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Kobe J. Med. Sci. 28, 65 - 73, April 1982

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INDEXING WORDS

SL/Ni mouse; SL/K mouse; mouse lymphoma; electronmicroscopic study

SYNOPSIS

Tumor cells of SL/Ni mice electronmicroscopically have the intimate intercellular relation such as tight junction or desmosome-like structure although morphologically their nuclei show different stages of maturation. They would belong to the centrofollicular cells of the spleen and lymph-nodes. Tumor cells of SL/K mice have the characteristics of free cells and no intimate intercellular relation as seen in those of SL/Ni mice. Tumor cells of the hybrids of SL/Ni and SL/K mice have the characteristics of SL/Ni mice. These tumor cells do not show B-cell or T-cell characteristics. Even immunologically in the immature stage, histogenesis of the tumor cells in SL/Ni mice will be confirmed by electronmicroscopic study.

Received for publication : February 1, 1982
Authors' names in Japanese : ジョコ・スーナルト・フィディアスモロ　木崎智彦
渡辺　信　武田善樹　浦野順文

INTRODUCTION

"SL" mouse is an inbred strain of albino mouse, established in 1955 by Dr. K. Tsuchikawa of the National Institute of Genetics in Japan. This strain is called SL/K and well known for its high incidence of lymphatic malignancy (60% to 70% of cases). This lymphatic malignancy is related to the Gross type of murine leukemia virus and does not originate in the thymus. Later, its substrain which has an high incidence of glomerulonephritis close to human SLE and also of arteritis close to human polyarteritis nodosa, is found and called SL/Ni, taking the initial of Dr. Nishizuka, founder of this substrain. But in this substrain, lymphatic malignancy occurs less frequently (under 30% of cases). [2, 4]

The immunological and virological studies of these lymphatic malignancies are well known. But little is known about their ultrastructural study and also about the relation between ultrastructural and immunological characteristics. [1, 5]

We examined electronmicroscopically the characteristics of the tumor cells of these lymphatic malignancies in SL/K, SL/Ni and hybrid of SL/K and SL/Ni mice and compared the results of the electronmicroscopic and immunological study.

EXPERIMENTAL MATERIALS AND METHODS

Lymphatic malignancies which occurred naturally in SL/K, SL/Ni and hybrid of SL/K and SL/Ni mice, and also lymphatic malignancy which was conserved by serial transplantation, were examined electronmicroscopically and immunologically.

These mice were as follows :

No. 1 Lymphoma derived from female SL/Ni mouse and serially transplanted into the peritonial cavity of male SL/Ni mice.
No. 2 Lymphoma developed spontaneously in female SL/Ni mouse.
No. 3 Lymphoma developed spontaneously in female SL/Ni mouse.
No. 4 Lymphoma developed spontaneously in female SL/Ni mouse.
No. 5 Lymphoma developed spontaneously in female SL/K mouse.
No. 6 Lymphoma developed spontaneously in female SL/K mouse.
No. 7 Lymphoma developed spontaneously in female SL/Ni-K mouse.

For electronmicroscopic study, the specimens were taken from the spleen, cervical and mesenteric lymphnodes, were fixed by 2.5% glutaraldehyde in 0.1 M phosphate buffer solution (pH 7.4) or 10% buffered

formalin (pH 7.4) for 2 hours at 4°C. They were refixed in 1% OsO_4 solution for 2 hours at 4°C. After dehydration through a series of ethylalcohol, they were embedded in epon by ordinary method. Ultrathin-sections were made by ultramicrotome Sorvall, stained with uranium acetate and lead citrate and finally observed by Hitachi HS-9 electronmicroscope.

For immunological study, the stamp preparations of the above specimens were stained by immunofluorescent method in order to detect terminal deoxynucleotidyl transferase (indirect method) and cytoplasmic immunoglobulin (IgG, IgA, IgM, direct method).

RESULTS

Electronmicroscopic findings of malignant lymphoma cells of mice

1. SL/Ni mice

The electronmicroscopic findings of the tumor cells in these 4 mice have approximately the same characteristics. According to nuclear differentiation, there are three types of tumor cells.

The first type of tumor cells has round or oval nuclei with shallow indentation. The heterochromatin is condensed marginally and sometimes located centrally. They have one central nucleole (Fig. 1).

