Pemetaan Profil Gen Resistansi Candida krusei terhadap Flukonazol dari Pasien: Pendekatan Whole Genome Sequencing = Mapping Fluconazole Resistance Gen Profile of Candida krusei from Patients: a Whole Genome Sequencing Approach

Julianty, author

Abstrak

Kandidiasis invasif yang disebabkan oleh Candida krusei merupakan salah satu penyebab kematian dengan angka kematian yang tinggi. Terjadinya resistansi terhadap flukonazol dilaporkan terkait dengan gen penanda resistansi intrinsik. Data epidemiologi molekular dengan Whole Genome Sequencing (WGS) yang mengidentifikasi gen dan varian yang terkait virulensi dan resistansi obat Candida krusei belum pernah dilaporkan di Jakarta, maupun di Indonesia. Berdasarkan permasalahan di atas, dilakukan penelitian lebih lanjut untuk menentukan profil gen resistansi dengan metode Whole Genome Sequencing. Hasil pemetaan MLST diperoleh ada 6 housekeeping gen yaitu ADE2, HIS3, LEU2, LYS2D, NMT1 dan TRP1. Berdasarkan hasil variant calling ditemukan beberapa gen yang berperan dalam resistansi yaitu ERG11 dan FKS1. Mutasi yang ditemukan meliputi missense, synonymous, stop gain dan indel. Sebagian besar adalah varian mutasi missense dan synonymous. Pola kepekaan Candida krusei dengan metode difusi cakram sebagian besar terdiri dari isolat yang resisten dan sensitif terhadap beberapa antijamur seperti flukonazol, itrakonazol, ketonazol, amfoterisin B, nistatin, vorikonazol dan mikonazol.
.....Invasive candidiasis caused by Candida krusei is one of the causes of death with a high mortality rate. The occurrence of resistance to fluconazole is reported to be related to intrinsic resistance marker genes. Molecular epidemiological data related to Whole Genome Sequencing (WGS) that identify genes and variants associated with Candida krusei virulence and drug resistance have never been reported in Jakarta, nor in Indonesia. Based on the problems above, further research was carried out to determine the resistance gene profile using the Whole Genome Sequencing method. The results of the MLST mapping showed that there were 6 housekeeping genes namely ADE2, HIS3, LEU2, LYS2D, NMT1, and TRP1. Based on the results of variant calling, several genes that play a role in resistance were found, namely ERG11 and FKS1. The mutations found include missense, synonymous, stop gain, and indel. Most are missense and synonymous mutation variants. The sensitivity pattern of Candida krusei by disc diffusion method mostly consisted of isolates that were resistant and sensitive to several antifungals such as fluconazole, itraconazole, ketoconazole, amphotericin B, nystatin, voriconazole, and miconazole.