226  | G       | A   | not_neo    | 13.3780 |     | OM,LV1            | HET         |           |        | SN                          | DLOH       |        |         |
| 3      | 75738689  | 75738689  | C       | A   | not_neo    | 2.4749  |     | LV2               | HET         |           |        | SN                          | NLOH       |        |         |
| 3      | 75738689  | 75738689  | C       | A   | not_neo    | 2.4749  |     | LV2               | HET         |           |        | SN                          | NLOH       |        |         |
| 3      | 75738689  | 75738689  | C       | A   | not_neo    | 2.4749  |     | LV2               | HET         |           |        | SN                          | NLOH       |        |         |
| 3      | 75739141  | 75739141  | T       | A   | neo        | 0.9330  |     | P1                | HET         |           |        | SN                          | NLOH       |        |         |
| 3      | 196803031 | 196803031 | G       | C   | neo        | 0.3683  |     | P2,OM,LN2         | HET         |           |        | LN3                         | NLOH       |        |         |
| 4      | 184638417 | 184638417 | T       | A   | neo        | 0.1199  |     | LV1,LV2           | HET         |           |        | SN                          | DLOH       |        |         |
| 7      | 100868687 | 100868687 | C       | T   | not_neo    | 4.0348  |     | P2                | HET         |           |        | SN                          | NLOH       |        |         |
| 7      | 101002450 | 101002450 | G       | A   | neo        | 0.1112  |     | LV1               | no_call     |           |        | SN                          | NLOH       |        |         |
| 7      | 132507597 | 132507597 | C       | T   | neo        | 0.9399  |     | P1,P2,LN3,LV1,LV2 | HET,GAIN    |           |        | SN                          | NLOH       |        |         |

Supplementary Table 3D

D

| seqnames | start     | end       | ref | alt | neo_status | min_el_mut | regions_called | cna_status_in_called_region | loh_regions | cna_status_in_loh_regions |
|----------|-----------|-----------|-----|-----|------------|------------|----------------|-----------------------------|-------------|---------------------------|
| 1        | 1046496   | 1046496   | T   | C   | neo        | 0.0425     | P3             | HET                         | C1,C3,P1,C2 | NLOH,ALOH                 |
| 18       | 49837547  | 49837547  | A   | G   | not_neo    | 5.3493     | P2             | HET                         | C1,C2,C3,P1 | NLOH                      |
| 19       | 15807836  | 15807836  | C   | T   | neo        | 0.0184     | P3             | HET                         | P1,C2,C1,C3 | NLOH                      |
| 19       | 35633856  | 35633856  | C   | T   | neo        | 0.1362     | P3             | HET                         | C2,P1,C3,C1 | NLOH                      |
| 19       | 50281747  | 50281747  | C   | T   | neo        | 0.4877     | P2             | HET                         | P1,C2,C1,C3 | NLOH                      |
| 19       | 52799708  | 52799708  | G   | T   | not_neo    | 8.2762     | C1             | HET                         | C2,P1,C3    | NLOH                      |
| 19       | 53353449  | 53353449  | G   | A   | neo        | 0.5508     | C1             | HET                         | C2,P1,C3    | NLOH                      |
| 20       | 1921646   | 1921646   | G   | A   | neo        | 1.8034     | C2             | no_call                     | P1,C3       | ALOH,NLOH                 |
| 20       | 3471186   | 3471186   | G   | T   | not_neo    | 3.7934     | P3             | HET                         | C3,C1,C2    | NLOH                      |
| 20       | 36197992  | 36197992  | C   | T   | neo        | 1.3177     | P1,P2,P3       | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 41488518  | 41488518  | C   | G   | neo        | 1.5468     | P1,P2,P3       | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 45963820  | 45963820  | G   | C   | not_neo    | 2.5415     | P1             | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 59042728  | 59042728  | C   | T   | not_neo    | 9.9821     | P1,P2,P3       | ASCNA,GAIN,HET              | C2,C1,C3    | ALOH                      |
| 21       | 46351441  | 46351441  | C   | G   | neo        | 0.3549     | P3             | HET                         | C1,C2,C3,P1 | ALOH,NLOH                 |
| 3        | 30671854  | 30671854  | G   | T   | neo        | 0.9108     | P2             | HET                         | P1,C3,C2,C1 | NLOH                      |
| 9        | 128333476 | 128333476 | G   | A   | neo        | 0.1884     | P2             | HET                         | C2,P1,C1,C3 | NLOH                      |

