Patient derived xenografts seem to have closer global expression profile to that of the patient tumors of the corresponding cancer types, than the equivalent cell lines do

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Introduction

Patient derived xenografts (PDXs) without *in vitro* manipulation are believed to mirror original patients' histopathologic and genetic profiles, thus to be predictive surrogate models for patients, with superiority over conventional cancer cell lines. We have built the largest commercially available comprehensive PDX library of >1,600 models with genetic profiles of major cancer types, including about 200 NSLCL[1], 200 CRC[2], 200 gastric[3], 100 HCC[4], 100 pancreatic, 30 ovarian, 10 brain tumors.

We set out to compare major types of our PDXs with the corresponding TCGA[5] patient tumor samples and CCLE[6] cancer cell lines on their genomic expression by calculating pairwise Spearman rank correlation coefficient ρ, in order to further explore/ confirm the similarity and difference among the three collections. Our PDXs were profiled by both RNAseq and microarray (Affymetrix Human Genome U219 Array); CCLE cell lines were profiled by microarray (Affymetrix Human Genome U133 Plus 2.0 Array); and TCGA samples were by RNAseq. For convenience, these 4 gene expression datasets are called "PDX, PDXchip, CCLE, and TCGA". Only genes common to all 4 datasets were used to compute ρ.

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Results

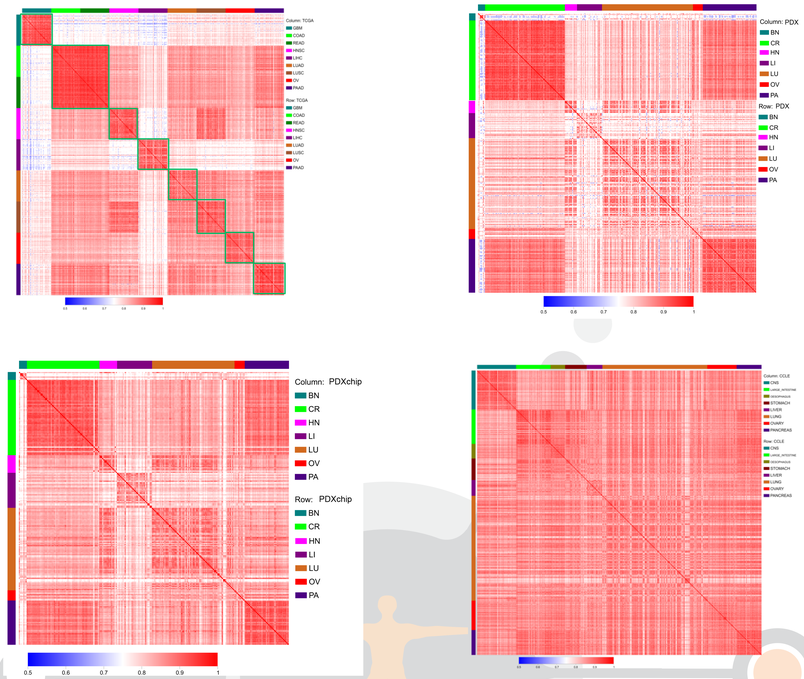

Figure 1. Pairwise genome-level expression correlation ρ for samples within 4 datasets (TCGA, PDX, PDXchip, and CCLE)

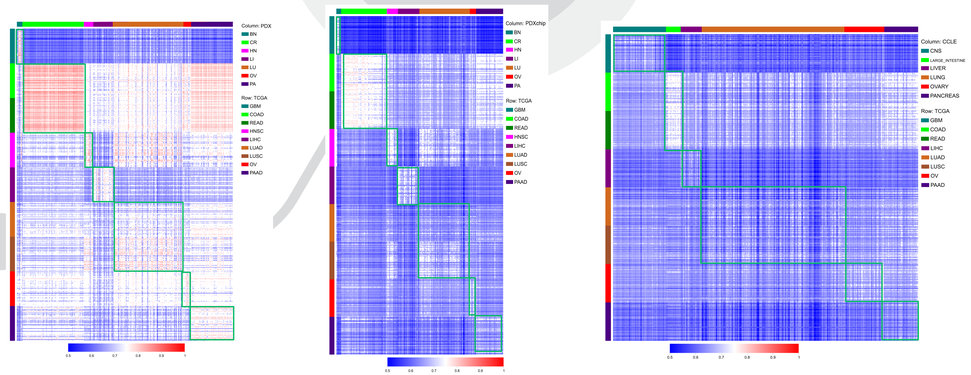

Figure 2. Pairwise genome-level expression correlation ρ for samples between TCGA and other 3 datasets (PDX, PDXchip, and CCLE)

Results

The preliminary data seems to lead to several observations. (1) Samples have higher ρ within the same cancer than between different cancers for TCGA, PDX, and PDXchip, but not so obvious for CCLE (Figure 1). (2) For all cancer types, there is always at least one different tumor CCLE-TCGA pair that has higher ρ than the same tumor CCLE-TCGA pair. For example, the TCGA colorectal, lung, and ovarian cancers have higher ρ with CCLE pancreatic cancer than the TCGA pancreatic cancer does. In contrast, for both PDX and PDXchip, only pancreatic cancer shows such behavior to TCGA colorectal cancer (COAD, READ) (Figure 2). (3) For same tumor type comparisons, ρ is 0.73-0.83 (average 0.772) between PDX and TCGA, 0.67-0.76 (average 0.698) between PDXchip and TCGA, 0.67-0.7(average 0.682) between CCLE and TCGA. (4) About 20% of CCLE lung cancers have much lower ρ with TCGA, PDX, and PDXchip lung cancers than the other CCLE lung cancers. In summary, these observations show that our PDX models are close in genomic expression profile to TCGA patient tumors per tumor types specifically, and more so than CCLE cancer cell lines, which is also less specific.

References

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