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(54) Title: METHODS FOR IDENTIFYING PATHWAYS OF DRUG ACTION

(57) Abstract

The present invention provides methods for identifying and representing the biological pathways of drug action on a cell by: (i) measuring responses of cellular constituents to graded exposures of the cell to a drug of interest; (ii) measuring the responses of cellular constituents to perturbations in one or more biological pathways of the cell; and (iii) scaling a combination of the measured pathway responses to fit the measured drug responses best according to an objective measure. In alternative embodiments, the present invention also provides for assessing the significance of the identified representation and for verifying that the identified pathways are actual pathways of drug action. In various embodiments, the effects on the cell can be determined by measuring gene expression, protein abundances, protein activities, or a combination of such measurements. In various embodiments, perturbation to a biological pathway in the cell can be made by use of titratable expression systems, use of transfection systems, modification to abundances of pathway RNAs, modifications to abundances of pathway proteins, or modifications to activities of the pathway proteins. The present invention also provides methods for drug development based on the methods for identifying biological pathways of drug action, and methods for representing the biological pathways involved in the effect of an environmental change upon a cell.