Supplementary Table 3E

E

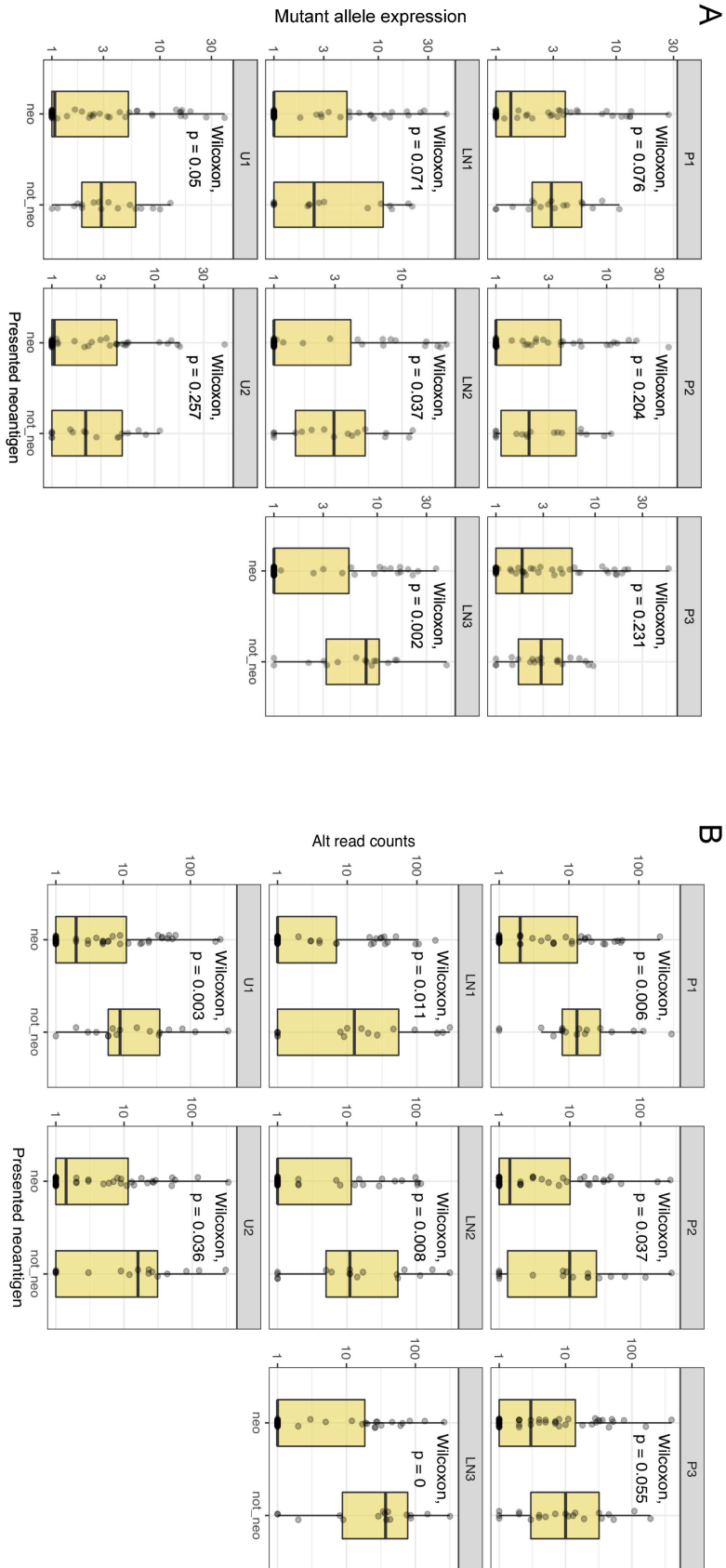
| seqnames | start     | end       | ref | alt | neo    | status | min     | del | mut               | regions | called | chr               | status | in | called | region      | loh | regions   | chr | status | in | loh | regions |
|----------|-----------|-----------|-----|-----|--------|--------|---------|-----|-------------------|---------|--------|-------------------|--------|----|--------|-------------|-----|-----------|-----|--------|----|-----|---------|
| 1        | 6245302   | 6245302   | C   | T   | neo    |        | 0.0794  |     | P1                |         |        | BCNA              |        |    |        | LV1         |     | DLOH      |     |        |    |     |         |
| 1        | 6413234   | 6413234   | A   | G   | neo    |        | 0.3322  |     | LV2               |         |        | GAIN              |        |    |        | LV1         |     | DLOH      |     |        |    |     |         |
| 1        | 21480217  | 21480217  | T   | G   | neo    |        | 0.2046  |     | LV2               |         |        | HET               |        |    |        | LV1         |     | DLOH      |     |        |    |     |         |
| 1        | 196828162 | 196828162 | G   | C   | neo    |        | 0.1974  |     | P1,LV3,NC1,NC2    |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 1        | 197104252 | 197104252 | G   | A   | neo    |        | 0.8617  |     | P1                |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 1        | 201209922 | 201209922 | A   | G   | noLneo |        | 2.5975  |     | P1                |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 1        | 228353056 | 228353056 | G   | A   | neo    |        | 0.0799  |     | NC1,NC2,NC3       |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 10       | 47312891  | 47312891  | G   | A   | neo    |        | 0.9891  |     | NC1,NC2,NC3       |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 10       | 133207180 | 133207180 | C   | T   | neo    |        | 0.8125  |     | P1                |         |        | HET               |        |    |        | LV3,LV1     |     | DLOH      |     |        |    |     |         |
| 11       | 280816    | 280816    | A   | T   | noLneo |        | 3.9977  |     | LV2               |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 11       | 71458501  | 71458501  | G   | C   | neo    |        | 0.5411  |     | LV2               |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 11       | 77112596  | 77112596  | C   | T   | neo    |        | 0.5455  |     | P1                |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 11       | 25096672  | 25096672  | G   | T   | neo    |        | 0.4546  |     | NC3               |         |        | no call           |        |    |        | LV1,LV3,LV2 |     | DLOH      |     |        |    |     |         |
| 14       | 77027406  | 77027406  | G   | C   | noLneo |        | 2.7479  |     | NC1               |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 16       | 20320413  | 20320413  | T   | C   | noLneo |        | 3.6038  |     | NC1,NC2,NC3       |         |        | no call           |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 18       | 35102094  | 35102094  | C   | G   | neo    |        | 0.5725  |     | NC1               |         |        | HET               |        |    |        | LV3,LV2,LV1 |     | DLOH      |     |        |    |     |         |
| 19       | 2917289   | 2917289   | C   | A   | neo    |        | 0.4972  |     | LV2               |         |        | HET               |        |    |        | LV1         |     | DLOH      |     |        |    |     |         |
| 19       | 22313623  | 22313623  | A   | G   | neo    |        | 0.0092  |     | P1                |         |        | BCNA              |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 19       | 55094775  | 55094775  | G   | C   | noLneo |        | 2.5358  |     | NC3               |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 2        | 128318303 | 128318303 | G   | T   | neo    |        | 0.1127  |     | P1,LV3,NC2        |         |        | HET               |        |    |        | LV1         |     | DLOH      |     |        |    |     |         |
| 3        | 14541920  | 14541920  | A   | T   | noLneo |        | 4.5713  |     | P1                |         |        | HET               |        |    |        | LV2,LV1,LV3 |     | DLOH      |     |        |    |     |         |
| 3        | 195781262 | 195781262 | G   | A   | neo    |        | 1.4083  |     | P2                |         |        | ASCNA             |        |    |        | LV3,NC1     |     | ALOH,NLOH |     |        |    |     |         |
| 3        | 195786302 | 195786302 | G   | A   | neo    |        | 1.2199  |     | P1                |         |        | no call           |        |    |        | LV3,NC1     |     | ALOH,NLOH |     |        |    |     |         |
| 4        | 70481468  | 70481468  | T   | C   | neo    |        | 1.0182  |     | P1,NC3            |         |        | HET               |        |    |        | LV3,LV1,LV2 |     | DLOH      |     |        |    |     |         |
| 4        | 75876552  | 75876552  | C   | T   | neo    |        | 0.0950  |     | P1,P2,NC1,NC2,NC3 |         |        | HET,UBCNA,no call |        |    |        | LV1,LV3,LV2 |     | DLOH      |     |        |    |     |         |
| 4        | 95219169  | 95219169  | T   | C   | noLneo |        | 14.0595 |     | P1                |         |        | HET               |        |    |        | LV2,LV3,LV1 |     | DLOH      |     |        |    |     |         |
| 6        | 33080864  | 33080864  | A   | G   | neo    |        | 1.3877  |     | P2,NC1            |         |        | UBCNA,GAIN        |        |    |        | LV3,LV2,LV1 |     | DLOH,NLOH |     |        |    |     |         |
| 6        | 75313139  | 75313139  | C   | T   | neo    |        | 1.6028  |     | NC1,NC2,NC3       |         |        | HET               |        |    |        | LV2,LV1,LV3 |     | DLOH      |     |        |    |     |         |
| 6        | 81752003  | 81752003  | T   | C   | neo    |        | 1.1642  |     | NC3               |         |        | HET               |        |    |        | LV2,LV1,LV3 |     | DLOH      |     |        |    |     |         |
| 6        | 128348470 | 128348470 | T   | A   | neo    |        | 0.0510  |     | NC1,NC2,NC3       |         |        | HET               |        |    |        | LV1,LV3,LV2 |     | DLOH      |     |        |    |     |         |
| 6        | 152325188 | 152325188 | T   | C   | neo    |        | 0.3887  |     | P1,P2,NC1,NC2,NC3 |         |        | HET,UBCNA         |        |    |        | LV1,LV3,LV2 |     | DLOH      |     |        |    |     |         |
| 6        | 152325244 | 152325244 | G   | A   | neo    |        | 0.8430  |     | NC2               |         |        | HET               |        |    |        | LV1,LV3,LV2 |     | DLOH      |     |        |    |     |         |
| 7        | 2264448   | 2264448   | G   | A   | neo    |        | 0.0465  |     | P1                |         |        | BCNA              |        |    |        | LV2,LV1     |     | DLOH      |     |        |    |     |         |
| 7        | 56086574  | 56086574  | G   | A   | neo    |        | 0.4527  |     | P1                |         |        | BCNA              |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 7        | 128409867 | 128409867 | C   | T   | neo    |        | 1.5376  |     | P1                |         |        | HET               |        |    |        | LV1         |     | NLOH      |     |        |    |     |         |
| 9        | 969448911 | 969448911 | T   | C   | neo    |        | 0.3242  |     | NC3               |         |        | ASCNA             |        |    |        | LV3,LV2,LV1 |     | DLOH      |     |        |    |     |         |
| 9        | 136501748 | 136501748 | C   | T   | neo    |        | 0.9122  |     | P2                |         |        | no call           |        |    |        | LV3,LV1,LV2 |     | DLOH      |     |        |    |     |         |
| 9        | 138023729 | 138023729 | A   | G   | neo    |        | 0.3511  |     | P1,P2             |         |        | BCNA,UBCNA        |        |    |        | LV3,LV1,LV2 |     | DLOH      |     |        |    |     |         |

Supplementary Table 3F

F

| seqnames | start     | end       | ref | alt | neo_status | min_el | mut          | regions_called | cna_status_in_called_region | loh_regions | cna_status_in_loh_regions |
|----------|-----------|-----------|-----|-----|------------|--------|--------------|----------------|-----------------------------|-------------|---------------------------|
| 11       | 1246233   | 1246233   | C   | T   | neo        | 0.3214 | LN3,P1       | HET            | P3,LN1                      | NLOH        |                           |
| 14       | 20143985  | 20143985  | G   | A   | neo        | 0.3001 | U1           | ASCNA          | LN1                         | ALOH        |                           |
| 18       | 31068961  | 31068961  | G   | A   | neo        | 0.0397 | LN1          | GAIN           | P3                          | NLOH        |                           |
| 18       | 47246972  | 47246972  | C   | T   | not_neo    | 3.2225 | LN1,U1,P1,P2 | GAIN,HET       | P3                          | NLOH        |                           |
| 18       | 62084534  | 62084534  | C   | A   | neo        | 1.3551 | U1           | HET            | P3                          | NLOH        |                           |
| 2        | 11197270  | 11197270  | G   | A   | neo        | 0.2225 | LN2,LN3,U1   | HET            | P3,LN1                      | NLOH        |                           |
| 2        | 130074871 | 130074871 | C   | A   | neo        | 0.3802 | U2,P1        | HET            | P3,LN1                      | NLOH        |                           |
| 4        | 1395164   | 1395164   | T   | C   | neo        | 0.5412 | LN2,LN3      | HET            | LN1                         | NLOH        |                           |
| 5        | 140841486 | 140841486 | G   | T   | neo        | 0.1783 | P2           | HET            | LN1,P3                      | NLOH        |                           |
| 9        | 33566372  | 33566372  | A   | G   | neo        | 0.2907 | LN2          | HET            | P3,LN1                      | NLOH        |                           |