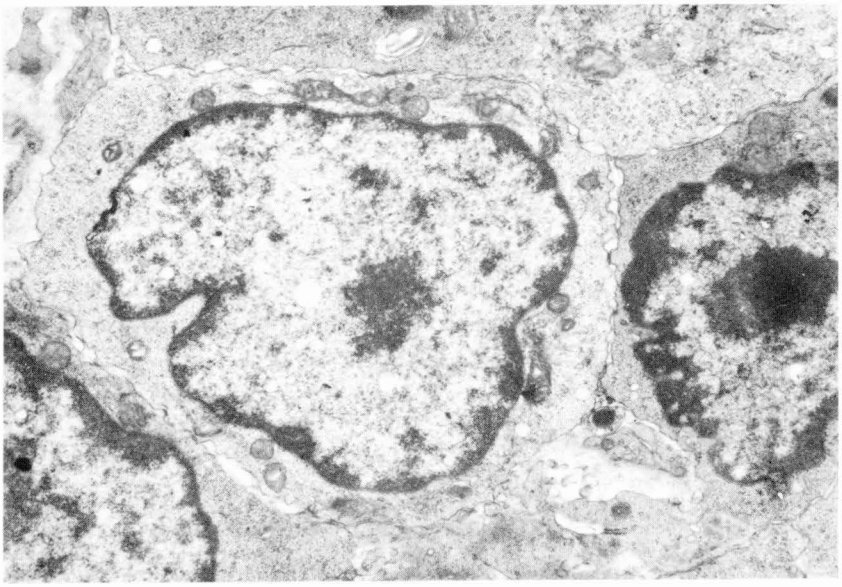

Fig. 1 Tumor cells of SL/Ni mouse (Case 2). X 5,200
The nuclear structure is more immature. Occasional tight junction is observed.

The second type of tumor cells has irregular shaped nuclei with one deep indentation. The heterochromatin is more widely condensed than that of the first type. The distribution of the heterochromatin is peripheral and central as seen in the first type (Fig. 2).

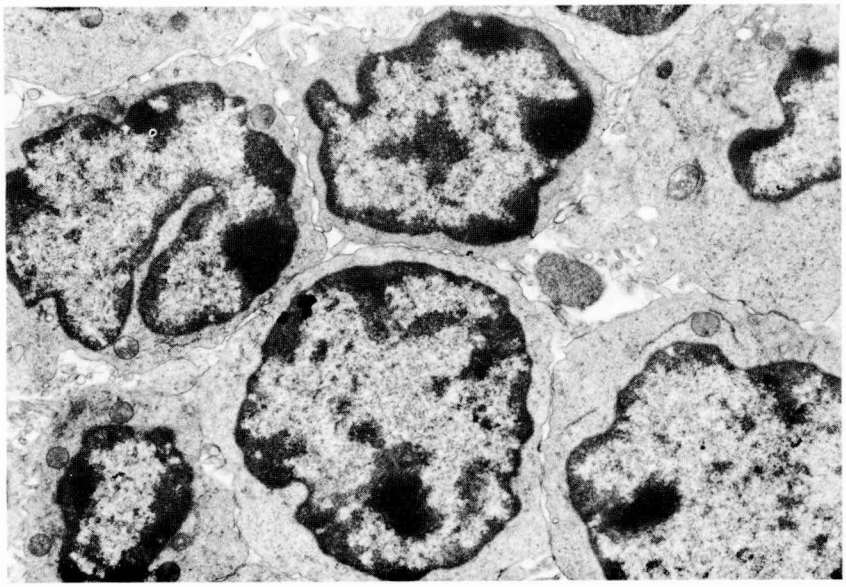

Fig. 2 Tumor cells of SL/Ni mouse (Case 1). X 3,500
The nuclear deep indentation is occasionally observed. Occasional tight junction is also observed.

The third type of tumor cells has irregular nuclear contour but without obvious indentation. The heterochromatin is well developed and irregular in distribution. The nucleoli are centrally situated (Fig. 3).

All three types of tumor cells have scanty cytoplasm. Mitochondria are frequently found. The ribosomes are found more frequently in form of monosome than in that of polysomes. There exist sparse straight rough endoplasmic reticulums. The tumor cells have intimate contact with each other with tight junction or desmosome-like apparatus (Figs. 1 and 2) and sometimes also interdigitation by microvillous buddings. There are type C virus particles in the cytoplasm.

2. SL/K mice

The electronmicroscopic findings of the tumor cells in these mice have approximately the same characteristics. Most of the cells have oval or round nuclei with irregular contour and occasionally small indentation. Small amount of heterochromatin is located in the marginal region of the

