EKSPLORASI MUTASI GEN FAKTOR VIII (*F8*) PADA KELUARGA DENGAN HEMOFILIA A DI YOGYAKARTA

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INTISARI

Hemofilia A adalah kelainan perdarahan kongenital yang diturunkan secara terangkai kromosom X resesif. Tingkat keparahan hemofilia A diklasifikasikan berdasarkan persentase faktor koagulasi VIII, yakni hemofilia ringan (>5-40%), hemofilia sedang (1-5%), dan hemofilia berat (<1%). Hemofilia A disebabkan karena defisiensi faktor koagulasi delapan akibat mutasi gen *F8*. Kajian terkait mutasi hemofilia A di Indonesia belum pernah dilaporkan, sehingga penting untuk dieksplorasi. Tujuan penelitian ini untuk mengetahui ada tidaknya mutasi dan jenis mutasi apa saja yang ditemukan pada gen *F8* ekson 19-22. Sumber DNA berupa sampel saliva dari 11 individu anggota Himpunan Masyarakat Hemofilia Indonesia Daerah Istimewa Yogyakarta. *FavorPrepTM 96-well Genomic DNA Kit* (Taiwan) digunakan untuk ekstraksi DNA dan Nanodrop Spektrofotometer digunakan untuk uji kuantitatif DNA serta metode *Polymerase chain reaction* (PCR) digunakan untuk amplifikasi gen *F8*. DNA hasil amplifikasi dilakukan sekuensing dan dianalisis menggunakan fasilitas analisis pensejajaran nukleotida yang tersedia di *website* Benchling. Hasil penelitian menunjukkan tidak terjadi mutasi ekson 19, 20, 21, dan 22 serta tidak terjadi mutasi pada penelitian paralel ekson 23, 24, 25, dan 26. Analisis lanjut dilakukan *long-read sequencing* menggunakan metode *next generation sequencing* (NGS) ditemukan mutasi *splice donor* c.1271+1G>A di intron 8 dan pada penelitian paralel ditemukan mutasi *missense* c.2095A>G di ekson 13. Mutasi *splice donor* c.1271+1G>A intron 8 menyebabkan terjadinya *splice donor cryptic*, sehingga mengakibatkan terbentuknya protein yang *out of frame*.

Kata kunci: hemofilia A, gen *F8*, ekson 19-22, mutasi *splice donor*, intron 8

EXPLORATION OF FACTOR VIII (*F8*) GENE MUTATIONS IN FAMILIES WITH HEMOPHILIA A IN YOGYAKARTA

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ABSTRACT

Hemophilia A is a congenital bleeding disorder caused by an inherited X-linked recessive. Hemophilia A is classified in mild hemophilia (>5-40%), moderate (1-5%), and severe (<1%). Hemophilia A is caused due to a mutation in the F8 gene. Information related to hemophilia A mutations in Indonesia have never been reported so it is important to explore this. The aim of this research is to determine whether there are mutations and what types of mutations are found in the F8 gene exon 19-22. The DNA source was saliva samples from 11 individual members of the Indonesian Hemophilia Society Association for the Special Region of Yogyakarta. FavorPrepTM 96-well Genomic DNA Kit (Taiwan) was used for DNA extraction and the Polymerase chain reaction (PCR) method was used for amplification. The amplified DNA was sequenced and analyzed using the nucleotide alignment analysis facility available on the Benchling. The results of the study showed that there were no mutations in exons 19, 20, 21 and 22 and there were no mutations in parallel studies of exons 23, 24, 25 and 26. Further analysis carried out long-read sequencing using the next generation sequencing (NGS) method and a splice donor mutation was found c.1271+1G>A in intron 8 and in parallel research a missense mutation c.2095A>G was found in exon 13. The splice donor mutation c.1271+1G>A intron 8 causes the appearance of a cryptic splice donor, that can results in the formation of proteins that are out of frame

Keywords: hemophilia A, *F8* gene, exon 19-22, splice donor mutation, intron 8