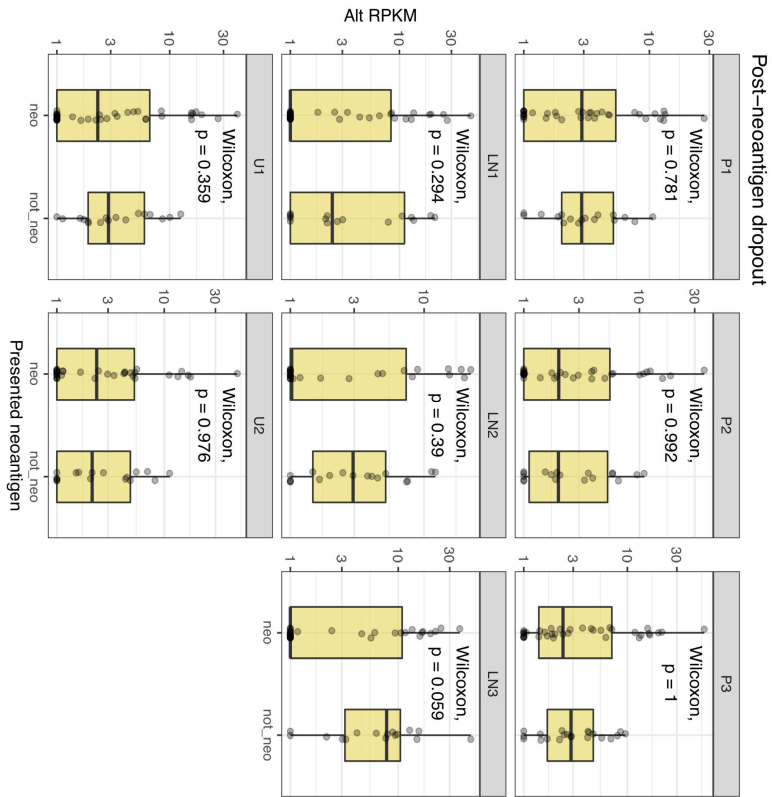
Supplementary Fig. 6





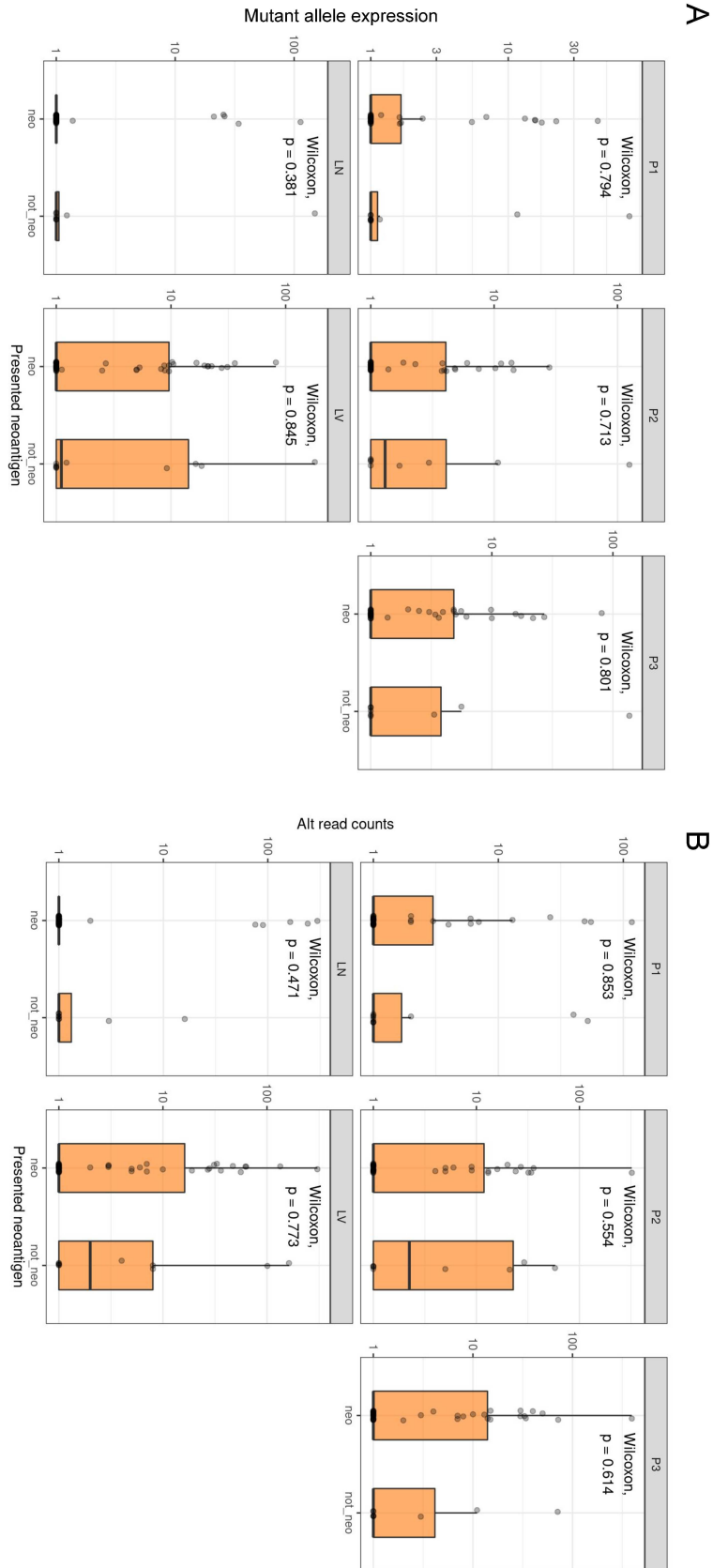
Supplementary Table 4

| chrom | pos       | ref alt | gene    | mut_peptide                   | min_el_mut | n_regions | expr_regions                      |
|-------|-----------|---------|---------|-------------------------------|------------|-----------|-----------------------------------|
| 2     | 162396927 | C T     | KCNH7   | IVVAILGKNDIFEEEMVHL YAKPGKS   | 0.0208     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 2     | 178718119 | G A     | TTN     | QCKVDGTPPEIRIFWYKKEHTTKLRSAAP | 0.1764     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 13    | 87676004  | G T     | SLITRK5 | NNLFRFVPLTHLYLRGNRRLKLLPYV    | 0.2527     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 6     | 31871375  | C T     | SLC44A4 | QQGISGLIDSLNTRDISVKIFEDFA     | 0.5174     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 17    | 29969201  | G A     | EFCAB5  | MLTQVEKKKKVLT KADTPSKFDPINIV  | 0.8164     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 12    | 8059594   | C G     | C3AR1   | DFYGDPLENRS LQINIVQPPGEMNDR   | 0.92       | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 6     | 39879403  | G A     | DAAM2   | LPLPQDPYPSSDIP L RKKRVQPSH    | 0.9732     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 5     | 159084705 | T A     | EBF1    | QAIVYEGQDKNPVMCRVLLTHEIMC     | 1.2098     | 8         | LN1, LN2, LN3, U1, U2, P1, P2, P3 |
| 19    | 13877273  | G T     | NANOS3  | MGTFDLWTVYV LGLAHLVRLAS       | 0.0115     | 7         | LN1, LN2, LN3, U2, P1, P2, P3     |
| 1     | 111414895 | T C     | OVGP1   | LTPVGHQSVTPVGHQSVSPGGTTMT     | 1.6476     | 7         | LN1, LN2, U1, U2, P1, P2, P3      |
| 5     | 180792305 | G A     | MGAT1   | DLEVAPDFEEYFWATYPL LKADPSL    | 0.0884     | 6         | LN1, LN3, U1, P1, P2, P3          |
| 11    | 116772934 | C G     | BUD13   | MAAAPPLSKAQYL KRYLSGADAG      | 0.752      | 6         | LN2, LN3, U1, U2, P1, P2          |
| 19    | 48462126  | C A     | KCNJ14  | PPPAPCFSHVASL LAFLFALETQT     | 0.0148     | 5         | LN2, LN3, U2, P1, P3              |
| 17    | 7673334   | C G     | TF53    | KPLDGEVFTIL QDHTSFQKENC       | 0.1465     | 5         | LN1, LN2, LN3, P1, P2             |

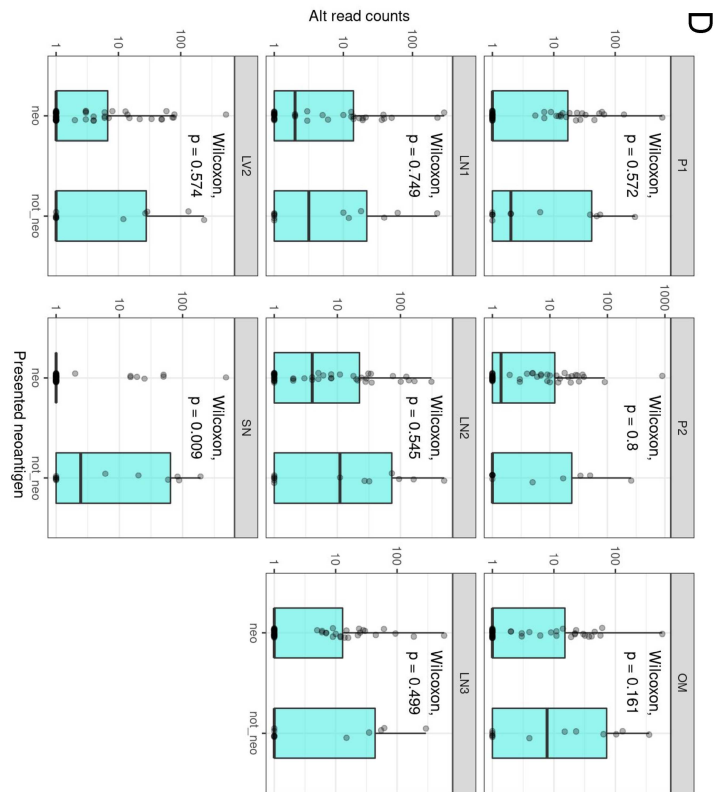
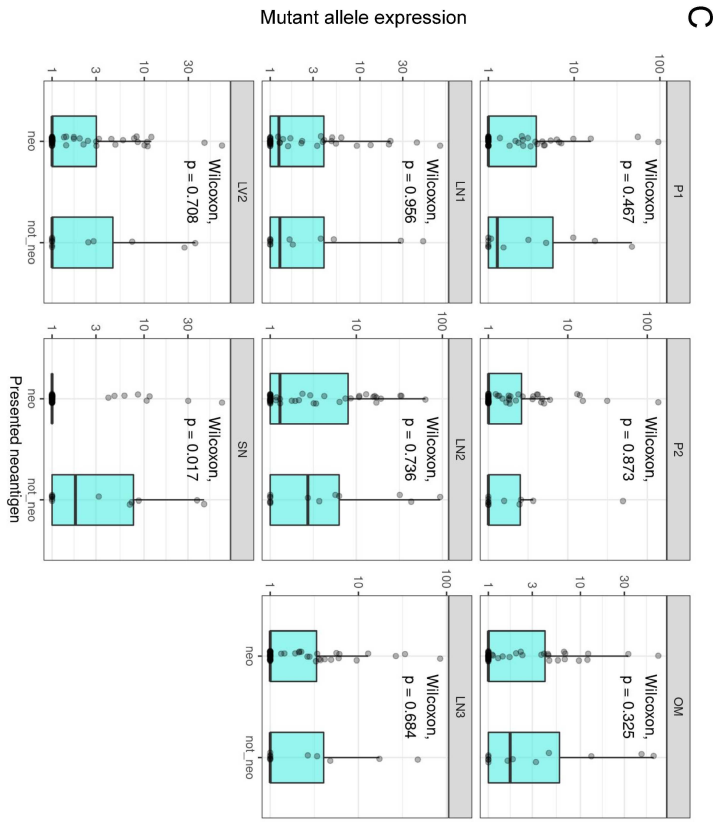