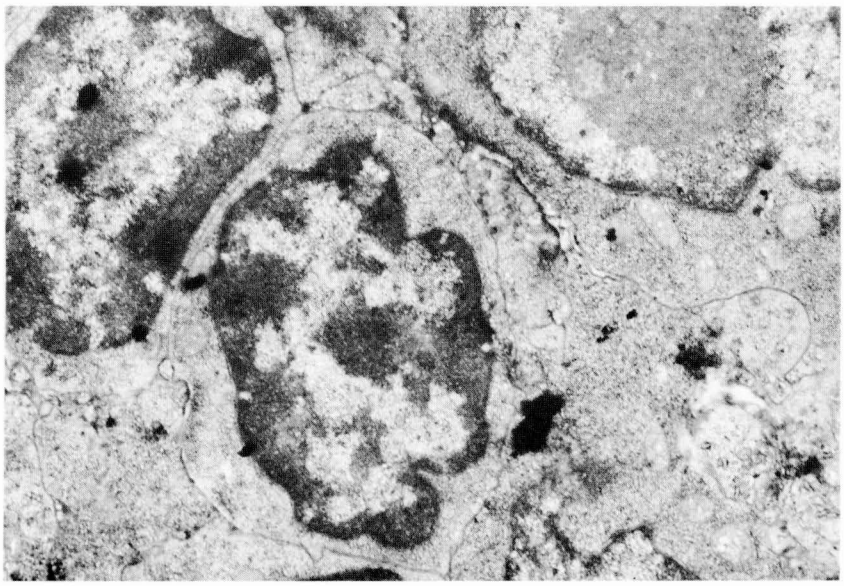

Fig. 3 Tumor cells of SL/Ni mouse (Case 3). X 5,200
The nuclear structure is more mature showing marked peripheral chromatin condensation.

nuclei. Some cells have nucleoli located in the nuclear center. The other cells have two or three nucleoli situated in the marginal part of the nuclei. The former type of nucleoli is more often found than that of the latter one. Cytoplasm is scanty with some mitochondrias and rare endoplasmic reticula. Some cells have well developed Golgi apparatus. The cytoplasmic border is irregular. There are cytoplasmic large projections but microvillous buddings are less developed (Fig. 4). There are virus particles of type C in the cytoplasm.

3. SL/Ni-K-F_1

Nuclei are round and oval. If there is an indentation, it is usually not too deep. Most of the cells have well developed heterochromatin which is distributed in the central and marginal parts of the nuclei. And some of the tumor cells have only less developed peripheral heterochromatin. The two types of tumor cells usually have nucleoli in the nuclear center. The cytoplasm is scanty. Ribosome and mitochondria are well developed. There is extensive direct contact between cells but only some microvillous budding (Fig. 5). There are type C virus particles in the cytoplasm.

4. Immunological study

Immunological studies show that terminal deoxynucleotidyl trans-

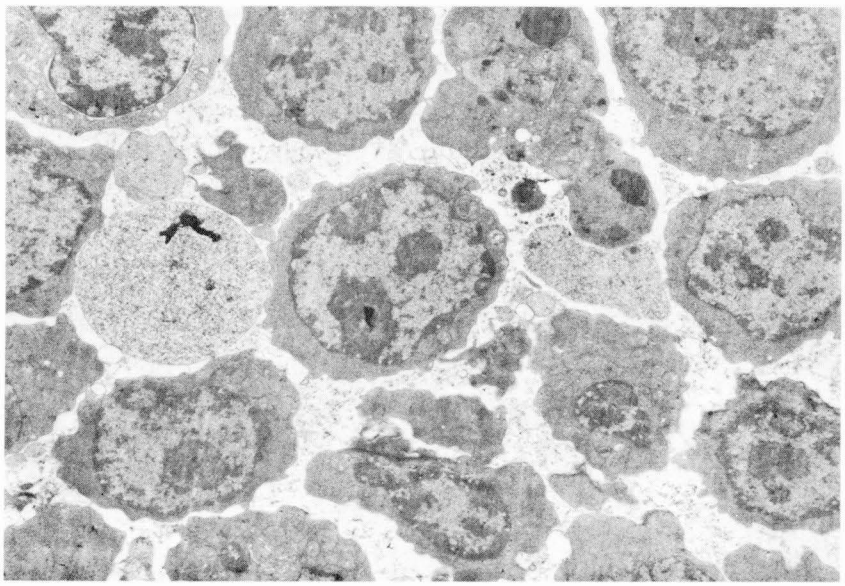

Fig. 4 Tumor cells of SL/K mouse (Case 5). X 2,200
The tumor cells are separated from each other. There is no intercellular intimate relation as seen in SL/Ni mouse tumor.

