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Azhar Rasul

Introduction

Chemotherapy is the current drug of choice to treat cancer. It kills cancer cells while trying to do as little damage as possible to healthy cells. Now there might be a better way to fight cancer. “The placenta and cancer have many things in common,” said Daugaard, an assistant professor of urologic science at UBC, a senior research scientist at the Vancouver Prostate Centre and the paper's principal investigator. “The placenta needs to grow from basically nothing to be a huge organ in a very short time.... It has rapid cell proliferation — that’s something we find in cancer. Then there is another thing also and that’s invasion. The placenta invades into the uterus tissue. Invasion is also something we see in cancer." The researchers can use the malaria protein diagnostically to attach and to identify cancer cells, but they took it one step further.

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Targeting Human Cancer by a Glycosaminoglycan Binding Malaria Protein

Salanti A[1], Clausen TM[2], Agerbæk M[3], Al Nakouzi N[4], Dahlbäck M[5], Oo HZ[4], Lee S[6], Gustavsson T[5], Rich JR[7], Hedberg BJ[7], Mao Y[8], Barington L[5], Pereira MA[5], LoBello J[9], Endo M[10], Fazli L[6], Soden J[11], Wang CK[6], Sander AF[5], Dagil R[5], Thrane S[5], Holst PJ[5], Meng L[8], Favero F[12], Weiss GJ[13], Nielsen MA[5], Freeth J[11], Nielsen TO[14], Zaia J[8], Tran NL[9], Trent J[9], Babcook JS[7], Theander TG[5], Sorensen PH[15], Daugaard M[16].

Summary

Plasmodium falciparum engineer infected erythrocytes to present the malarial protein, VAR2CSA, which binds a distinct type chondroitin sulfate (CS) exclusively expressed in the placenta. Here, we show that the same CS modification is present on a high proportion of malignant cells and that it can be specifically targeted by recombinant VAR2CSA (rVAR2). In tumors, placental-like CS chains are linked to a limited repertoire of cancer-associated proteoglycans including CD44 and CSPG4. The rVAR2 protein localizes to tumors in vivo and rVAR2 fused to diphtheria toxin or conjugated to hemiasterlin compounds strongly inhibits in vivo tumor cell growth and metastasis. Our data demonstrate how an evolutionarily refined parasite-derived protein can be exploited to target a common, but complex, malignancy-associated glycosaminoglycan modification.