Scientists publish seminal paper and announce project to develop biomarkers of aging

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Today the Biogerontology Research Foundation announced the international collaboration on signaling pathway perturbation-based transcriptomic biomarkers of aging. On November 16th scientists at the Biogerontology Research Foundation alongside collaborators from Insilico Medicine, Inc, the Johns Hopkins University, Albert Einstein College of Medicine, Boston University, Novartis, Nestle and BioTime Inc. announced the publication of their proof of concept experiment demonstrating the utility of a novel approach for analyzing transcriptomic, metabolomic and signalomic data sets, titled iPANDA, in *Nature Communications*.

"Given the high volume of data being generated in the life sciences, there is a huge need for tools that make sense of that data. As such, this new method will have widespread applications in unraveling the molecular basis of age-related diseases and in revealing biomarkers that can be used in research and in clinical settings. In addition, tools that help reduce the complexity of biology and identify important players in disease processes are vital not only to better understand the underlying mechanisms of age-related disease but also to facilitate a personalized medicine approach. The future of medicine is in targeting diseases in a more specific and personalized fashion to improve clinical outcomes, and tools like iPANDA are essential for this emerging paradigm," said Joao Pedro de Megalhaes, PhD, a trustee of the Biogerontology Research Foundation.

The algorithm, iPANDA, applies deep learning algorithms to complex gene expression data sets and signal pathway activation data for the purposes of analysis and integration, and their proof of concept article demonstrates that the system is capable of significantly reducing noise and dimensionality of transcriptomic data sets and of identifying patient-specific pathway signatures associated with breast cancer patients that characterize their response to Toxicol-based neoadjuvant therapy.

The system represents a substantially new approach to the analysis of microarray data sets, especially as it pertains to data obtained from multiple sources, and appears to be more scalable and robust than other current approaches to the analysis of transcriptomic, metabolomic and signalomic data obtained from different sources. The system also has applications in rapid biomarker development and drug discovery, discrimination between distinct biological and clinical conditions, and the identification of functional pathways relevant to disease diagnosis and treatment, and ultimately in the development of personalized treatments for age-related diseases.

"iPANDA represents a significant contribution to the emerging application of deep learning algorithms to transcriptomic and signalomic data analysis, and is a substantial extension of the approach the team put forward previously through their OncoFinder algorithm. The capacity of iPANDA to reduce the dimensionality of transcriptomic and signalomic data sets makes it a very useful tool in rapid biomarker development and accelerated drug discovery, in formulating personalized treatments to promote improved clinical outcomes, in bringing the results of in silico analyses closer to their experimental counterparts, and in the analysis of transcriptomic and signalomic data originating from multiple sources. While the team predicted and compared the response of breast cancer patients to Taxol-based neoadjuvant therapy as their proof of concept, the application of this approach to patient-specific responses to biomedical gerontological interventions (e.g. to geroprotectors, which is

a clear focus of the team's past efforts), to the development of both generalized and personalized biomarkers of ageing, and to the characterization and analysis of minute differences in ageing over time, between individuals, and between different organisms would represent a promising and exciting future application" said Franco Cortese, Deputy Director of the Biogerontology Research Foundation.

"This latest achievement on the part of Alex Zhavoronkov and his team is yet another step toward greater heights and bolder frontiers in the application of deep learning to personalized medicine, biomarker characterization and accelerated drug discovery. The publication of this proof-of-concept experiment in *Nature Communications* is a testament to the importance of their latest accomplishment, to the substantial progress that the team has made over the past 2 years, and to the great heights and ground-breaking achievements that they are sure to reach in the years to come. It represents yet another successful validation of the usefulness of their entire approach - namely, the application of deep learning to biomedicine, geroscience and P3 (personalized, precision and preventative) medicine." said Dmitry Kaminskiy, Managing Trustee of the Biogerontology Research Foundation.

More information: Ivan V. Ozerov et al, In silico Pathway Activation Network Decomposition Analysis (iPANDA) as a method for biomarker development, *Nature Communications* (2016). DOI: 10.1038/NCOMMS13427

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