DDRnet utilises the xgboost model to explore genetic interactions with and amongst DDR genes, offering a complementary approach to CRISPR screen analyses. The xgboost model identifies interactions with a target gene, such as ATM, by predicting its z-scores based on those of other genes across all screens within the DDRcs. Through a training process, the xgboost model autonomously constructs an ensemble of regression trees with a select few important genes, which are considered to interact with the target gene (e.g. ATM). DDRnet applies this procedure to all genes in the human genome to infer genetic interactions with DDR genes.

The DDRnet web app offers two modes of network visualization: (1) gene query and (2) cluster. In gene query mode, users select a list of genes of interest and query all the genes interacting with these input genes. Users have the flexibility to adjust the network confidence by setting frequency and importance threshold. Higher frequency and importance yield more stringent analyses but result in fewer interacting genes. Additionally, users can choose from various display options to customize the network visualisation. In cluster mode, users can explore subsets of Pendragon genes, which have been pre-clustered offline (frequency ≥ 3 and importance ≥ 0.08). Adjusting the frequency and importance threshold results in different display of gene interactions within the clusters.

Since we filtered out some genes to maintain high consistency of the data across multiple CRISPR screens, DDRnet does not encompass a complete genetic network of all gene pairs. If you cannot locate your genes of interest in the networks or if they only interact with few others, it is likely that these genes were not included in our analysis. The list of genes utilised in the DDRnet can be found in the “Genes” tab.