INTEGRATIVE MODELING OF NEURODEGENERATIVE DISORDERS

The American University in Cairo
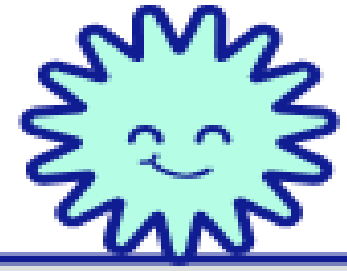
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The National Human Genome Research Institute shared a vision that by 2030 predictive models should incorporate multi-omics and epigenetic data features into phenotype prediction[1]. The convergence of large publicly available clinical, omics, and demographic datasets, along with the advances in artificial intelligence (AI) and machine learning (ML), allows biomedical researchers to maximize the value of the readily available datasets.

What Do We Know?

- Neurodegenerative disorders are caused by the progressive loss of function or structure of neurons[3]. Affecting the body's functions, manifesting in loss of movements, cognition, and autonomous muscular control. The most common is Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis .
- They are the leading cause of disability and the second leading cause of death globally, with approximately 9 million deaths per year, as reported by the WHO[6,7].
- Machine Learning & Modeling is a powerful tool that has emerged from AI and involves using computer algorithms that can improve and learn through pattern recognition.
- ML can find signatures and patterns at a quicker rate than can be performed by one single individual.
- Integrating diverse data modalities like genomics, transcriptomics, and epigenetics into a single model is vital for disease prediction, as each modality contributes unique insights – genomics reveals genetic variations, transcriptomics captures gene expression patterns, and epigenetics unveils modifications influencing gene function, collectively providing a comprehensive view essential for accurate disease predictions.

What Do We Need to Do?

- A fully contextualized framework that can be used to make disease predictions related to population health.
- Develop a diagnostic framework that correlates complex multi-modality data will capitalize on the available resources, including the currently available ML algorithms.
- Leading to implementation in clinical early diagnosis of neurodegenerative disorders for public health practice.

