

CASE STUDY

# Pathway Studio

Exploring Autophagy in Cancer with Pathway Studio



Dr. Philip Lorenzi, who holds a doctorate in pharmaceutical sciences, knows that research that's already been done can be mined and extended for continued drug discovery work.



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**DR. PHILIP LORENZI**

Beginning as a post-doctoral researcher at the NIH in 2006, Dr. Lorenzi began using Elsevier’s Pathway Studio for analysis of microarray and siRNA screening data. His experience with molecular profiling and technology development has led him to his current role at MD Anderson Cancer Center, where he serves as co-director of the Proteomics and Metabolomics Core Facility and heads a laboratory in the Department of Bioinformatics and Computational Biology. In those roles, he began focusing his use of Pathway Studio to blaze a trail in the field of autophagy research, especially as it relates to cancer.

MD Anderson previously used mass spectrometry to analyze samples for ‘omic’ profiling, which can be very expensive. In addition to the expense, Dr. Lorenzi and his colleagues were not satisfied with the results or the quality of the data received from that method. From previous work using Pathway Studio he knew the depth of analysis it provided was a great fit for his current research focused on understanding a complex biological system like autophagy. Based upon his recommendations, MD Anderson secured funding to investigate different methods of data analysis. “Because biologists are increasingly expected to conduct pathway analysis of their experimental results, users of our facility stand to benefit greatly from some guidance about how to do that.”

Cancer cells, Dr. Lorenzi points out, are sophisticated in ensuring their own survival. When cell damage exceeds a critical mass, the cell starts to use autophagy pathways – processes designed to recycle damaged cellular components – to its advantage, often leading to more aggressive cancer.

Dr. Lorenzi recently published results of his extensive work to create a complete catalogue of the cellular components of the autophagy process. His workflow included using several of the commercially available products for data analysis: Pathway Studio, Thomson Reuters’ MetaCore, and Qiagen’s Ingenuity Pathway Analysis (IPA). He also reviewed siRNA data from a range of experiments previously conducted.

Analyzing pathways involves huge numbers of individual transactions, and all software packages have various limitations. When compared head-to-head, there was only moderate overlap in the data collected from the three software packages, and very little overlap between the experimental results. Pathway Studio, though, was vastly superior to IPA, identifying nearly twice as many proteins and triple the number of small molecules; it also identified almost ten times more proteins than MetaCore.

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Understanding these complex pathways and the specifics of the regulation are very important to his research, says Dr. Lorenzi. Text mining sets Pathway Studio apart from other options, both commercial and open source. Large numbers of full-text articles from Elsevier’s journals, and those of other publishers, are mined to provide the information in Pathway Studio. “Text mining really improves quality of analysis,” says Dr. Lorenzi, “It more comprehensively interrogates the pathway. It helps reduce false negative results dramatically, at slight cost of higher false positives.”

For example, in his Autophagy research, admittedly a very complex topic, Dr. Lorenzi found that 19 percent of the relations were incorrect – the direction of regulation needed to be changed either from positive to negative or vice-versa. Fortunately, the ability for an end user to review all the relationships, and to include or exclude specific information based on their own knowledge — a feature that is unique to Pathway Studio— allows for that change. This capability improves the quality of the analysis that goes into the decision to characterize the pathway.

“Power is in the user’s hand to interpret results with text mining,” says Dr. Lorenzi. “With manual curation done by others, the researcher often assumes the results are 100 percent accurate, that there are no false positives, and that false negatives are limited. But in reality, the false positives are not zero. Even manually curated databases have errors in them.”

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“False negative interpretation is where it really stands out,” adds Dr. Lorenzi. “I suspect that when using other major curation software manual curators go through these types of sentences and might discard an unknown result because it can’t be rescued due to lack of access to additional data.”

In his experience, Pathway Studio is most useful to post-doctoral fellows, experimental bench scientists, and other researchers who are working with a particular drug, especially when trying to understand all the genes mediating sensitivity to that drug.

“It’s a great starting point for generating hypotheses so that researchers can get back to the bench and test them.”

Are you interested in learning how  
Pathway Studio can support your  
drug discovery efforts?

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ASIA AND AUSTRALIA

Tel: + 65 6349 0222

Email: [sginfo@elsevier.com](mailto:sginfo@elsevier.com)

JAPAN

Tel: + 81 3 5561 5034

Email: [jpinfo@elsevier.com](mailto:jpinfo@elsevier.com)

KOREA AND TAIWAN

Tel: +82 2 6714 3000

Email: [krinfo.corp@elsevier.com](mailto:krinfo.corp@elsevier.com)

EUROPE, MIDDLE EAST AND AFRICA

Tel: +31 20 485 3767

Email: [nlinfo@elsevier.com](mailto:nlinfo@elsevier.com)

NORTH AMERICA, CENTRAL AMERICA AND CANADA

Tel: +1 888 615 4500

Email: [usinfo@elsevier.com](mailto:usinfo@elsevier.com)

SOUTH AMERICA

Tel: +55 21 3970 9300

Email: [brinfo@elsevier.com](mailto:brinfo@elsevier.com)