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Identifikasi Varian Genetik Menggunakan Metode Long-Read Sequencing Pada Subjek Suspected Alfa-Thalassemia
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IDENTIFIKASI VARIAN GENETIK MENGGUNAKAN METODE *LONG-READ SEQUENCING* PADA SUBJEK *SUSPECTED* α-THALASSEMIA

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INTISARI

α-thalassemia merupakan salah satu penyakit genetik akibat mutasi pada gen *α-globin* yang berperan penting dalam pembentukkan hemoglobin. Tingkat keparahan α-thalassemia bergantung pada jenis dan kombinasi varian mutasi yang dimiliki oleh individu. Penelitian ini dilakukan dengan tujuan menganalisis hasil *Long-Read Sequencing* (PromethION, Oxford Nanopore Technologies) dari genom subjek *suspected* α-thalassemia menggunakan pendekatan bioinformatika. Selain itu, penelitian ini juga bertujuan untuk mengidentifikasi status varian genetik pada subjek. Berdasarkan hasil analisis pada subjek, teridentifikasi 15 varian pada gen-gen terkait globin yang berkaitan dengan thalassemia, meliputi 14 *single nucleotide polymorphism* (SNP) dan satu *structural variant* (SV). Salah satu SNP yang teridentifikasi adalah varian *HBA1*:c.326C>A (p.Thr109Asn) atau Hb Rogliano, yang diklasifikasikan sebagai *likely pathogenic*. Hb Rogliano dilaporkan berkontribusi terhadap α-thalassemia dengan frekuensi alel global kurang dari 1%. Selain itu, teridentifikasi beberapa varian heterozigot pada subjek berstatus *benign* atau *likely benign* yang hanya muncul pada fragmen yang sama dengan Hb Rogliano, yaitu *HBA1*:c.-41C>G, *HBA2*:c.-41C>G, *HBA2*: c.300+55T>G, dan *HBA2*:c.301-24delinsCTCGGCCC.

KATA KUNCI: α-thalassemia, WGS, *amplicon sequencing*, ONT, Hb Rogliano

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IDENTIFICATION OF GENETIC VARIANTS USING THE LONG-READ SEQUENCING METHOD IN A SUBJECT SUSPECTED OF HAVING α-THALASSEMIA

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ABSTRACT

α-thalassemia is a genetic disorder caused by mutations in the α-globin genes, which play a crucial role in hemoglobin synthesis. The clinical severity of α-thalassemia depends on the type and combination of genetic variants present in an individual. This study was conducted to analyze the whole genome of a subject suspected of having α-thalassemia using Long-Read Sequencing (PromethION, Oxford Nanopore Technologies) and bioinformatics approaches. In addition, this study was conducted to identify the subject's genetic variant status. Based on the analysis of the subject, 15 variants were identified in globin-related genes associated with thalassemia, including 14 single nucleotide polymorphisms (SNPs) and one structural variant (SV). One of the identified SNPs was variant *HBA1*:c.326C>A (p.Thr109Asn), also known as Hb Rogliano, which is classified as likely pathogenic. Hb Rogliano has been reported to contribute to α-thalassemia and has a global allele frequency of less than 1%. Furthermore, several heterozygous variants classified as benign or likely benign were also identified in the subject, which only appeared in the same fragment as Hb Rogliano, namely *HBA1*:c.-41C>G, *HBA2*:c.-41C>G, *HBA2*: c.300+55T>G, and *HBA2*:c.301-24delinsCTCGGCCC.

KEYWORDS: α-thalassemia, WGS, amplicon sequencing, ONT, Hb Rogliano