Supplementary Fig. 7

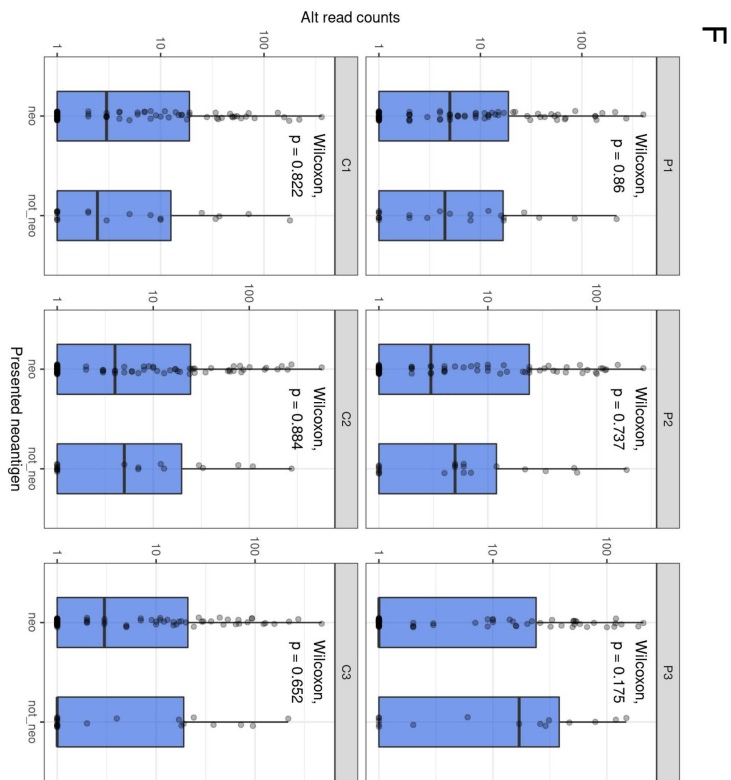
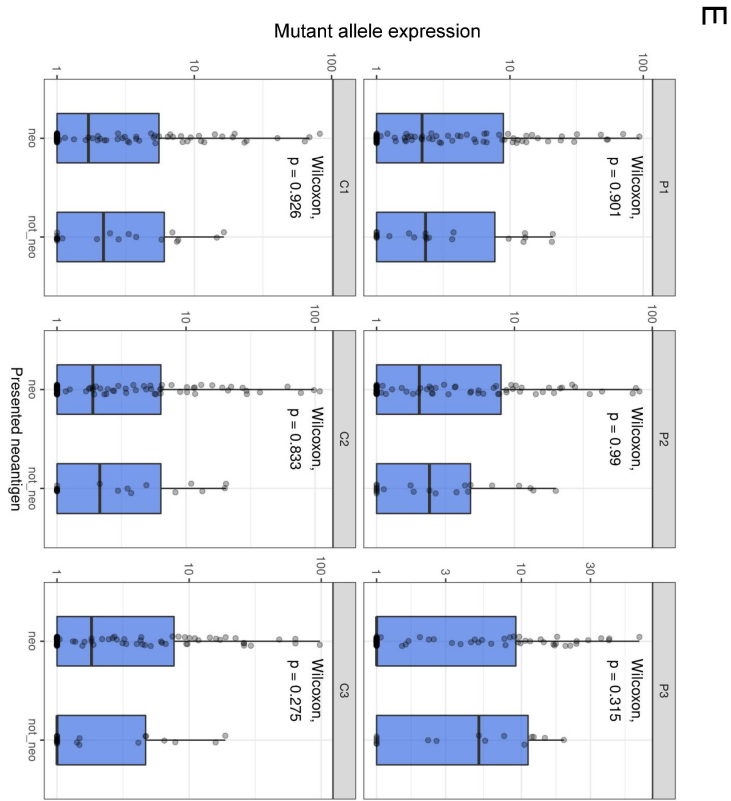
Supplementary Fig. 8A,B.



Supplementary Fig. 8C,D.

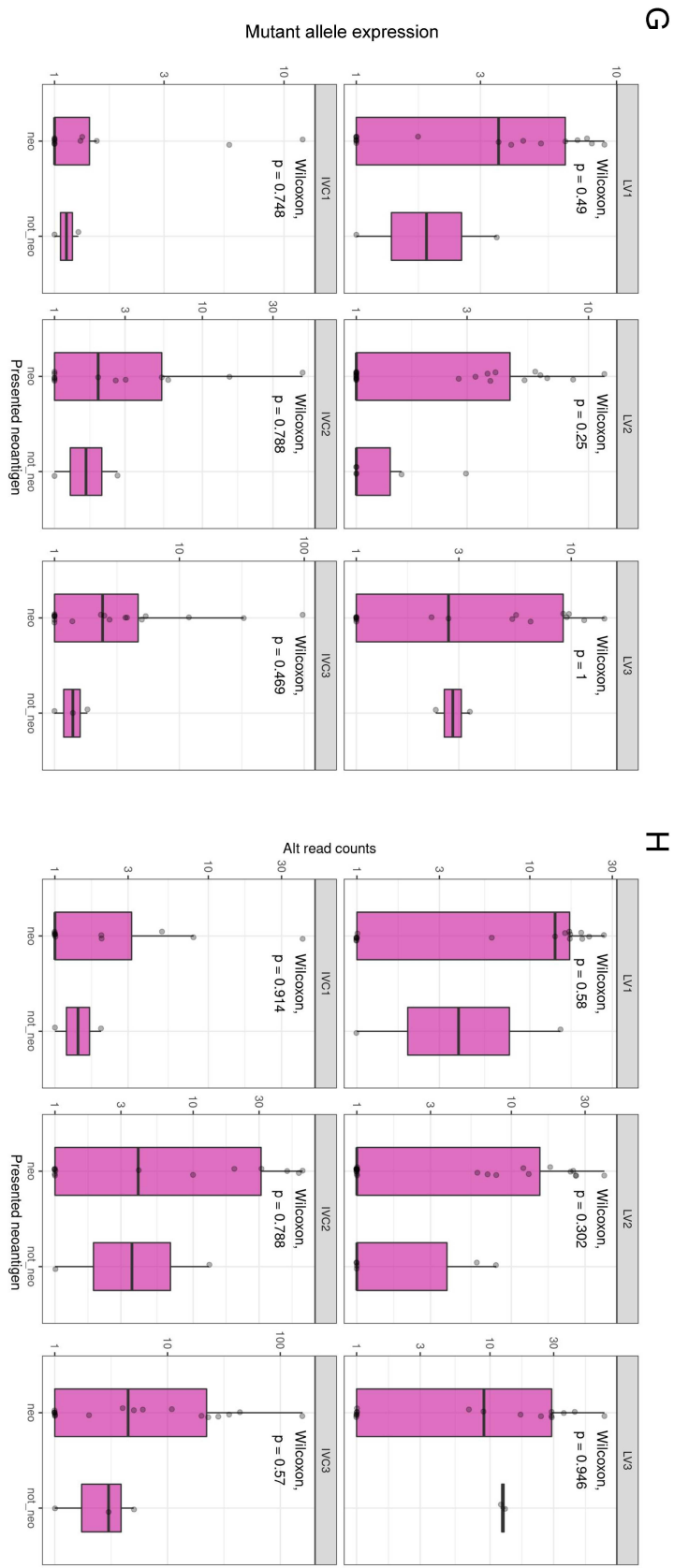


Supplementary Fig. 8E,F.



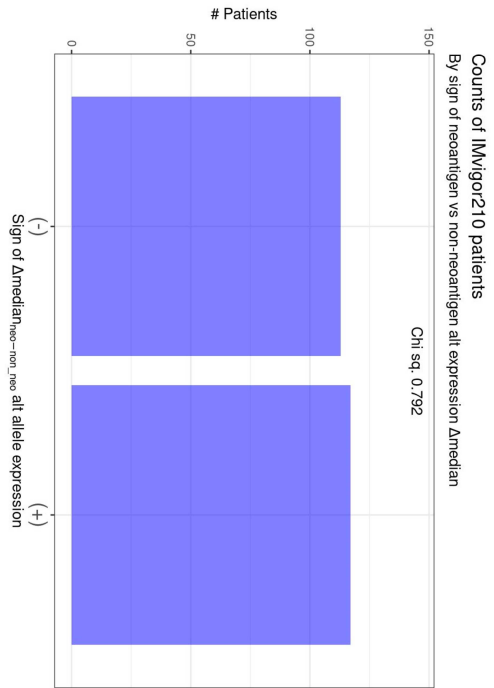


Supplementary Fig. 8G,H.

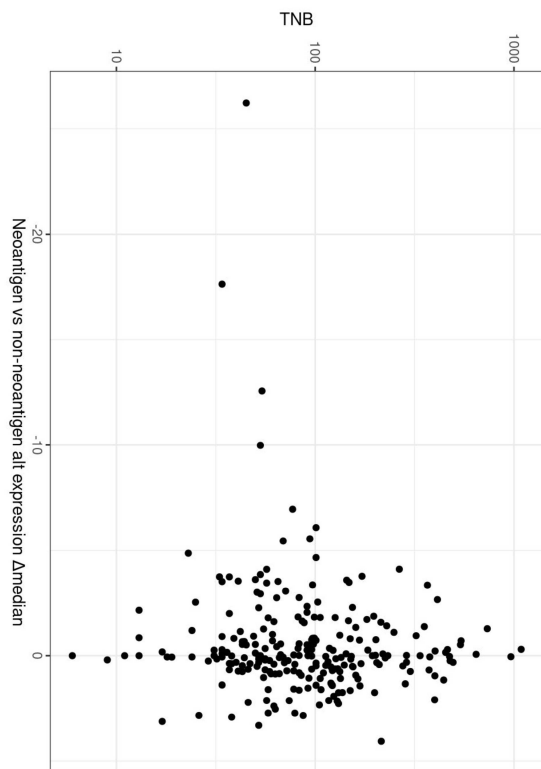


Supplementary Fig. 9A,B,C.

