血清タンパクを利用した薬物担体の担癌マウスにおける体内動態

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The Disposition of Serum Proteins as Drug-Carriers in Mice Bearing Sarcoma 180

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Abstract The tumor distribution and the disposition of serum proteins, such as albumin, fetuin, transferrin, and IgG, were investigated in mice bearing Sarcoma 180. Serum proteins labeled with fluoresceinisothiocyanate (FITC) were administered to the mice. The FITC-labeled proteins acylated with glutaric anhydride were also administered to the mice in order to investigate the effect of chemical modification. The plasma concentration of each glutarylated serum protein was significantly lower, about 15 to 46-fold, in comparison to that of the non-acylated protein at 24 h after administration. The tissue distributions of the glutarylated serum proteins were also decreased compared to those of the non-acylated proteins. Especially, the hepatic distribution of albumin and IgG was significantly reduced with glutarylation. The urinary excretion of albumin and transferrin, and fecal excretion of IgG, were significantly increased with glutarylation. The serum proteins were accumulated effectively in the tumor tissue in mice bearing Sarcoma 180. It was found that the tumor distributions were not impaired by the glutarylation, except involving fetuin. It was suggested, therefore, that the glutarylated serum proteins were valuable for relative tumor-selectivity and might be utilized in a macromolecular carrier system for antitumor drugs.

アルブミン、フェツイン、トランスフェリンおよびIgGに、無水グルタル酸を用いて化学修飾(グリタル化)を行った。これらのグリタル化した血清タンパクでは、元の

タンパクに比べて循環血中からの消失速度が顕著に増大し、正常臓器への分布量は有意に減少した。血清タンパクの低分子代謝物の排泄量はグルタル化により増加した。このことから、グリタル化により血清タンパクの低分子化が亢進し、血中からの消失が促進すると考えられた。これに対して、腫瘍組織への分布はグルタル化の影響を受けなかった。これらの知見から、血清タンパクはグルタル化により腫瘍への指向性を相対的に向上させることが可能であり、グルタル化した血清タンパクは腫瘍集積性の薬物担体として有用であることが示唆された。