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Comparative Study between Nude Mice and Immunosuppressed Hamsters as Recipients of Human Tumor Xenografts

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ABSTRACT

We comparatively examined nude mice and hamsters as to their suitability as recipients of human cancers. CD-1 nude mice and golden hamsters immunosuppressed with anti-hamster thymocyte serum were used. Nude mice were superior in the areas of primary transplantation and subsequent transfer and maintenance. However, growth of tumors transplantable to both animals (a lung cancer line LC-1, a colon cancer line RPMI4788) tends to be better in hamsters than in nude mice. The better development of LC-1 and RPMI4788 cells in hamsters than in nude mice appears to be related to the superior gain in body weight shown by hamsters.

Since a serially transplantable human tumor was first established in nude mice by Rygaard and Povlsen in 1969[16], nude mice have come to be recognized as suitable recipients of human tumor-xenografts[6,15]. Before the general use of nude mice, hamsters were often used as recipients of human tumor xenografts[1-3,14,17,18]. In 1954, Patterson serially transplanted a human malignant tumor in the cheek pouches of hamsters administered steroid hormones[13]. The hamster-human tumor xenograft system has not developed, however, because of problems with tumor growth and the unsuitability of the cheek pouch[19]. Since 1976, Miyoshi and Hiraki have developed immunosuppressed hamster-human hematopoietic cell systems which appear to be promising[10].

In the present study, we comparatively examined hamsters and nude mice as to their suitability as recipients of human cancers.

MATERIALS AND METHODS

Animals. Male nude CD-1 (nu/nu) mice were obtained from Charles River Japan, Inc. (Atugi, Kanagawa, Japan) at the age of 4-6 weeks. Golden hamsters were obtained from Hayashibara Biochemical Labolatories, Inc., less than 24 hr of birth. The hamsters were injected intraperitoneally twice weekly with rabbit anti-hamster thymocyte serum (ALS)[7].

Tumors. RPMI4788, a human colon cancer line, was kindly supplied by Roswell Park Memorial Institute[12]. The karyotype of RPMI4788 cells was stable, with a mode of 64 and range of 60-69. The karyotype was originally reported to have a mode of 70 and range 65-72 after 10 passages. RPMI4788 have human transferrin receptors recognized by OKT-9 (Ortho Diagnostic Systems, Inc., Tokyo). Nude mice and hamsters were injected with 2×10^6 tumor cells in 0.1 ml PBS. Other fresh tumors were obtained from cancer patients during surgery. These tumors were divided into blocks (2-3 mm) with sterile scissors. Nude mice and hamsters were inoculated with two or three tumor blocks.

Histological examination. Sections were stained with hematoxyline and eosin (H.E.).

RESULTS

Growth of RPMI4788 cells in nude mice and hamsters. Tumors grown in nude mice and hamsters showed histologically poorly differentiated adenocarcinoma (Fig. 1). The relation between the number of days after inoculation and the weight of resected RPMI4788 tumors is shown

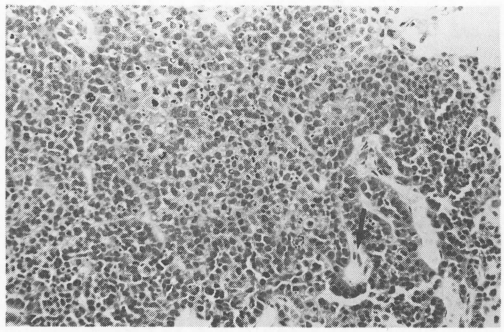

Fig. 1. RPMI4788 cells grown in nude mice. Histological examination shows poorly differentiated adenocarcinoma. Arrow indicates a tubulus.

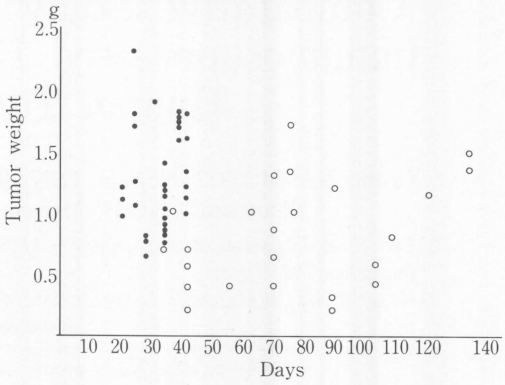

Fig. 2. Tumor growth in nude mice (○) and hamsters (●). The relationship between resected tumor weights and the period (days) after tumor inoculation.