A



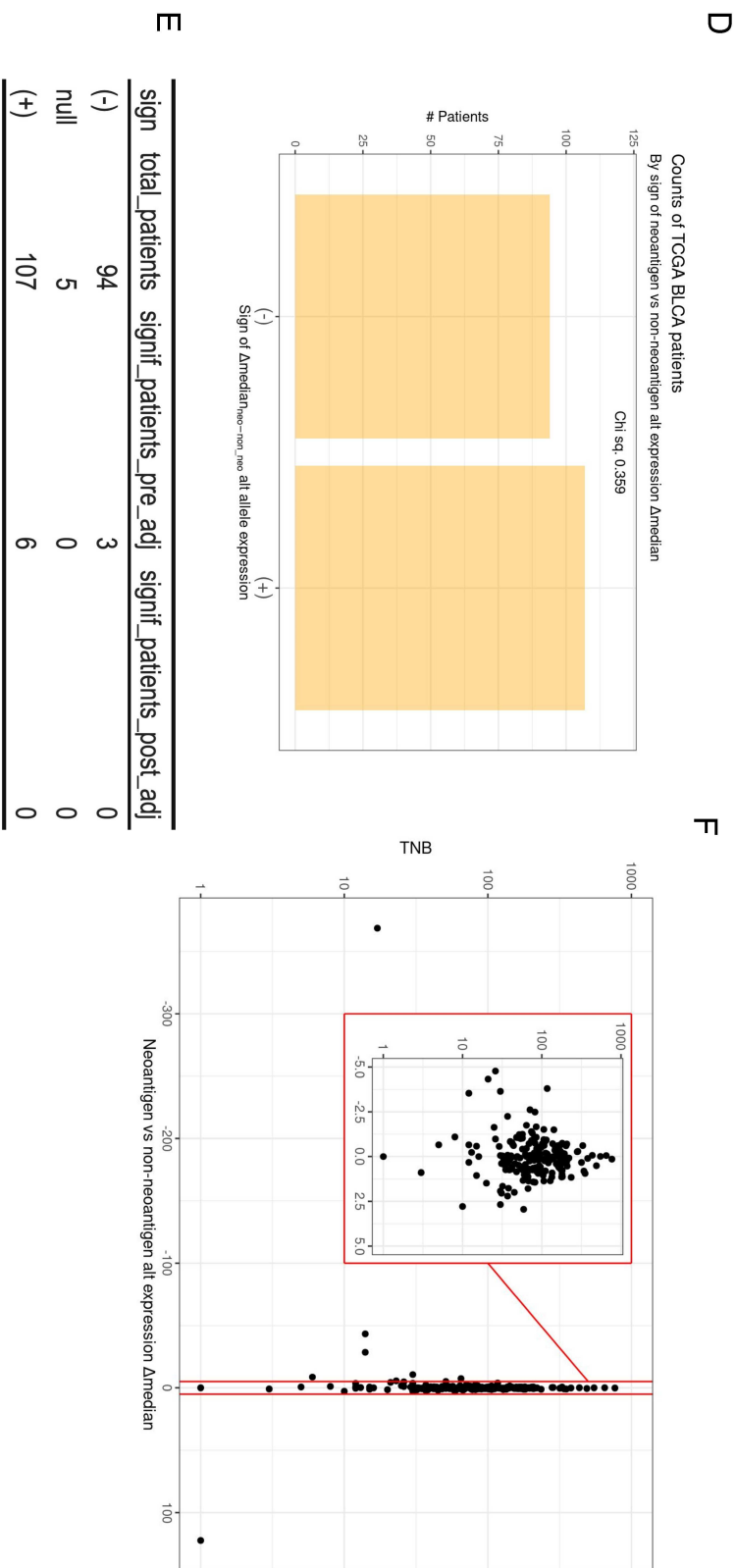
C



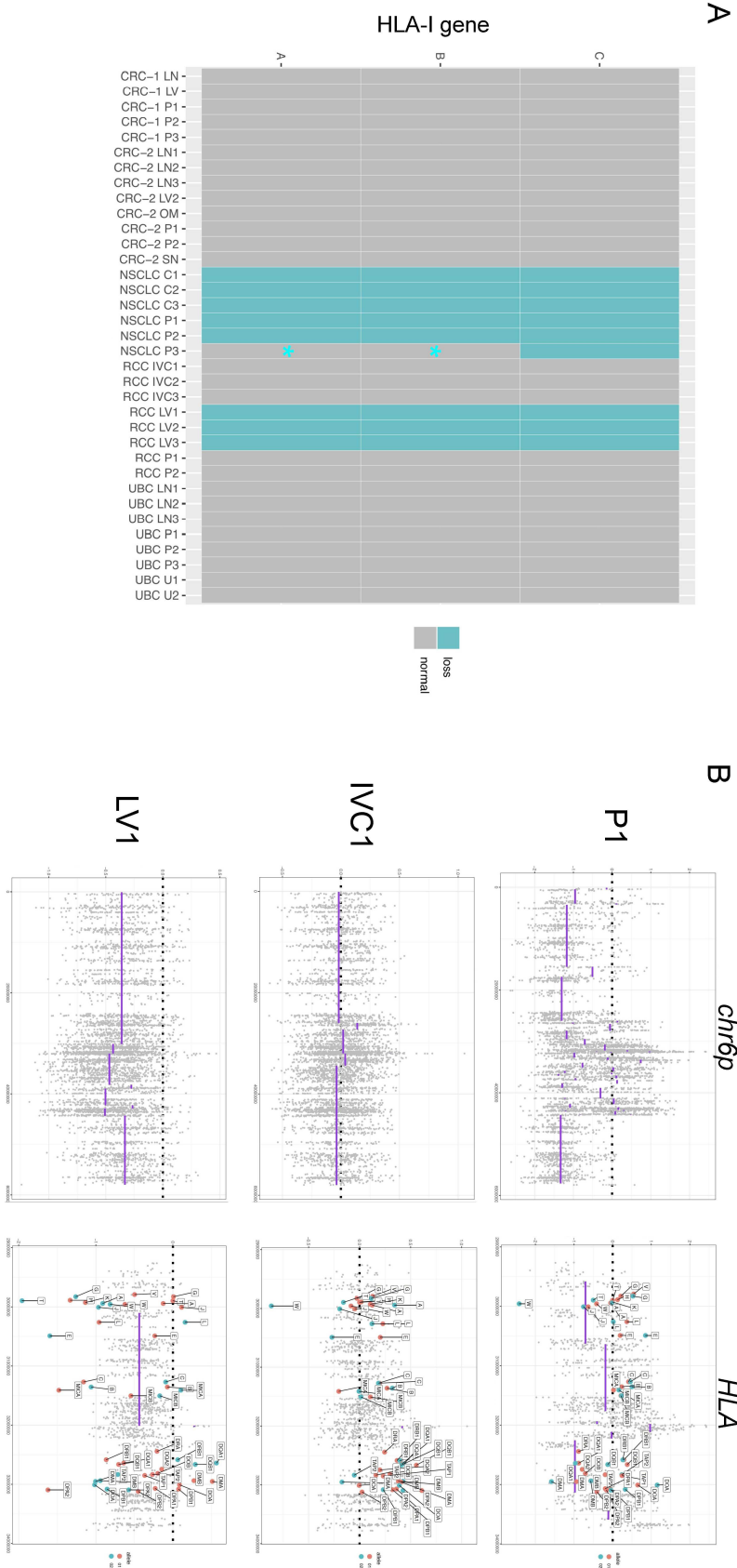
B

| sign | total_patients | signif_patients_pre_adj | signif_patients_post_adj |
|------|----------------|-------------------------|--------------------------|
| (-)  | 113            | 8                       | 0                        |
| null | 8              | 0                       | 0                        |
| (+)  | 117            | 11                      | 0                        |

Supplementary Fig. 9D,E,F.