What We Did
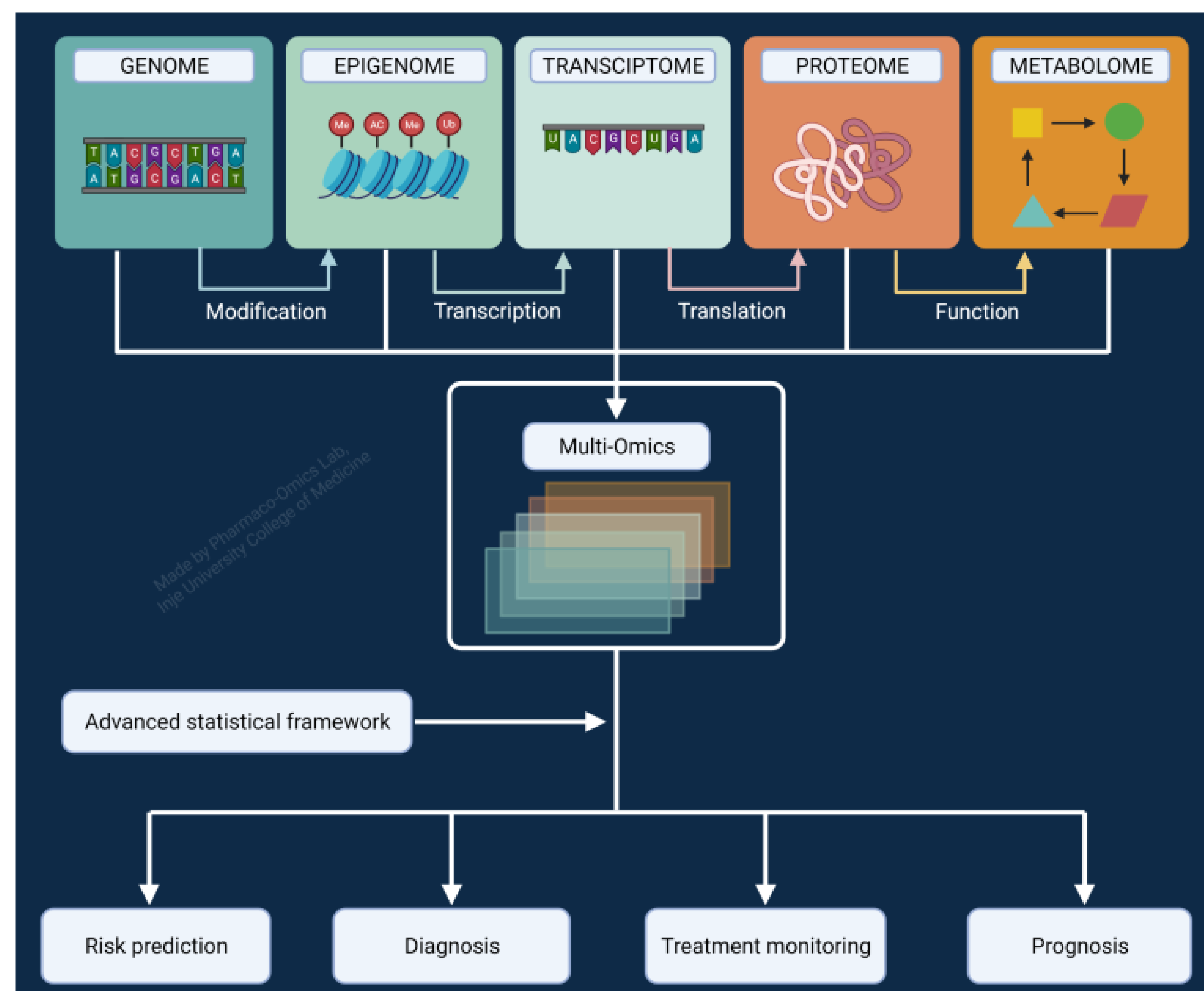
Did we achieve our goal?

- The combination of genetic and transcriptomic data in a two-modality network outperforms the single modality biomarker approach with 89% accuracy of disease prediction of Parkinson, proving that multi-modality approaches show higher accuracy rates and are potentially more informative.
- Further incorporation of additional modalities is our next goal.

How Can we Do It?

1. Combine data from different omics levels (genetics, transcriptomics, metabolomics, etc) of various ND into one large dataset.
2. Utilize different Machine learning algorithms on the combined dataset.
3. This allows for the identification of disease specific markers and universal biomarkers of neurodegenerative disorders.

References: 1.Green, E. D. *et al*. Strategic vision for improving human health at The Forefront of Genomics. *Nature* **586**, 683–692 (2020). 2.Bycroft, C. *et al*. The UK Biobank resource with deep phenotyping and genomic data. *Nature 2018 562:7726* **562**, 203–209 (2018). 3.Gitler, A. D., Dhillon, P. & Shorter, J. Neurodegenerative disease: models, mechanisms, and a new hope. *Dis Model Mech* **10**, 499 (2017). 4.Hansson, O. Biomarkers for neurodegenerative diseases. *Nat Med* **27**, 954–963 (2021).
5.Dorsey, E. R., Sherer, T., Okun, M. S. & Bloemd, B. R. The emerging evidence of the Parkinson pandemic. *J Parkinsons Dis* **8**, S3–S8 (2018). 6.Burden of Neurological Conditions - PAHO/WHO | Pan American Health Organization. https://www.paho.org/en/enlace/burden-neurological-conditions. 7.Health Organization, W. Follow-up to the political declaration of the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases: Annex 7. (2022) doi:10.1016/S1474-4422(18)30499-X. 8.Poewe, W. *et al*. Parkinson disease. *Nat Rev Dis Primers* **3**, 1–21 (2017).