Model offers new understanding of cell signaling

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Looking for answers in the bright light of day, rather than the confined beam of a street light at night. That's how University of Michigan researcher Sofia Merajver, M.D., Ph.D., describes the power of a new mathematical model that could have far-reaching impact on how scientists study cellular signaling pathways.

"This has the potential to be a true paradigm shift," says Merajver, a professor in the U-M Department of Internal Medicine and co-director of the Breast Oncology Program at the U-M Comprehensive Cancer Center. She is the senior author of a study about the new model published online March 21 in *PLoS Computational Biology*.

Around the world, researchers scrutinize the pathways inside cells where signals travel and activate or suppress thousands of cell functions. The researchers want to learn which cellular processes are key in causing disease conditions and how to target them with new drugs. Understanding the full complexity of signaling pathways and their interactions is critical in discovering effective treatments for cancer, inflammation and other conditions that affect millions of people.

The full description of the new model in the article immediately offers scientists the opportunity to improve current mathematical models with a superior tool that can take advantage of advances in computing power, says Merajver.

"I would hope that it may help guide us much better than our own

intuition to decide what our targets are," she says. "If we can understand these pathways better, we should be able to pick more effective targets. This is the step before screening a drug. Until now, there have been very few tools to help us choose a target."

Merajver's collaborators in the study are first author Alejandra C. Ventura, Ph.D., a post-doctoral fellow in the U-M Department of Internal Medicine, Division of Hematology and Oncology and Comprehensive Cancer Center; and Jacques-A. Sepulchre, a mathematical physicist at the Institut Non Lineaire de Nice at the Universite de Nice Sophia-Antipolis in Valbonne, France.

The authors developed the model and tested it using experimental data from a well-known signaling pathway involved in many disease states, the MAPK pathway. They found that this kind of signaling pathway naturally transmits information not just in a forward direction, but also backwards. That implies new considerations if drugs are to adequately address key targets.

In addition, the study will enable scientists to construct models that take into account interactions between two pathways, or "cross-talk," Merajver says.

A specialist in inflammatory breast cancer, Merajver previously has discovered oncogenes that foster metastasis. Her lab has numerous plans to put the model to work immediately.

"We hope it will broaden our understanding on how to inhibit metastasis, since our lab studies this aspect of cancer; this work has many applications for normal and disease conditions," she says.

Source: University of Michigan Health System