Supplementary Fig. 10



Supplementary Table 5

|           | Total reads | High qual. reads | rRNA reads | Processed reads | Total mapped | Uniquely mapped | Mitochondrial reads |
|-----------|-------------|------------------|------------|-----------------|--------------|-----------------|---------------------|
| HP-210866 | 5036064     | 49669461         | 1048775    | 48620866        | 46579338     | 38207102        | 21505               |
| HP-210867 | 52821959    | 52080524         | 1098165    | 50982359        | 50983356     | 39668705        | 97450               |
| HP-210868 | 59546345    | 58721069         | 965414     | 57765655        | 577690547    | 45662118        | 81341               |
| HP-210869 | 57435497    | 56864491         | 816233     | 56048298        | 55962139     | 43368259        | 53466               |
| HP-210871 | 56396996    | 55675339         | 468959     | 55206380        | 55150357     | 41587712        | 17209               |
| HP-210872 | 51144291    | 50600000         | 1382129    | 49207871        | 49172953     | 38973855        | 9464                |
| HP-210873 | 56008464    | 55422983         | 1376576    | 54046407        | 54002920     | 43921331        | 15952               |
| HP-210874 | 51478213    | 50760554         | 1756717    | 49004837        | 48970726     | 30798288        | 22660               |
| HP-210875 | 56277722    | 55591111         | 1351351    | 54239780        | 54219147     | 44596658        | 10532               |
| HP-210876 | 48570098    | 47290028         | 3130459    | 44159569        | 44108729     | 35642386        | 46331               |
| HP-210877 | 51531915    | 50846550         | 3539917    | 47306633        | 47249606     | 38023534        | 72091               |
| HP-210878 | 51932811    | 51378146         | 1604232    | 49773914        | 49747411     | 39884044        | 16528               |
| HP-210879 | 50987167    | 50162438         | 2792980    | 47368448        | 47344480     | 38245094        | 41280               |
| HP-210880 | 57980164    | 57292610         | 1726229    | 55566381        | 55541302     | 45455397        | 14582               |
| HP-210882 | 55865542    | 55295412         | 622803     | 54672509        | 54632087     | 42575965        | 3274                |
| HP-210883 | 49283138    | 48472911         | 1577485    | 46895426        | 46841139     | 38181496        | 11736               |
| HP-210884 | 61005884    | 60275191         | 1106429    | 59168762        | 59102910     | 44741042        | 4866                |
| HP-210885 | 51114676    | 50323023         | 1453234    | 48868789        | 48819196     | 36400418        | 18810               |
| HP-210886 | 51912865    | 5148173          | 988403     | 50159770        | 50128884     | 42317916        | 3968                |
| HP-210887 | 62352760    | 61628254         | 896321     | 60771933        | 60712088     | 48027898        | 4550                |
| HP-210888 | 57974848    | 57169331         | 7267951    | 55901380        | 55787328     | 44479953        | 8661                |
| HP-210889 | 49728613    | 48838866         | 1063271    | 47775595        | 47695228     | 38479932        | 17506               |
| HP-210890 | 52266691    | 51589239         | 1679048    | 49920191        | 49793750     | 38688016        | 39058               |
| HP-210895 | 57096568    | 56433477         | 1392636    | 55040851        | 55005930     | 44668026        | 3195                |
| HP-210896 | 52067861    | 51331487         | 1433740    | 49891747        | 49872179     | 40408727        | 50283               |
| HP-210897 | 56865437    | 56066855         | 1537293    | 54529562        | 54482874     | 44301014        | 43107               |
| HP-210898 | 50127096    | 49330035         | 1286014    | 48034021        | 47949182     | 37732763        | 46095               |
| HP-210899 | 53013888    | 52887269         | 1013918    | 51273551        | 51181281     | 40097530        | 40204               |
| HP-210900 | 60946196    | 60012510         | 1792104    | 58220406        | 58138828     | 45749068        | 85349               |
| HP-210902 | 57946388    | 56936250         | 1514290    | 55421980        | 55383251     | 43526321        | 30401               |
| HP-210903 | 53374234    | 52445712         | 1330095    | 51144717        | 51092525     | 39317158        | 17314               |
| HP-210904 | 60928649    | 60049215         | 1588454    | 58450761        | 58361386     | 44545208        | 41001               |
| HP-210905 | 60516883    | 59471573         | 2246614    | 57006659        | 56921161     | 42545208        | 69336               |
| HP-210906 | 55655183    | 54123520         | 3973469    | 50250051        | 50141680     | 38473983        | 37141               |
| HP-210907 | 60389354    | 59379870         | 3293433    | 55099927        | 55030991     | 44696609        | 135273              |
| HP-210908 | 68282925    | 67337240         | 3019582    | 64317658        | 64291811     | 50688898        | 58416               |
| HP-210909 | 63177648    | 62882852         | 4005892    | 58676960        | 58636649     | 48813648        | 78600               |
| HP-210910 | 60415201    | 59397153         | 2668388    | 56869765        | 56602918     | 41804980        | 58111               |
| HP-210911 | 55254266    | 54296521         | 2203632    | 52092889        | 52014874     | 38619173        | 52091               |

## Supplementary Tables 6A,B

A

| Patient | Tissue Abstr. | Wilcoxon P-value | Adjusted P-value (within-patient) |
|---------|---------------|------------------|-----------------------------------|
| CRC-1   | LV            | 0.8446547        | 0.8446547                         |
| CRC-1   | P1            | 0.7936131        | 0.8446547                         |
| CRC-1   | P2            | 0.7127719        | 0.8446547                         |
| CRC-1   | P3            | 0.8010851        | 0.8446547                         |
| CRC-1   | LN            | 0.3810733        | 0.8446547                         |
| CRC-2   | P1            | 0.4669977        | 0.9464703                         |
| CRC-2   | P2            | 0.8732703        | 0.9559919                         |
| CRC-2   | OM            | 0.3245311        | 0.9464703                         |
| CRC-2   | LN1           | 0.9559919        | 0.9559919                         |
| CRC-2   | LN2           | 0.7361436        | 0.9464703                         |
| CRC-2   | LN3           | 0.6840069        | 0.9464703                         |
| CRC-2   | LV1           | 0.4463424        | 0.9464703                         |
| CRC-2   | LV2           | 0.7080822        | 0.9464703                         |
| CRC-2   | SN            | 0.0172880        | 0.1554120                         |
| NSCLC   | P1            | 0.9010240        | 0.9896837                         |
| NSCLC   | P2            | 0.9896837        | 0.9896837                         |
| NSCLC   | P3            | 0.3146956        | 0.9440867                         |
| NSCLC   | C1            | 0.9256716        | 0.9896837                         |
| NSCLC   | C2            | 0.8332084        | 0.9896837                         |
| NSCLC   | C3            | 0.2751837        | 0.9440867                         |
| RCC     | LV1           | 0.4901167        | 0.9459376                         |
| RCC     | LV2           | 0.2498910        | 0.9459376                         |
| RCC     | LV3           | 1.0000000        | 1.0000000                         |
| RCC     | IVC1          | 0.7475504        | 0.9459376                         |
| RCC     | IVC2          | 0.7882813        | 0.9459376                         |
| RCC     | IVC3          | 0.469507         | 0.9459376                         |
| UBC     | LN1           | 0.0707651        | 0.1215934                         |
| UBC     | LN2           | 0.936727         | 0.1215934                         |
| UBC     | LN3           | 0.0023588        | 0.0188461                         |
| UBC     | U1            | 0.0496528        | 0.1215934                         |
| UBC     | U2            | 0.2569331        | 0.2569331                         |
| UBC     | P1            | 0.0759959        | 0.1215934                         |
| UBC     | P2            | 0.2039102        | 0.2569331                         |
| UBC     | P3            | 0.2314699        | 0.2569331                         |

B

| Patient | Tissue Abstr. | Wilcoxon P-value | Adjusted P-value (within-patient) |
|---------|---------------|------------------|-----------------------------------|
| CRC-1   | LV            | 0.7732900        | 0.8534200                         |
| CRC-1   | P1            | 0.8534200        | 0.8534200                         |
| CRC-1   | P2            | 0.5536233        | 0.8534200                         |
| CRC-1   | P3            | 0.6142980        | 0.8534200                         |
| CRC-1   | LN            | 0.4714011        | 0.8534200                         |
| CRC-2   | P1            | 0.5715550        | 0.7382067                         |
| CRC-2   | P2            | 0.7999913        | 0.7999913                         |
| CRC-2   | OM            | 0.1605321        | 0.7223946                         |
| CRC-2   | LN1           | 0.7488708        | 0.7999913                         |
| CRC-2   | LN2           | 0.5448204        | 0.7382067                         |
| CRC-2   | LN3           | 0.4993582        | 0.7382067                         |
| CRC-2   | LV1           | 0.4616425        | 0.7382067                         |
| CRC-2   | LV2           | 0.5741608        | 0.7382067                         |
| CRC-2   | SN            | 0.0091749        | 0.0825745                         |
| NSCLC   | P1            | 0.8600336        | 0.8838148                         |
| NSCLC   | P2            | 0.7366613        | 0.8838148                         |
| NSCLC   | P3            | 0.1747156        | 0.8838148                         |
| NSCLC   | C1            | 0.8219721        | 0.8838148                         |
| NSCLC   | C2            | 0.8838148        | 0.8838148                         |
| NSCLC   | C3            | 0.6516619        | 0.8838148                         |
| RCC     | LV1           | 0.5799825        | 0.9455936                         |
| RCC     | LV2           | 0.3015753        | 0.9455936                         |
| RCC     | LV3           | 0.9455936        | 0.9455936                         |
| RCC     | IVC1          | 0.9140005        | 0.9455936                         |
| RCC     | IVC2          | 0.7882813        | 0.9455936                         |
| RCC     | IVC3          | 0.5695880        | 0.9455936                         |
| UBC     | LN1           | 0.0109205        | 0.0174727                         |
| UBC     | LN2           | 0.0078581        | 0.0157162                         |
| UBC     | LN3           | 0.0001787        | 0.0009499                         |
| UBC     | U1            | 0.0032892        | 0.0131566                         |
| UBC     | U2            | 0.0361100        | 0.0423381                         |
| UBC     | P1            | 0.0055066        | 0.0146843                         |
| UBC     | P2            | 0.0370459        | 0.0423381                         |
| UBC     | P3            | 0.0553739        | 0.0553739                         |

Supplementary Tables 7A,B,C.

