Prostate cancer (PC) is the most common malignancy in men and the second leading cause of cancer-related deaths. The majority of PCs are classified as adenocarcinomas characterized by the expression of androgen receptor (AR) and prostate-specific antigen (PSA). Two of the most commonly used cell lines are LNCaP and PC-3 cells, derived from lymph node and bone metastases, respectively. In addition to these, VCaP cells, derived from vertebral metastases, are widely used in prostate cancer research. It has been well established that LNCaP and VCaP cells represent the conventional indolent form of PC expressing AR and PSA and are androgen-dependent. PC-3 cells, on the other hand, do not express AR and PSA, are androgen-independent, and represent the highly aggressive form of PC.

Aim of the Study

Our goal was to compare the response of LNCaP, VCaP and PC-3 cells to a large panel of known anti-cancer compounds and determine the differences and similarities in sensitivity between these cell lines.

Materials and Methods

Drug sensitivity of the cell lines was assessed by applying a large panel of drugs covering both cancer chemotherapeutics and many clinically available and emerging molecularly targeted drugs including conventional chemotherapy, kinase inhibitors, metabolic modifiers, rapalogs, differentiating/epigenetic modifiers, kinesin inhibitors, apoptotic modulators, NSAIDs, hormone therapy, immunomodulations and HSIF inhibitors. A panel of about 460 compounds was tested in five concentrations covering a 10,000-fold drug-relevant concentration range in 384-well format. Cells were seeded to pre-drugged plates, followed by cell viability measurements (CellTiter-Glo) after 72 hours. Maximal and minimal viability (1-3).

Results / Drug sensitivity score (DSS)

Figure 1: Drug sensitivity score (DSS) profile of A) LNCaP, B) VCaP and C) PC-3 cells. D) Heatmap of DSS values in PC-3, VCaP and LNCaP cells. Twenty highest DSS values of E) LNCaP, F) VCaP and G) PC-3 cells.

Results / Selective drug sensitivity score (sDSS)

Figure 2: Selective drug sensitivity score (sDSS) profile of A) LNCaP, B) VCaP and C) PC-3 cells. D) Heatmap of sDSS values in PC-3, VCaP and LNCaP cells. Twenty highest sDSS values of E) LNCaP, F) VCaP and G) PC-3 cells.

Conclusions

We conclude that the cell-based compound screening combined with DSS analysis provides a possibility to profile cellular responses to an extensive collection of anti-cancer compounds. In addition, sDSS value can be used to identify the selective drug response pattern of different cancer cell lines. This enables identification of new indications for already existing drugs, finding vulnerabilities in different lines of cancer cells, and functional investigation of cellular pathways behind drug sensitivity or resistance.

References