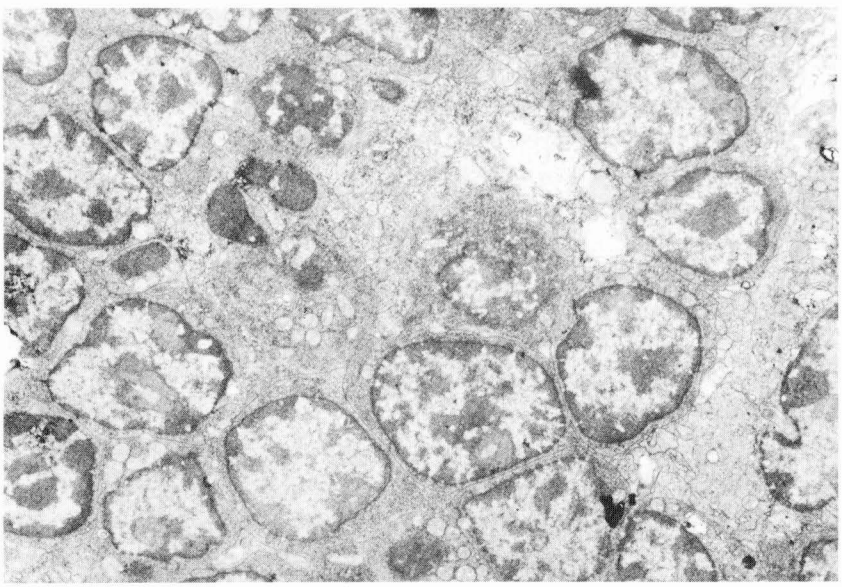

Fig. 5 Tumor cells of hybrid of SL/Ni and SL/K mice (Case 7). X 2,200
The tumor cells have the same intercellular relation as seen in SL/Ni mouse tumor.

ferase is positive in the tumor cells of case 2 (SL/Ni mouse), case 5 (SL/K mouse) and case 7 (hybrid of SL/Ni and SL/K mouse). The cytoplasmic immunoglobulin is negative in all the cases (Table 1).

Table 1 Electron-microscopic and immunological characteristics of tumor cells.

Case	Mice	Sex	Organ	TdT	cIg	Virus Particles	Intimate cell interaction
1*	SL/Ni	M	L.N.	-	-	+	+
1	SL/Ni	M	Spleen	-	-	++	+
2	SL/Ni	F	Spleen	+	-	++	+
3	SL/Ni	F	L.N.	-	-	+	+
4	SL/Ni	F	Spleen	-	-	++	+
5	SL/K	F	L.N.	+	-	+	-
6	SL/K	F	L.N.	-	-	+	-
7	SL/Ni-SL/K	F	L.N.	+	-	+	+

Case 1 : Serially transplanting tumor

Case 2-7 : Spontaneously induced primary tumor

M : Male

F : Female

L.N. : Lymphnode

TdT : Terminal deoxynucleotidyl transferase

cIg : Cytoplasmic immunoglobulin

DISCUSSION

The tumor cells of the SL/K mice have the characteristics of free cells. They have large cytoplasmic projections. They proliferate apart from each other. There is no intimate intercellular interaction. There are no desmosomes nor tight junctions, nor interdigitating cell membranes. The nuclei are oval or round in shape without deep indentation. Cytoplasmic organellas are sparse. They are electronmicroscopically immature cells without specific differentiation.

Some of the tumor cells of SL/Ni mice have the characteristics of

desmo-dendric cells, but in abortive or incomplete form. They have occasionally abortive interdigitating cell membranes between adjacent cells. There exist tight junctions or desmosome-like apparatus. The nuclei often have one deep indentation. These are the characteristics of desmo-dendric cells in the follicle center. Usually in the spleen there are cohesive cell populations with extensive cytoplasmic contact with microvillous budding. These tumor cells also have the characteristics of the splenic cohesive cells. Tumor cells in the hybrids of SL/K and SL/Ni mice have the characteristics of SL/Ni mice in the intercellular relation. The tight junctions or desmosome-like apparatus are observed, but the nuclear deep indentations are lacking. They belong to the follicle center cells in the histogenesis of the tumor although abortive in their morphological characteristics.[2, 6, 7]

Immunologically, tumor cells of the SL/K mice are said to be either of B-cell or T-cell origin and most of the tumor cells of SL/Ni mice are said to be of B-cell origin. The immunological studies of our cases are not sufficient enough to decide whether the tumor cells belong to B-cell or T-cell or non T·non-B cells.

From both the immunological and electronmicroscopic studies of our cases, it will be suggested that the tumor cells of SL/K mice will be immunologically variable although morphologically they would belong to the one group of cells. However their histogenesis cannot be resolved from electronmicroscopic cytological findings. On the other hand, tumor cells of SL/Ni mice and hybrids SL/K and SL/Ni mice will also belong to one group of cells and they will originate from centrofollicular cells with abortive desmo-dendric cell characteristics.

The detailed electronmicroscopic observation of these tumor cells has not yet been reported. They are classified morphologically in the category of reticulum cell sarcoma or Dunn's type B neoplasm.[1, 4, 5] The detailed analysis of immunological and morphological characteristics will be necessary in order to disclose the histogenesis of these tumors in SL/Ni, SL/K mice and their hybrid mice.

ACKNOWLEDGEMENTS

This work was supported in part by the grant of the Japan Society for the Promotion of Science (JSPS).

The authors are grateful to Mr. S. Tanioka, Miss C. Ikeuchi, Miss M. Kato, and Mrs. A. Kawashima for their technical assistance.

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