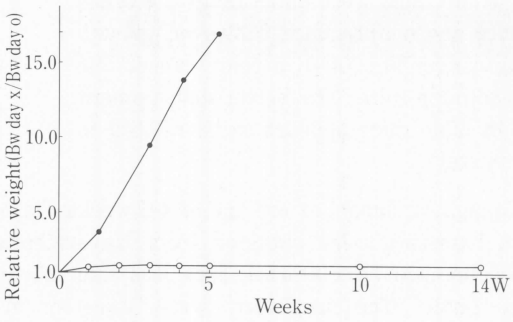

Fig. 3. Growth (body weight) of recipient nude mice (○) and hamsters (●) after birth.

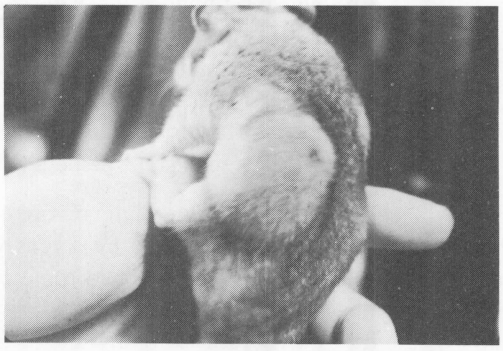

Fig. 4. A hamster bearing LC-1 tumor.

Table 1. Serially transplantable tumors in nude mice and/or hamsters

Tumor	Primary Site	Histology	Nude Mouse	Hamster	Patient
GC-1	Lung	mod. diff. adeno. ca.	take s.t.	reject	59y.o. M.
CC-2	Colon	well diff. adeno. ca.	take s.t.	reject	52y.o. F.
LC-1	Lung	mod. diff. squamous ca.	take s.t.	take s.t.	67y.o. M.
PC-1	Pancreas	por. diff. adeno. ca.	take s.t.	reject	60y.o. F.
His-1	Hip	malignant histiocytoma	take s.t.	take s.t.	57y.o. M.

s.t.; serially transplantable
well diff. adeno. ca.; well differentiated adenocarcinoma
mod. diff. adeno. ca.; moderately differentiated adenocarcinoma
por. diff. adeno. ca.; poorly differentiated adenocarcinoma
mod. diff. squamous ca.; moderately differentiated squamous cell carcinoma

