Prolongation of Skin Graft Survival in Mice by 6-Mercaptopurine Riboside

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OGATA, M. and YANAGIMOTO, S. Prolongation of Skin Graft Survival in Mice by 6-Mercaptopurine Riboside. Tohoku J. exp. Med., 1974, 112 (2), 129-131 — 6-Mercaptopurine riboside (6-MPR), which is thought to be a powerful metabolic antagonist of the nucleic acid synthesis and to have a lower toxicity than 6-mercaptopurine (6-MP), prolongs the survival time of skin homografts in mice when administered after grafting. Treatment must be continued to maintain graft reliability. —— 6-mercaptopurine riboside; skin graft survival

In the previous reports (Ogata and Kumashiro 1970; Ogata 1971), the authors reported that the circulating antibody to bovine serum albumin is completely suppressed in rabbits by 6-MPR with lower toxicity. In addition, the authors therein compared 6-MPR with 6-MP and Azathiopurine (Imuran).

As to the effect of 6-MP on the allograft reaction, Meeker et al. (1959) reported on the prolongation of skin homograft survival in rabbits.

In this experiment, the effect of 6-MPR on the survival time of skin homograft in inbred mice is described.

MATERIALS AND METHODS

Animals: Skin-graft experiments were performed using male strong A mice weighing about 20 g. AKR mice were used as skin-graft donors.

6-MPR: 6-MPR solution used in this study was prepared freshly by dissolving 6-MPR in 0.04 N NaOH in physiological saline solution.

Skin grafting: Male strong A mice were grafted on their skin with 20×20 mm skin patches from male AKR donors. The technique used was that described by Billingham et al. (1951). The allografts were inspected daily and the same criteria for rejection were used. The initial slough time is defined as the time when the margin of skin graft is dried, and the end slough time is defined as the time when 2/3 part of skin graft is completely dried, the mean slough time being defined as the intermediate of the initial and end slough times.

All mice were housed in groups in the cages air-humidity-controlled.

RESULTS

The data are summarized in Table 1. The initial, end and mean slough times in treated animals were 7.6, 9.8 and 8.7 days, respectively and those in untreated
TABLE 1. Effect of 6-MPR on skin graft rejecting reaction

<table>
<thead>
<tr>
<th>Rejection Group</th>
<th>Onset (day)</th>
<th>Completion (day)</th>
<th>Mean (day)</th>
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<td>Case</td>
<td>Control</td>
<td>Treated</td>
<td>Control</td>
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m±σ: 5.6±0.5 7.6±1.1 7.8±0.5 9.8±1.8 6.7±0.4 8.7±1.4

P: *<0.01 †<0.05

The experimental animals received daily intraperitoneal injection of 60 mg 6-MPR/kg body weight.

The control (animals) received no immunosuppressive agents.

Animals were 5.6, 7.8 and 6.7 days, respectively. And the differences of initial, end and mean slough times between treated and untreated animals were significant within 1%, 5% and 5% levels, respectively. From the above results, it can be concluded that treated animals obtain a longer prolongation in the graft survival than untreated ones.

**DISCUSSION**

The results clearly established that 6-MPR in the dose levels employed, produced an inhibitory effect on the immune response to skin homografts in inbred mice.

Properties of 6-MPR to interfere with the nucleic acid synthesis may be inferred to produce the predominant action to suppress a humoral antibody production as well as a homograft reaction.

Pierre et al. (1967) described that the nucleoside formation of thionisone would involve a reaction requiring a nucleoside kinase instead of a nucleoside pyrophosphorylase in cell-free extract from a thioguanine-resistant subline of Ehrlich ascites carcinoma which lacked inosine monophosphate-guanosine monophosphate pyrophosphorylase. From these results, it is inferred that thioinosic acid which is thought to be an inhibitor of the nucleic acid biosynthesis was formed by nucleoside kinase from thioinosine.

**References**


