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NJIT professor finds engineering technique to identify disease-causing genes

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Scientists believe that complex diseases such as schizophrenia, major depression and cancer are not caused by one, but a multitude of dysfunctional genes. A novel computational biology method developed by a research team led by Ali Abdi, PhD, associate professor in NJIT's department of electrical and computer engineering, has found a way to uncover the critical genes responsible for disease development.

The research appeared in "Fault Diagnosis Engineering of Digital Circuits Can Identify Vulnerable Molecules in Complex Cellular Pathways," the current cover article of *Science Signaling*, a new publication of the American Association for the Advancement of Science, publisher of *Science*.

"We see our research developing a novel technology holding high promises for finding key molecules that contribute to human diseases and for identifying critical targets in drug development," said Abdi. "The key to success was our collaboration among researchers with different backgrounds in engineering and medical sciences."

The scientists analyzed large cellular molecular networks whose dysfunction contributed to the development of certain complex human disorders. Molecules--genes or proteins—communicate through interconnected pathways via different biochemical interactions, explained Abdi. Through these interactions, molecules propagate regulatory signals. The function of cells in the body is vulnerable to the dysfunction of some molecules within a cell. "In other words," he added,

"different diseases may arise from the dysfunction of one or several molecules within an interconnected network system."

To better understand how dysfunctional molecules pass on their problems and which ones are key players, the scientists developed a novel, biologically-driven vulnerability assessment method. This novel algorithm is capable of calculating the vulnerability levels of all molecules in a network. Using a computer, they analyzed the vulnerability of several signaling networks.

"We found few molecules with the highest vulnerability level," said Ali. "Nevertheless, we observed that if each of these molecules failed to function, the entire molecular network would not work." These critical molecules, he said, also held the key to better and more effective treatments. "By understanding their roles and functions better, we would be able to develop more effective treatments for complex disorders with such unknown molecular basis," Abdi said. "Many mental illnesses fall within this category."

Effat Emamian, MD, founder and CEO of Advanced Technologies for Novel Therapeutics, a start-up company in NJIT's business incubator, and Mehdi Tahoori, assistant professor at Northeastern University, contributed to the research.

"In the field of medical research, we face enormous challenges for finding the causes and curative treatments for complex human disorders" said Emamian, whose research focuses on mental disorders. "We believe that complex human disorders, such as cancer, different mental disorders and some neurodegenerative disorders, are not caused by a single gene but rather many. Our most important task is to figure out which genes are critical for disease development and which molecules are the most promising therapeutic targets."

Tahoori noted that it was exciting to see how circuit engineering research can contribute to finding the possible causes and treatments of complex human diseases. "Modeling a problem in a different domain and using tools, methods, and techniques available in the other modeling domain can lead to breakthrough solutions for the original problem," he said. "This is what cross-disciplinary research is all about."

Source: New Jersey Institute of Technology

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