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Drug repurposing: Discovery and development of new anticancer drugs from old drugs

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The discoveries of new pharmacological activity of known drugs, sometimes referred to as the "off target" effects, have appeared in the literature from time to time. Recent years have witnessed an increase in frequency of the appearance of such discoveries. Finding new indications for existing drugs offers a number of advantages. First, since the drug is already in use in humans, it is bioavailable and has tolerable side effects. Second, the well-established toxicity and bioavailability of the drug in humans will significantly reduce the time and cost to test the drug for the new indications in the clinic. Last but not least, the extensive knowledge on the mechanism of action of a known drug and the availability of a large number of analogs during the development of the drug facilitates the understanding of the molecular basis of the new pharmacological activity and enable rapid structure/activity relationship study to develop new generations of the drug in the context of the new indication. We began a new initiative to systematically collect and assemble a library of clinical drugs in 2003. To date, we have to date collected over 2,700 existing drugs and assembled them into the Johns Hopkins Drug Library. We have screened this library in a number of cell-based assays for new antimalarial, anti-angiogenic and immiunosuppressive agents. Novel and unexpected hits have been identified in each of the screens performed. Mechanistic deconvolution of those hits has shed light on the regulation of different biological processes with which they interfere. Moreover, some of the hits have entered Phase 2 and 3 human clinical trials, underscoring the prowess of this approach to rapidly translating discoveries at the bench to the bedside.