Karakterisasi antibodi bispecific menargetkan reseptor epha2 dan x pada kanker prostat dan kanker otak = Characterisation of bispecific antibodies targeting epha2 and x receptors on prostate and brain cancers / Ni Made Rahayu Maitri

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Abstrak

[Kanker prostat dan kanker otak adalah salah satu penyebab utama kematian pada penderita kanker. Hasil penelitian menunjukkan bahwa aktivasi dan penurunan jumlah reseptor EphA2 dan X pada sel-sel kanker otak dan kanker prostat dapat mengurangi proliferasi sel dan pembentukan tumor. Reseptor EphA2 diekspresikan pada sel kanker prostat, PC-3, dan reseptor X diexpresikan pada sel kanker prostat, LNCaP. Reseptor EphA2 juga diekspresikan pada sel-sel kanker otak, U-251. Proyek ini ditujukan untuk melihat kemampuan ikatan antara sel kanker dan antibodi bispecific (BsAb), 4B3-X, yang disusun dengan cara menggabungkan fragmen antibodi 4B3-scFv (khusus mengikat pada reseptor EphA2) dengan fragmen antibodi X-scFv (khusus mengikat pada reseptor X). Pada susunan BsAb ini, satu sisi antibodi akan mengikat EphA2 dan sisi lainnya akan mengikat reseptor X. Studi ikatan ini dilakukan menggunakan flow cytometry dan hasil studi menunjukkan bahwa 4B3-X berhasil mengikat pada reseptor EphA2 dan X yang diekspresikan pada sel kanker. 4B3-X berhasil terikat pada sel kanker prostat PC-3 yang megekspresikan reseptor EphA2 dan sel kanker prostat LNCaP yang mengekspresikan reseptor X, juga pada sel kanker otak U-251 yang mengekspresikan reseptor EphA2. Yang menarik, fragmen antibodi X-scFv (yang khusus mengikat pada reseptor X) juga terbukti terikat pada sel kanker otak, U-251; ini menunjukkan bahwa sel-sel ini mengekspresikan reseptor X dan EphA2 secara bersamaan. Dengan ini dapat disimpulkan bahwa 4B3-X berhasil mengikat pada kedua reseptor EphA2 dan X. Hal ini dapat menjadi sarana yang berpotensial untuk mengaktivasi reseptor ganda dan mengurangi jumlah reseptor EphA2 dan X pada sel kanker dan membunuh sel kanker tersebut.

;Prostate and brain cancers are among the leading causes of cancer-related deaths. Studies have revealed that the activation and subsequent reduction of the EphA2 and X receptors on advanced brain and prostate cancer cells reduce cell proliferation and tumourigenesis. EphA2 and X are overexpressed on prostate cancer cells PC-3 and LNCaP, respectively. EphA2 is also overexpressed in U-251brain cancer cells. This project assesses the binding of a bispecific antibody (BsAb), 4B3-X, which were created by separately combining the 4B3 scFv antibody fragments (targeting EphA2) with the X scFv fragment, targeting X. In the BsAb format, one arm binds EphA2 and the other binds X receptors. Binding studies using flow cytometry showed that 4B3-X BsAb binding to EphA2 and X receptors was maintained; 4B3-X BsAb successfully bound to EphA2 -expressing PC-3 cells and X-expressing LNCaP cells as well as U-251. Interestingly, the X scFv (specific for X) was shown to bind to U-251 cells, indicating that these cells express X, as well as overexpressing EphA2. In summary, the 4B3-X BsAb, that binds both EphA2 and X, may provide potential means of dual receptor activation and subsequent reduction of the EphA2 and X receptors in cancer cells.

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