IMMUNOPATHOLOGICAL STUDIES ON THE SPECIFICITY AND STRENGTHENING OF THE TYPE SPECIFIC ANTIGENICITY OF ASCITES TUMORS OF RAT

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As reported several times before, ascites tumor cells of rat contain two kinds of antigens, one is species specific to normal tissues of rat and is common to all tumors of rat. The other is specific only to those tumors which have the same characteristics, perhaps common to the tumors which are originated from the same tissue cell, even if the tumor was generated in other animals. This is Tumor Type Specific Antigenicity. However, this antigenicity did not correspond to the organ specificity of normal cells.

To ascertain the tumor type specific antigenicity, the following 3 postulates should be satisfied. 1) It should not exist in normal cells, 2) it should exist only in tumor cells and 3) it should be differently antigenic according to the type of tumors. These postulates were confirmed by means of re- and cross-transplantation in immunized animals, by neutralization test, immunotherapy with immune sera and by follow up test with I¹³¹ labeled immune sera.

According to the tumor type specific antigenicity the 12 strains of rat tumors could be classified in 3 types as follows: 1) Yoshida sarcoma type (Yoshida sarcoma, MTK 1, 2, 3., Hirosaki sarcoma), 2) Takeda sarcoma, Usubuchi sarcoma and 3) ascites hepatoma type (AAT 1, 2., DAB 1, 2., HT 1).

The species specific and tumor Type specific antigens show different physico-chemical features. The species specific antigen is stable to damage of tumor cells, freezing and melting, lyophilizing and heating (60°C), but is labile to fixation and trichloroacetic acid (TCA). On the contrary the tumor type specific antigen is labile to cell damage, freezing and melting, and to heating, even to the mild treatment avoiding the denaturation of cell protein, the type specificity degenerates soon after the death of cells. However, it is stable to the treatment with formalin or trichloroacetic acid (2-10%) for 10 days.

This is apparently demonstrated when the tumor cells were treated with TCA,
and the mice, immunized with such antigen of 0.2 g x 5 times dilution, were inoculated with tumor cells of the corresponding type. In these cases no takes were shown, while the inoculation of other types of tumor took as in normal mice.

For the purpose of strengthening the antigenicity, Freund's adjuvant was combined with TCA-treated tumor cells. In this case the takes of corresponding tumor were strongly inhibited during 30 days, even by immunization with antigen of 0.05-0.1 g x 1 time dilution, while the takes of other types in these animals were not inhibited at all.

The tumor cells were fractionated by Potter-Elevehjem's method to protoplasm and nucleus, and the mice were immunized with each antigen. In these cases mice inhibited the takes of all rat tumors, in cases of immunization with cytoplasm as well as with nucleus, and there was no inhibition by the immunization with TCA-treated protoplasm or nucleus. Therefore, this inhibition was caused by species specific immunity, and the tumor type specific antigen must have disappeared during the fractionation.

However, when the mice were immunized with TCA-treated nucleus combined with Freund's adjuvant, they indicated an apparent inhibition against the takes of the transplantation of the same type tumor, but no inhibition was shown against the take of other types of tumor. Mice, immunized with TCA-treated protoplasm combined with Freund's adjuvant, indicated almost no inhibition, even in the case of the transplantation of corresponding tumor. From this result, it is suggested that the type specific antigenicity of tumor cells originated from nucleus antigen.

The 12 strains of ascites tumors of rat which were used for immunization were originally induced in separate uniform hybrid rat respectively. Therefore, a problem remains as to whether or not the genetic difference between these rats, in which tumors were induced, influences the type specific antigenicity of tumor cells.

To solve this problem, the uniform hybrid rats were fed with butter yellow, and the part of hepatoma, normal part of liver, kidney and spleen of the same rat were treated with TCA, and the mice were immunized with these antigens respectively. The mice immunized with normal part of liver, or kidney, did not inhibit the take of all ascites tumors of rat, even the hepatoma. However, the mice immunized with a part of induced hepatoma inhibited the take of ascites hepatoma of all strains slightly, but not the take of Yoshida and Takeda sarcomas.

When the mice were immunized with a small amount of induced hepatoma treated with TCA combined with Freund's adjuvant, they did not inhibit the take of Yoshida and Takeda sarcomas at all, but inhibited apparently all strains of hepatomas.
As control, mice were immunized with TCA-treated normal part of liver, kidney and spleen combined with Freund’s adjuvant, and they inhibited neither the take of hepatoma nor that of Yoshida and Takeda sarcomas.

From these results, it can be said that the hepatoma cells contain a new specific antigen (hapten ?) common only to that of hepatoma of other rat, and not common to normal part of liver and other organs of the same rat.

**Various Aspects of the Immunity Against Takeda Sarcoma**

**I. Immunological Reacton of Takeda Sarcoma**

**NOBUHISA SATO**

9. **武田肉腫免疫の諸相（第一報）武田肉腫の免疫血清学的反応**

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使用武田肉腫は当教室で dd 系マウスに 200 代以上経代移植した腫瘍である。

1) 人工免疫によって得た抗血清では沈降反応、凝聚反応、補体結合反応、Middlebrook & Dubos の血球凝聚反応および溶血反応の結果、抗腫瘍血清は腫瘍と高く反応するが、また宿主動物組織（マウスおよびラットの各臓器、胎児）とも高く反応する。ただしこの際抗原性は腫瘍の方が組織乳剤より高い、また抗腫瘍血清より抗組織抗体を除去した吸収血清では力価が著明に低下するが、なお腫瘍特異性抗体を認め腫瘍特異性抗原の存在を確認した。この特異性抗体については凝集反応で最も高い値を示した。なお凝聚反応に補体を加えても力価に著明な差がなくやや高い値を示すのみであった。沈降反応、補体結合反応（諸方法）では抗原価および抗体価について同時に検したが、反応の場は階段状をなし反応系が多数あることを認めた、抗ホルモル化腫瘍血清は組織抗原と低い値で反応せずホルモル化により腫瘍特異性が高まる。

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