a Experimental design of 6 TNBC PDX Tumours Untreated / cisplatin treated / cisplatin holiday series Untreated series Х3 Pt4 BRCA2 type UnRx Pt1 X7 Rx X5 Pt2 Pt5 BRCA1 type X6 **X8** X9 X10 X8 X6 X7 X1 Pt3 X4 Pt6 APOBEC (HRD-Like) type X5 X8 **b** Data analysis workflow Joint Single-Cell Tumour Populations (DLP+ & scRNA-seq) Trajectory Analysis (slingshot, tradeSeq) DLP+ Phylogenetic Tree Inference (sitka) Gene Module 1 Clone Resistant Rx, RxH UnRx RxH Gene Module 2 Root Clone Sensitive UnRx UnRx Rx UnRx Rx **RxH** Pseudotime Significant Pathways Integration of scRNA-seq & scDNA-seq (clonealign) X4 X5 X6 X7 Differential Expression Analysis (edgeR) Copy Number Genotype Dependent / Independent Gene Classification Rx vs UnRx-RxH vs UnRx-Rx vs UnRx-RxH vs UnRx-Rx vs UnRx -RxH vs UnRx -Rx vs UnRx Gene Set Enrichment Analysis (GSEA)