A

| patient | n_neo_mutex_loh | n_non_neo_mutex_loh | frac_mutex_loh_muts_that_are_neo | frac_all_nonsyn_muts_that_are_neo |
|---------|-----------------|---------------------|----------------------------------|-----------------------------------|
| CRC-1   | 2               | 1                   | 0.67                             | 0.86                              |
| CRC-2   | 5               | 0                   | 1.00                             | 0.81                              |
| NSCLC   | 5               | 3                   | 0.62                             | 0.78                              |
| RCC     | 6               | 1                   | 0.86                             | 0.88                              |
| UBC     | 2               | 0                   | 1.00                             | 0.70                              |

B

| seqnames | start    | end      | ref | alt | neo_status | min_el_mut | regions_called | ona_status_in_called_region | loh_regions | ona_status_in_loh_regions |
|----------|----------|----------|-----|-----|------------|------------|----------------|-----------------------------|-------------|---------------------------|
| 16       | 78691263 | 78691263 | G   | A   | not_neo    | 4.3743     | LV,P1,P2,P3    | GAIN,HET                    | LN          | NLOH                      |
| 6        | 31356262 | 31356262 | C   | T   | neo        | 0.0205     | P3             | GAIN                        | LN,P1,P2    | ALOH,NLOH                 |
| 6        | 31356284 | 31356284 | G   | T   | neo        | 1.3549     | LV             | HET                         | LN,P1,P2    | ALOH,NLOH                 |

C

| seqnames | start     | end       | ref | alt | neo_status | min_el_mut | regions_called    | ona_status_in_called_region | loh_regions | ona_status_in_loh_regions |
|----------|-----------|-----------|-----|-----|------------|------------|-------------------|-----------------------------|-------------|---------------------------|
| 13       | 41193155  | 41193155  | G   | A   | neo        | 0.0111     | P1,P2,LN3,LV1,LV2 | HET                         | SN          | DLOH                      |
| 13       | 113636697 | 113636697 | A   | G   | neo        | 0.4878     | LV1,LV2           | HET                         | SN          | DLOH                      |
| 17       | 17816293  | 17816293  | C   | T   | neo        | 0.0406     | P2                | HET                         | SN          | DLOH                      |
| 2        | 53700454  | 53700454  | C   | T   | neo        | 0.0092     | LV1,LV2           | HET                         | SN          | NLOH                      |
| 4        | 184638417 | 184638417 | T   | A   | neo        | 0.1199     | LV1,LV2           | HET                         | SN          | DLOH                      |



Supplementary Tables 7D,E,F

**D**

| seqnames | start    | end      | ref | alt | neo_status | min_el_mut | regions_called | cna_status_in_called_region | loh_regions | cna_status_in_loh_regions |
|----------|----------|----------|-----|-----|------------|------------|----------------|-----------------------------|-------------|---------------------------|
| 11       | 1246233  | 1246233  | C   | T   | neo        | 0.3214     | LN3,P1         | HET                         | P3,LN1      | NLOH                      |
| 2        | 11197270 | 11197270 | G   | A   | neo        | 0.2225     | LN2,LN3,U1     | HET                         | P3,LN1      | NLOH                      |

**E**

| seqnames | start     | end       | ref | alt | neo_status | min_el_mut | regions_called       | cna_status_in_called_region | loh_regions | cna_status_in_loh_regions |
|----------|-----------|-----------|-----|-----|------------|------------|----------------------|-----------------------------|-------------|---------------------------|
| 1        | 196828162 | 196828162 | G   | C   | neo        | 0.1974     | P1,LV3,IVC1,IVC2     | HET                         | LV1         | NLOH                      |
| 1        | 228353056 | 228353056 | G   | A   | neo        | 0.0799     | IVC1,IVC2,IVC3       | HET                         | LV1         | NLOH                      |
| 19       | 55094775  | 55094775  | G   | C   | not_neo    | 2.5358     | IVC3                 | HET                         | LV1         | NLOH                      |
| 6        | 33080864  | 33080864  | A   | G   | neo        | 1.3677     | P2,IVC1              | UBCNA,GAIN                  | LV3,LV2,LV1 | DLOH,NLOH                 |
| 6        | 126348470 | 126348470 | T   | A   | neo        | 0.0510     | IVC1,IVC2,IVC3       | HET                         | LV1,LV3,LV2 | DLOH                      |
| 6        | 152325188 | 152325188 | T   | C   | neo        | 0.3887     | P1,P2,IVC1,IVC2,IVC3 | HET,UBCNA                   | LV1,LV3,LV2 | DLOH                      |
| 6        | 152325244 | 152325244 | G   | A   | neo        | 0.8430     | IVC2                 | HET                         | LV1,LV3,LV2 | DLOH                      |

**F**

| seqnames | start    | end      | ref | alt | neo_status | min_el_mut | regions_called | cna_status_in_called_region | loh_regions | cna_status_in_loh_regions |
|----------|----------|----------|-----|-----|------------|------------|----------------|-----------------------------|-------------|---------------------------|
| 19       | 35633856 | 35633856 | C   | T   | neo        | 0.1362     | P3             | HET                         | C2,P1,C3,C1 | NLOH                      |
| 20       | 3471186  | 3471186  | G   | T   | not_neo    | 3.7934     | P3             | HET                         | C3,C1,C2    | NLOH                      |
| 20       | 36197992 | 36197992 | C   | T   | neo        | 1.3177     | P1,P2,P3       | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 41488518 | 41488518 | C   | G   | neo        | 1.5468     | P1,P2,P3       | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 45963820 | 45963820 | G   | C   | not_neo    | 2.5415     | P1             | HET                         | C1,C2,C3    | NLOH                      |
| 20       | 59042728 | 59042728 | C   | T   | not_neo    | 9.9821     | P1,P2,P3       | ASCNA,GAIN,HET              | C2,C1,C3    | ALOH                      |
| 21       | 46351441 | 46351441 | C   | G   | neo        | 0.3549     | P3             | HET                         | C1,C2,C3,P1 | ALOH,NLOH                 |
| 3        | 30671854 | 30671854 | G   | T   | neo        | 0.9108     | P2             | HET                         | P1,C3,C2,C1 | NLOH                      |

Supplementary Table 8A.

