A Highly Efficient Pharmaceutical Drug Screening System using Numerous Bacterial Biosensors

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We assessed the applicability of multi-strain bacterial bioreporter bioassays to drug screening. To this end, we investigated the reactions of a panel of 15 luminescent recombinant Escherichia coli bacterial bioreporters to a library of 420 pharmaceuticals. The panel included bacterial bioreporters associated with oxidative stress, DNA damage, heat shock, and efflux of excess metals. Eighty nine drugs elicited a response from at least one of the panel members and formed distinctive clusters, some of which contained closely related drugs. In addition, we tested a group of selected drugs against a collection of fluorescent transcriptional reporters that covers the great majority of gene promoters in E. coli. The sets of induced genes were in accord with the in vitro toxicity of the tested drugs, as reflected by the response patterns of the 15-member panel, and provided more insights into their toxicity mechanisms. Facilitated by microplates and robotic systems, all assays were conducted in high-throughput. Our results thus suggest that multi-strain assemblages of bacterial bioreporters have the potential for playing a significant role in drug development alongside current in vitro toxicity tests.