M; Male
F; Female

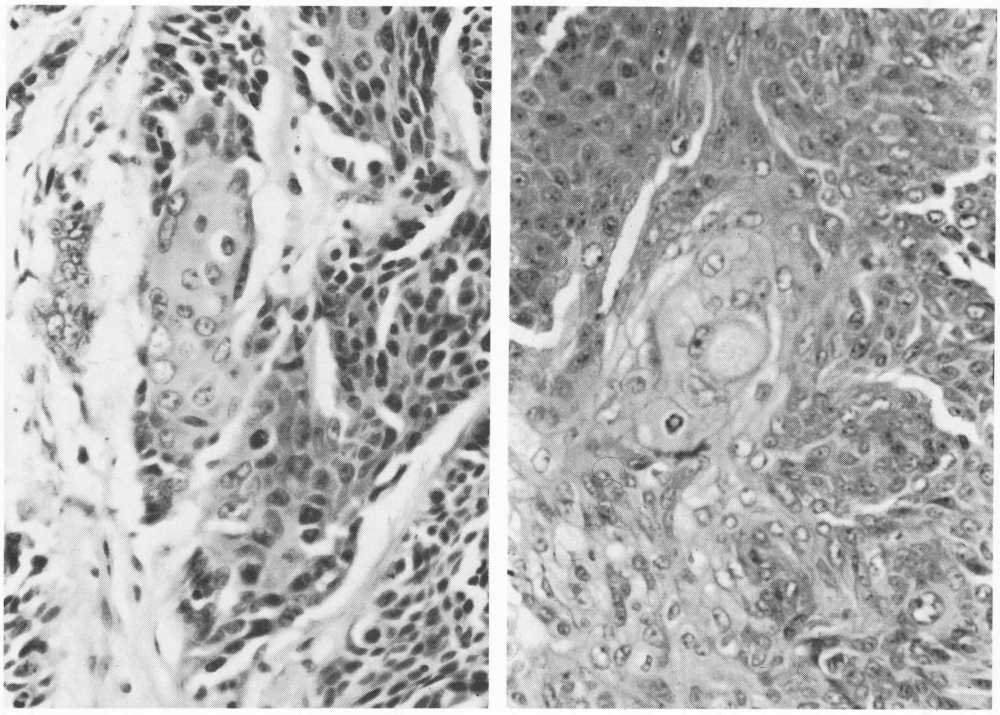

Fig. 5. Left, Histology of LC-1 in the patient. Right, Histology of LC-1 in the hamster. Both show moderately differentiated squamous cell carcinoma.

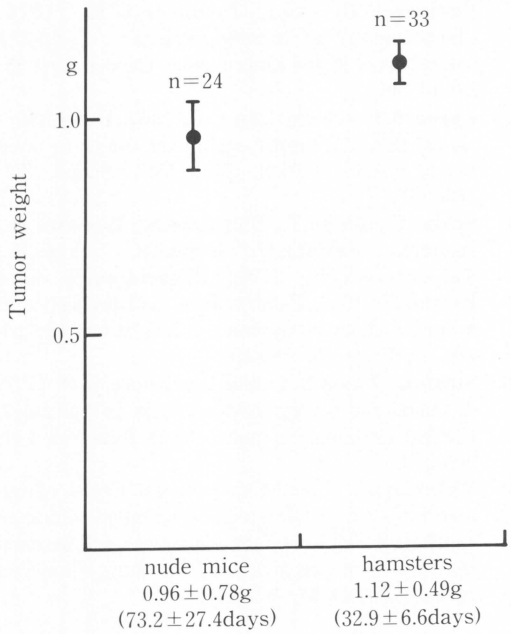

Fig. 6. The growth of LC-1 in nude mice and hamsters. The relationship between tumor weights and resected day after tumor inoculation.

in Fig. 2. The growth of RPMI4788 cells in hamsters was obviously good. The change in body weight of hamsters was good, as can be seen in Fig. 3, which shows a comparison of the body weights of hamsters and nude mice.

Primary inoculation. In nude mice, 23.3% (10/43) of the primary tumors took, while in hamsters only LC-1 and His-1 tumors took. A list of serially transplantable primary tumors is given in Table 1. Five tumors (5/43, 11.6%), GC-1, CC-2, LC-1, PC-1 and His-1, were serially transplantable in nude mice.

Fig. 4 is a photograph of a hamster bearing an LC-1 tumor. Histological examinations of an LC-1 tumor excised from a patient and an LC-1 tumor born by a hamster revealed both to be moderately differentiated squamous cell carcinomas (Fig. 5). As can be seen from Fig. 6, the growth of LC-1 tumors was much better in hamsters than in nude mice. The karyotype of LC-1 had a mode of 70.

DISCUSSION

When comparing nude mice and hamsters as

recipients of human tumors, especially tumors of epitherial origin, nude mice are superior in the areas of primary transplantation and subsequent transfer and maintenance. However, growth of tumors transplantable to both animals (LC-1, RPMI4788) tends to be better in hamsters than in nude mice[19]. The better development of LC-1 and RPMI4788 cells in hamsters than in nude mice appears to be related to the superior gain in body weight shown by hamsters.

Hematopoietic tumors are recognized as being difficult to transfer and maintain *in vivo*. Miyoshi and Hiraki et al have succeeded in establishing hematopoietic tumor cell lines, including normal cells, in hamsters[4,5,8,9]. They have also reported the availability of this system to the mass production of human lymphokines[11]. The use of hamsters in assay systems has the advantage of being inexpensive, but the problem of frequent cannibalism within 2 weeks often makes the experimental use of hamsters impractical.

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