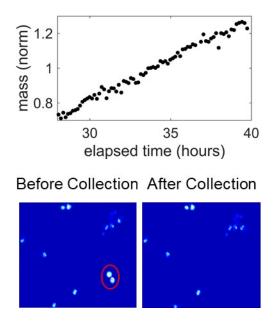
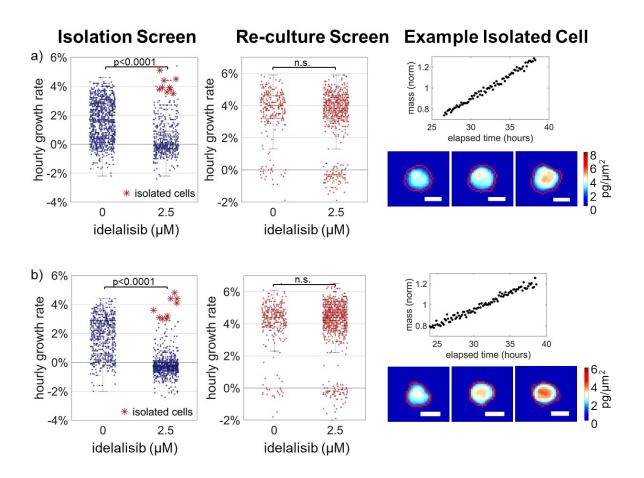
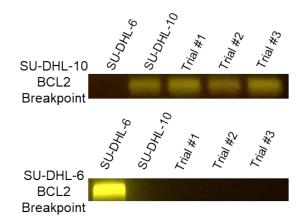
Electronic Supplementary Material (ESI) for Analyst. This journal is © The Royal Society of Chemistry 2021



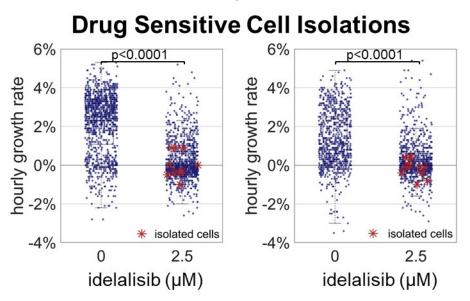
**Supplementary Figure #1:** An isolated cell cluster (tracked together) from the experiment in Fig. 3 grew at 4.8% +/- 0.06% per hour with before and after collection images shown demonstrating specificity of micropipette collection



**Supplementary Figure #2:** Replicates of resistant cell isolation. a) The 1:100 SU-DHL-10/-6 mixture was exposed to 2.5  $\mu$ M idelalisib for 24 hours with mass accumulation measured from 24-40 hours post dosing. Of 814 cells exposed to 2.5  $\mu$ M idelalisib with biomass growth measured, 9 were isolated. Isolated cells were grown for 20 days and then rescreened at 2.5  $\mu$ M of idelalisib with median growth rate of treated cells increased to 3.8% +/- 0.1% per hour from 0% +/- 0.07% per hour in the isolation screen. An example of an isolated cell grew at 4.5% +/- 0.06% per hour. b) In an identical experiment, of 1,310 cells exposed to 2.5  $\mu$ M idelalisib with biomass growth measured, 9 were isolated. Isolated cells were grown for 20 days and then rescreened at 2.5  $\mu$ M idelalisib with biomass growth measured, 9 were isolated. Isolated cells were grown for 20 days and then rescreened at 2.5  $\mu$ M idelalisib with median growth rate of 1,310 cells exposed to 2.5  $\mu$ M idelalisib with biomass growth measured, 9 were isolated. Isolated cells were grown for 20 days and then rescreened at 2.5  $\mu$ M of idelalisib with median growth rate of treated cells increasing to 4.4% +/- 0.07% per hour from was -0.3% +/- 0.02% per hour in the isolation screen. An isolated cell which grew at 3.1% +/- 0.05% per hour.



Supplementary Figure #3: PCR of re-cultured cells from all replicates (Trials #1-3) with controls. Trials #1-3 demonstrated amplification at the SU-DHL-10 breakpoint but not the SU-DHL-6 breakpoint further confirming that SU-DHL-10 cells were isolated.



**Supplementary Figure #4:** Replicates of drug sensitive isolation a) median growth rate of untreated cells is 2.5% +/- 0.1% per hour while the median growth of treated cells was -0.1% +/- 0.05%. 12 cells were isolated. b) median growth rate of untreated cells was 1.1% +/- 0.2% per hour while the median growth of treated cells was 0% +/-0.05%. 10 cells were isolated. Isolated cells were re-cultured for 20 days and no cell replication was observed.

| Cell Line | Breakpoint | Genomic Location           | Primer                              |
|-----------|------------|----------------------------|-------------------------------------|
| SU-DHL-6  | MBR (BCL2) | chr18: 63126367: 63126401  | CTATGGTGGTTTGACCTTTAGAGAGTTGCTTTACG |
|           | MBR (IGH)  | chr 14: 105861506-10586154 | CTAGGCCAGTCCTGCTGACGCCGCATCGGTGATTC |
| SU-DHI-10 | ICR (BCL2) | chr18: 63107355-63107377   | TCGTTCTCAGTAAGTGAGAGTGC             |
|           | ICR (IGH)  | chr14:105863199-105863214  | TGAGGAGACGGTGACC                    |

**Supplementary Table #1:** Locations and sequences of PCR primers for t(14:18) for SU-DHL-6 and SU-DHL-10.