A

| patient  | sequenans | start     | end | ref | alt                        | Mut. peptide | symbol            | Regions losing presentation | Expression (counts) | EL             |                        | All regions | Alteration |
|----------|-----------|-----------|-----|-----|----------------------------|--------------|-------------------|-----------------------------|---------------------|----------------|------------------------|-------------|------------|
|          |           |           |     |     |                            |              |                   |                             |                     | min (pre-loss) | min EL mut (post-loss) |             |            |
| NSCLC 1  | 11838896  | 11838896  | C   | T   | VPLALVSSQSRATFRLLCPREMLLE  | CLCN6        | C1,C2,C3,P1,P2,P3 | 0.3,0.1,1.0                 | 0.2842              | 2.0378         | C1,C2,C3,P1,P2,P3      | S92F        |            |
| NSCLC 1  | 31756497  | 31756497  | G   | A   | HYLVNFTQLRPPSEEMVAQAESEVG  | A0GRB2       | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 0.8278              | 2.3842         | C1,C2,C3,P1,P2,P3      | P114S       |            |
| NSCLC 1  | 40190795  | 40190795  | C   | T   | GRLLVSCFELLIVSESELPOEWWL   | ELF          | C1,C2,C3,P1,P2    | 33.26,23.21,21              | 1.2015              | 5.6849         | C1,C2,C3,P1,P2,P3      | S138L       |            |
| NSCLC 1  | 52921631  | 52921631  | G   | A   | RVLCLLRPWRPRLWARGCAGSDGAMG | ECHDC2       | C1,C2,C3,P1,P2    | 7.6,4,11,7                  | 0.5955              | 2.6015         | C1,C2,C3,P1,P2,P3      | R15W        |            |
| NSCLC 10 | 59245331  | 59245331  | C   | A   | HYVILVAPVAGSTGDFEFCQRLPOL  | PHYHPL       | C1,C2,C3,P1       | 0.0,0.0                     | 0.2534              | 6.4171         | C1,C2,C3,P1            | P65T        |            |
| NSCLC 12 | 43425588  | 43425588  | G   | T   | LEDHNGEIVNKPSPVIOGHMHPQ    | ADAMTS20     | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 0.6195              | 2.4806         | C1,C2,C3,P1,P2,P3      | P1404T      |            |
| NSCLC 12 | 69610072  | 69610072  | G   | T   | TPEPRPKARRELVRESEDELOAP    | LRRC10       | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 0.7582              | 2.3883         | C1,C2,C3,P1,P2,P3      | A256E       |            |
| NSCLC 15 | 83263764  | 83263764  | G   | T   | TVQPVLPFRYSPDPAEVAWTFGL    | BNC1         | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 0.8157              | 2.1377         | C1,C2,C3,P1,P2,P3      | A496D       |            |
| NSCLC 15 | 97969220  | 97969220  | T   | A   | KYAFQIOTYLARGKTKTRHMAN     | ARRDC4       | C1,C2,C3          | 0.0,0                       | 0.8805              | 6.2571         | C1,C2,C3               | S247R       |            |
| NSCLC 18 | 13067919  | 13067919  | AC  | A   | GMKALPLKLNRSNPLCOLD        | CEP192       | C2,P2             | 7.6                         | 0.2931              | 2.1509         | C2,P2                  | T1051X      |            |
| NSCLC 19 | 22180832  | 22180832  | C   | A   | CEEGKASNSSSLMHEHKRHITGEK   | ZNF676       | C2                | 0                           | 1.4688              | 4.2567         | C2                     | K256N       |            |
| NSCLC 19 | 41088499  | 41088499  | A   | G   | MASGLLVALLACLTYMVLNS       | CYP2A13      | C1                | 0                           | 1.2765              | 5.4701         | C1                     | T10A        |            |
| NSCLC 19 | 41088509  | 41088509  | C   | T   | MLASGLLVTLVCLTYMVLNSVWR    | CYP2A13      | C1                | 0                           | 0.4682              | 4.7881         | C1                     | A13V        |            |
| NSCLC 2  | 73927008  | 73927008  | A   | G   | SPLEGVSSRRGLRGRGRRLSIEG    | DGLOK        | C1,C2,C3,P1,P2,P3 | 17.18,11.11,9.25            | 1.6243              | 5.1094,2.3805  | C1,C2,C3,P1,P2,P3      | H33R        |            |
| NSCLC 2  | 130916483 | 130916483 | C   | A   | RENPPAAAGRDADPLHHGGASWPE   | ARRGFE4      | C1,C2,C3,P1,P2    | 4.5,4,16,13                 | 1.9202              | 3.3333         | C1,C2,C3,P1,P2,P3      | P846Q       |            |
| NSCLC 20 | 1921646   | 1921646   | G   | A   | TREDVHSQVIGEMAHVTLQDPLRG   | SIRPA        | C2                | 0                           | 1.8034              | 2.5388         | C2                     | V230M       |            |
| NSCLC 21 | 37166575  | 37166575  | C   | T   | NNKCEVPESTSVWTPHVMQWAI     | TTC3         | C1,C2,C3,P1,P2    | 0.2407                      | 2.2259              | 0.2407         | C1,C2,C3,P1,P2,P3      | A1454V      |            |
| NSCLC 22 | 36822244  | 36822244  | C   | A   | MVAQGLSMALMLQWERSLGAIE     | CSF2RB       | C1,C2,C3          | 0.0,0                       | 0.6880              | 4.2002         | C1,C2,C3,P3            | L13M        |            |
| NSCLC 3  | 30671854  | 30671854  | G   | T   | FSEHKALIEDLSIDISTGANNIN    | TGFRB2       | P2                | 3                           | 0.9108              | 3.1781         | P2                     | R224L       |            |
| NSCLC 4  | 78407833  | 78407833  | C   | T   | RHSQGAQSDSFCFEVSSASNAQTR   | FRAS1        | P2                | 0                           | 1.0012              | 5.3149         | P2,P3                  | R1434C      |            |
| NSCLC 4  | 82429412  | 82429412  | G   | C   | RRPDLFRRHFKRSRIGR5AAAAAT   | HNRNPDL      | C1,C2,C3,P1,P2,P3 | 59.82,67.42,51.9            | 0.2777              | 4.9357,2.4301  | C1,C2,C3,P1,P2,P3      | S83R        |            |
| NSCLC 4  | 119502949 | 119502949 | C   | T   | ITPWPVQQRKAKLVATEFDQGDQR   | PDE5A        | C1,C2,C3,P1,P2    | 38.59,12.28,23              | 0.1882              | 2.202          | C1,C2,C3,P1,P2,P3      | E738K       |            |
| NSCLC 4  | 140657098 | 140657098 | T   | C   | EVDIFRLRTSYGKGFTRADLEQ     | TBC1D9       | C1,C2,C3,P1       | 5.16,6.8                    | 1.8573              | 2.8352         | C1,C2,C3,P1            | E779G       |            |
| NSCLC 5  | 149250489 | 149250489 | G   | A   | LISKASALPAYRNKGLHRTPSADLF  | ABLIM3       | C1,C2,C3,P1,P2    | 6.9,10,0.1                  | 0.0563              | 5.1305         | C1,C2,C3,P1,P2         | R891K       |            |
| NSCLC 6  | 28572912  | 28572912  | C   | T   | SEVITQKELAPKCKRTHCFHRES    | ZEBD9        | C1,C2,C3,P1       | 3.7,0.2                     | 0.8007              | 4.16           | C1,C2,C3,P1            | E993K       |            |
| NSCLC 7  | 88145131  | 88145131  | G   | A   | GACIFKFKPSKLLNPECGNGEIEG   | ADAM22       | C1,C2,C3,P1,P2    | 3.0,0.5,0                   | 1.6394              | 4.6524         | C1,C2,C3,P1,P2,P3      | D443N       |            |
| NSCLC 7  | 89333473  | 89333473  | C   | A   | PNKGRKKSQMKMTLLKGNLPR      | ZNF804B      | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 1.1861              | 4.485          | C1,C2,C3,P1,P2         | S164T       |            |
| NSCLC 7  | 128941320 | 128941320 | G   | A   | VKMPPLTQPTLQPTLQPTLQPP     | IRF5         | C2,P1,P2          | 0.0,0                       | 0.8228              | 9.1729         | C2,P1,P2,P3            | R175Q       |            |
| NSCLC 8  | 43422322  | 43422322  | T   | A   | QHSVDNLDITRPSASJEDYLLD     | POTEA        | C1,C2,C3,P1,P2    | 0.0,0.0,0                   | 1.2131              | 2.4979         | C1,C2,C3,P1,P2,P3      | W442R       |            |
| NSCLC 8  | 54626563  | 54626563  | C   | T   | ILSKQHTTRANFELASIKKPFDEEA  | RP1          | C1,C2,C3,P1,P2,P3 | 2.0,1.0,2.0                 | 0.0620              | 2.1374         | C1,C2,C3,P1,P2,P3      | S894F       |            |
| NSCLC 9  | 128333476 | 128333476 | G   | A   | GAFFGRRLGAQNLQVLSLEIPVA    | COO4         | P2                | 0                           | 0.1894              | 2.4328         | P2                     | S210N       |            |

Supplementary Table 8B.

B

| patient | seqnames | start     | end       | ref  | alt | Mut. peptide               | symbol   | Regions losing presentation | Expression (counts) | min EL         |                    | All regions                             | Alteration |
|---------|----------|-----------|-----------|------|-----|----------------------------|----------|-----------------------------|---------------------|----------------|--------------------|---|------------|
|         |          |           |           |      |     |                            |          |                             |                     | mut (pre-loss) | min EL (post-loss) |   |            |
| RCC     | 1        | 21480217  | 21480217  | T    | G   | SLQEQHLGLALDVRMKKKDQEEED   | NBPF3    | LV2                         | 0                   | 0.2046         | 4.3407             | LV2                                     | L459V      |
| RCC     | 1        | 39427601  | 39427601  | T    | G   | PVGTQTAKIQQOSIRHKALEEDIEN  | MACF1    | LV1, LV2, LV3               | 21, 39, 71          | 0.8051         | 3.9881             | LV1, LV2, LV3                           | I3928S     |
| RCC     | 10       | 3138934   | 3138934   | C    | T   | DIDEAKLSYFSTIDAPVAPSDKGM   | PITRM1   | LV2                         | 0                   | 0.9846         | 3.5659             | LV2                                     | V963I      |
| RCC     | 12       | 11393380  | 11393380  | T    | C   | PQGPPOQDNKSRARSPPGKPOGP    | PRB2     | LV2, LV3                    | 0.1                 | 0.2569         | 22.84              | IVC1, IVC2, IVC3, LV2, LV3, P1, P2      | Q233R      |
| RCC     | 12       | 64127665  | 64127665  | G    | C   | DSEASSGPVTEIDNSSSKDMNSPTDR | SRGAP1   | LV1, LV2, LV3               | 6.1, 10             | 0.6790         | 8.2087             | IVC1, IVC2, IVC3, LV1, LV2, LV3, P1, P2 | K827N      |
| RCC     | 17       | 43091462  | 43091462  | C    | G   | EERGTGLEENNQOEGMDSNLGIGT   | BRCA1    | LV1, LV2, LV3               | 13.6, 23            | 1.3151         | 3.7598             | LV1, LV2, LV3                           | E1357Q     |
| RCC     | 19       | 10986534  | 10986534  | C    | G   | PPSVSATGPGRGPGRGPGRGPAP    | SMARCA4  | LV1, LV2, LV3               | 5.0, 1              | 1.5231         | 12.5212            | LV1, LV2, LV3, P2                       | P234R      |
| RCC     | 20       | 59206957  | 59206957  | C    | T   | LOSCVQLRASRLCTPTWVRRSRHP   | ZNF831   | LV3                         | 0                   | 1.0094         | 5.0535             | LV3                                     | R1310C     |
| RCC     | 3        | 42686652  | 42686652  | A    | G   | PAANECYCASLSSQVPKNHVSLVTK  | KLHL40   | LV2                         | 0                   | 0.0290         | 2.7966             | LV2                                     | N345S      |
| RCC     | 3        | 52409576  | 52409576  | CGTA | C   | DFGKGVQVEEIDLQSKCQGFVYG    | BAP1     | LV1, LV2, LV3               | 13.2, 27            | 1.4224         | 7.7321             | IVC1, IVC3, LV1, LV2, LV3, P1, P2       | Y3-        |
| RCC     | 4        | 24895036  | 24895036  | C    | T   | MVVVIVIIIIIRAAATWD         | CCDC149  | LV2                         | 0                   | 1.1643         | 3.3868             | LV2                                     | V7I        |
| RCC     | 4        | 56315829  | 56315829  | C    | T   | AGVRELKGGPEKLEMHREPADTTEG  | KIAA1211 | LV2                         | 0                   | 1.6818         | 6.7485             | LV2                                     | S776L      |
| RCC     | 8        | 24917368  | 24917368  | G    | A   | EEKEEPEPEEKEKVAAKKSPVKAITA | NEFM     | LV1, LV2, LV3               | 0.0, 0              | 0.7140         | 4.7753             | LV1, LV2, LV3                           | E505K      |
| RCC     | 8        | 104499497 | 104499497 | C    | T   | IITSFODFIQSRRCNLDWLTIE     | LRP12    | LV1, LV2, LV3               | 26, 12, 8           | 1.0487         | 6.639              | LV1, LV2, LV3                           | G99R       |
| RCC     | 8        | 142879800 | 142879800 | G    | T   | MALREKAEVCMAMPVLS          | CYP11B1  | LV1, LV2, LV3               | 0.0, 0              | 1.7779         | 2.2302             | IVC2, LV1, LV2, LV3, P1                 | ASE        |

Supplementary Fig. 11

