Improving genetic diagnostics for patients with negative exome sequencing using AI- powered genome analysis

Joana Ribeiro[1,2*], Brígida Mónica Faria[1,3], Pedro Pinto[2], Joaquim Sá[4]

1. ESS – Polytechnic of Porto, Porto, Portugal; 2. Quilaban, Sintra, Portugal; 3. LIACC – Artificial Intelligence and Computer Science Lab (member of LASI), Porto, Portugal.4. Unilabs Genetics, Porto, Portugal.

* Corresponding author email: 10220100@ess.ipp.pt

Introduction: Next-generation sequencing (NGS) can be performed using several different platforms. Detecting DNA alterations that affect human health is now possible because of NGS technologies [1]. Despite the advancements in NGS, challenges persist, particularly in cases where traditional exome sequencing yields negative results. Sequencing of the entire genome provides global information about exons and introns, which can reveal the regulatory components of genes, such as promoters, enhancers, and intronic regulators, and structural variants, like copy number variants, inversions, and translocations [2],[3]. As with any technology, DNA sequencing has its limitations. Despite these limitations, DNA sequencing technology has revolutionised our understanding of cellular physiology in health and disease [1]. Although these steps do not directly involve bioinformatics per se, they may have downstream consequences on the bioinformatics algorithms used. **Objectives:** This study focuses on the analysis and performance of genome sequencing in patients with negative exome results. Leveraging AI technology, our study explores both non-coding and coding regions of the genome, aiming to unlock hidden insights. **Methods:** For this project, the data were collected from patients with a negative result for Whole Exome sequencing (WES) and who were resequenced for the Whole Genome Sequencing (WGS) approach. After, the raw data was treated by Emedgene (AI- algorithm-based software) and afterwards the results between techniques were compared and statistically treated using SPSS software. **Results:** The results were based on 16 selected cases with a negative exome diagnosis but with a diagnosis result from other complementary techniques. The first analysis appreciation shows that at least in 80% of the cases, the diagnosis could be assumed with WGS using this specific AI- algorithm. **Conclusions:** The implications of AI genome analysis, showcase the potential to provide more accurate and conclusive genetic diagnoses, improving patient care and treatment decisions. Bridging the gap left by traditional exome sequencing offers a promising avenue for precision medicine and personalized healthcare.

Keywords: Artificial Intelligence; Genetics; Whole-genome sequencing; Bioinformatics.

References:

1. O. Akintunde, T. Tucker, and V. J. Carabetta, "The evolution of next-generation sequencing technologies," ArXiv, p. arXiv:2305.08724v1, May 2023. D. A. Wheeler et al., "The complete genome of an individual by massively parallel DNA sequencing," Nature, vol. 452, no. 7189, pp. 872–876, Apr. 2008, doi: 10.1038/nature06884.
2. J. Chou, T. K. Ohsumi, and R. S. Geha, "Use of whole exome and genome sequencing in the identification of genetic causes of primary immunodeficiencies," Current Opinion in Allergy & Clinical Immunology, vol. 12, no. 6,
3. pp. 623–628, Dec. 2012, doi: 10.1097/ACI.0b013e3283588ca6.
4. N. B. Larson, A. L. Oberg, A. A. Adjei, and L. Wang, "A Clinician's Guide to Bioinformatics for Next- Generation Sequencing," Journal of Thoracic Oncology, vol. 18, no. 2, pp. 143–157, Feb. 2023, doi: 10.1016/j.jtho.2022.11.006.
5. K. F. Oakeson, J. M. Wagner, M. Mendenhall, A. Rohrwasser, and R. Atkinson-Dunn, "Bioinformatic Analyses of Whole-Genome Sequence Data in a Public Health Laboratory," Emerg. Infect. Dis., vol. 23, no. 9, pp. 1441–1445, Sep. 2017, doi: 10.3201/eid2309.170416.
6. A. M. Kanzi et al., "Next Generation Sequencing and Bioinformatics Analysis of Family Genetic Inheritance," Front. Genet., vol. 11, p. 544162, Oct. 2020, doi: 10.3389/fgene.2020.544162.
7. E. L. Van Dijk, H. Auger, Y. Jaszczyszyn, and C. Thermes, "Ten years of next-generation sequencing technology," Trends in Genetics, vol. 30, no. 9, pp. 418–426, Sep. 2014, doi: 10.1016/j.tig.2014.07.001.
8. H.-G. Klein, P. Bauer, and T. Hambuch, "Whole genome sequencing (WGS), whole exome sequencing (WES) and clinical exome sequencing (CES) in patient care," LaboratoriumsMedizin, vol. 38, no. 4, pp. 221–230, Jul. 2014, doi: 10.1515/labmed-2014-0025.