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SCREENING

# High-throughput screen identifies a roadmap for combination drug trials

Effective cancer therapy often relies on the use of drug combinations to increase response rates and decrease the likelihood of resistant cancer cells appearing. Researchers at the NIH NCATS Center performed high-throughput screening of thousands of drug–drug pairs to identify molecules that would cooperate with ibrutinib (an inhibitor of the Bruton's tyrosine kinase) to kill activated B-cell-like diffuse large B-cell lymphoma (ABC DLBCL) cells.

According to the researchers, such approaches "are critical as the number of potential drug combinations is overwhelming". They add that "combination screening has the ability to prioritize drug–drug pairs with appropriate properties for more in-depth vetting prior to a clinical trial." The method involved plating the individual agents in matrix blocks and exploring a wide range of concentrations for each drug. The investigators explain that "when two agents have a positive combination outcome (synergy or additivity) at concentrations achievable *in vivo*, the pair is flagged for follow-up evaluation". Surprisingly, an enhancement of ibrutinib activity was observed when the drug was combined with components of the R-CHOP regimen, the standard of care for DLBCL, suggesting that an ibrutinib/R-CHOP combination should be investigated.

Of note, both the method and the results generated in this study are publicly available and, as the investigators highlight, "these results should impact both translational and basic research by providing researchers with a roadmap of drugs that are synergistic, additive or antagonistic with ibrutinib".

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