

Digital communication technology helps clear path to personalized therapies

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Researchers at the Burnham Institute for Medical Research (Burnham) have shown that search algorithms used in digital communications can help scientists identify effective multi-drug combinations. The study, led by Giovanni Paternostro, M.D., Ph.D., was published in the December 26, 2008, issue of *PLoS Computational Biology*.

Using the stack sequential algorithm, which was developed for digital communications, the team of scientists searched for optimal drug combinations. This algorithm can integrate information from different sources, including biological measurements and model simulations. This differs from the classic systems biology approach by having search algorithms rather than explicit quantitative models as the central element. The variability of biological systems is the fundamental motivation for this strategy.

"Combination therapies have demonstrated efficacy in treating complex diseases such as cancer and hypertension, but it is difficult to identify safe and effective combination treatment regimens using only trial and error," said Dr. Paternostro. "As personalized medicine moves from the present emphasis on diagnosis and prognosis to therapy, the problem of searching for optimal drug combinations uniquely suited to the genetic and molecular profile of each patient will need to be solved. This research is a first step in that direction."

Current methodology for identifying effective combination therapies involves exhaustive testing. However, the exponential expansion of

possibilities precludes exploring large combinations using this approach. For example, many chemotherapy regimens include six drugs from a pool of 100. A study that included all combinations (including partial combinations containing only some of these compounds) at three different doses would have to digest 8.9×10^{11} possibilities. The problem requires a new approach rather than more efficient screening technology.

In the study, a small subset of the possible drug combinations identified using the algorithms were tested in two biological model systems. One system studied improvement in the physiological decline associated with aging in *Drosophila melanogaster* (fruit flies) and the other system tested for selective killing of cancer cells. In both cases, effective drug combinations were identified by combining the algorithm with biological tests.

"Our work was greatly helped by collaborators with expertise in medicine, engineering and physics from Burnham, University of California, San Diego and Michigan State University," said Dr Paternostro. "We especially benefited from suggestions from Dr. Andrew Viterbi, inventor of the Viterbi algorithm so widely used in digital communications, who pointed to parallels between this biological problem and signal decoding." Dr. Andrew Viterbi cofounded Linkabit Corporation and Qualcomm Inc., with Dr. Irwin Jacobs. He is currently the president of the venture capital firm, The Viterbi Group.

Source: Burnham Institute

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