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CancerDR: An overview of the online database for cancer drug resistance

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U.S. President Richard Nixon signed the National Cancer Act of 1971 that galvanized efforts aimed at seeking a cure for the disease and better understand the biological events that lead to it.It has been 40 years since the eventful declaration by the Nixon Administration, however despite significant progress in terms of understanding the mechanisms of the disease and some notable treatment successes at early onset of the disease; cancer continues to be a major cause of death[1]. Chemotherapy has been the mainstays of treatment for cancer patients, which is fraught with numerous side effects and is associated with poor quality of life for patients. With an increasing understanding of the molecular mechanisms of cancer, targeted therapies aimed at disrupting signaling pathways and molecules have emerged in the last few decades.

However, this has met with limited success owing to extensive molecular diversity that spans genetic and epigenetic alterations. The advent of genomic and proteomic technologies provide a comprehensive perspective of the disease; revealing a host of unique attributes including somatic and inherited mutations, polymorphisms, gene expression, amplification or copy number variations, and protein over-expression, loss, mutations and copy number variations.Interpreting this deluge of information is challenging both in terms of data management and retrieval. It is in this regard that databases catering exclusively to dissemination of cancer associated data that would assist efforts aimed at testing new chemotherapy treatments have emerged recently[2]. However, there have been few efforts at collecting and compiling valuable information to manage drug resistance data, especially the ones that are based on specific mutations in drug targets.

The latest article in Nature Science Reports titled “CancerDR: Cancer Drug Resistance Database” attempts to offer a prospective solution to identifying specific drug molecules that can target wide range of cancer cells., CancerDR(http://crdd.osdd.net) is a database of 148 anticancer drugs and their effectiveness against around 1000 cancer

cell lines. The 148 anti-cancer drugs include 36 FDA approved drugs, 48 drugs in clinical trials and 64 experimental drugs, of which, 130 are being used in targeted therapies and the remaining are cytotoxic drugs. Cancer cell lines used for pharmacological profiling in the databaseare distributed across major tissue types allowing users to access a wide range of information. The CancerDR database allows users to understand the effectiveness of drugs against specific cancer types based on pharmacological profiling data of anticancer drugs on different cell lines (http://www.nature.com/srep/2013/130313/srep01445/full/srep01445.html). The clustering module in the database allows the user to cluster mutants of a drug target to understand similarity among targets obtained from different sources or cell lines.These clusters are based on sequence similarity and represented via a visual alignment tree of wild type sequences of each target with their mutants. This feature helps users to view the distance of different mutant sequences in the alignment against selected targets in CancerDR. The authors also provide a comprehensive list of effective anti-cancer drugs against various tissue types obtained by clustering module, which is a valuable resource for the community.

One of the major aims of the database is to provide the users with a comprehensive understanding of the effect of mutations in drug targets on acquired drug resistance. The integrated NGS mapping tool allows users to map short reads, contigs and sequences on drug targets. This is particularly useful to detect mutations in drug targets of defined patient subsets, based on which, one can identify anti-cancer drugs for those patients. Since mutations in drug targets are known to cause structural changes that in turn are responsible for acquired drug resistance, the database has an in-built repository of predicted tertiary structures of all the drug targets, and their mutants/variants. This allows rapid identification of structural deviation due to individual mutations. As an extension of this tool, the database also allows users to predict and compare structures for user-defined protein sequences with preexisting protein structures available in CancerDR.

The authors claim that the database would allow extension of the concept of personalized medicine in cancer treatment by allowing users to select best therapeutic options for a particular cancer type. A major shortcoming of the CancerDR database is its exclusive cancer cell line based content. Having access to information about how different cancer cell lines respond to different chemotherapy treatments will no doubt assist scientists and physicians to suggest the best drug options for patients. However, in practice, this conceptual extension based on information derived from cancer cell lines has received mixed reactions. A recent commentary has emphasized that cell line data is only the first step in bringing new treatments into the clinic[3]. It states that even large numbers of cell lines cannot predict how immune mechanisms and the tumor micro-environment will factor into a drug's effectiveness, which renders wide-sweeping

conjectures based on cell lines extremely unreliable. That being said, the authors do acknowledge the deficiency and outline the necessity to integrate cancer patient data into their database. However, drug resistance information on cells lines from the database can be applied to explore new mechanisms that could be relevant in improving drug delivery and distribution.

In my own experience, CancerDR is a very valuable resource for the cancer research community and would definitely advance molecular and pharmacological research in the area. The tools are extremely user friendly and the format of data output makes analysis very intuitive. The authors allow/invite contributions from the community which makes the database very dynamic in terms of content. In summation, CancerDR is a valuable resource and offers a compilation of valuable scientific information while providing a free accessible platform with user-friendly tools.

1. Tiwari, A.K. and H.K. Roy, *Progress against cancer (1971-2011): how far have we come?* J Intern Med, 2012. **271**(4): p. 392-9.
2. Barretina, J., et al., *The Cancer Cell Line Encyclopedia enables predictive modelling of anticancer drug sensitivity.* Nature, 2012. **483**(7391): p. 603-7.
3. Begley, C.G. and L.M. Ellis, *Drug development: Raise standards for preclinical cancer research.* Nature, 2012. **483**(7391): p. 531-3.