Forum Minireview

Microminipig, a Non-rodent Experimental Animal Optimized for Life Science Research: Preface

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Received August 23, 2010; Accepted October 25, 2010

Abstract. Fuji Micra Inc. has recently achieved success in a challenging and prospective project that produces the smallest pig in the world, the “Microminipig”, at a breeding farm at the foothills of Mt. Fuji in Japan. Microminipigs weigh approximately 7.0 kg at 6 months of age when they are mature. Microminipigs have been provided to several research organizations in Japan as a non-rodent experimental animal optimized for life science research.

Keywords: Microminipig, animal model, life science research

Life science research often directly investigates processes of life phenomena by using in vitro research techniques. To confirm whether a principle generated from in vitro experiments are applicable under physiological conditions, in vivo studies are definitely required. However, such in vivo proof is particularly difficult to obtain under the current situation of promoting 3R (Reduction, Replacement, and Refining) and alternatives to animal testing (1). Particularly for safety and tolerability evaluations, no researcher can predict unexpected adverse reactions and/or toxicity of new molecular entities without conducting animal studies.

Miniature pigs such as Göttingen are well known as an ideal experimental animal from the similarities to humans including skin, cardiovascular, respiratory, metabolic, gastrointestinal systems, and so on (2). To our knowledge, unfortunately, it may be hard to use not only regular pigs but also minipigs for in vivo proof because they still require larger dosage of test article. In this review, we introduce a promising experimental animal, the Microminipig (Fig. 1). The Microminipig will contribute to the health and welfare of mankind as an experimental animal very suitable for life science research.

A female minipig named “Catherin”, the “Eve” of Microminipig, was born by the mating of Pot-bellied pig and another type of minipig. Strangely enough, extremely small pigs were born without fail from Catherin regardless of gender. There are six strains of Microminipig at the moment. All strains are the littermate from Mother Catherin (Fig. 2).

The growth curve of the Microminipig is shown in Fig. 3. In Microminipigs, a first estrus was observed at 2 – 3 months after birth. Therefore, the age thought to be this animal’s youth would be 4 – 6 months after birth. Generally, young mature animals are used for an animal experiment including those for pharmacology, toxicology, and pharmacokinetics, so that Microminipigs with body weights of approximately 6.0 – 7.0 kg are suitable for the experiments. Their size is less than that of young mature beagle dogs.

The use of Microminipigs is effective with respect to cost/benefit from the financial point of view. For example, in a pre-clinical toxicity study, toxicologists usually give a maximum dose of 2,000 mg/kg, p.o., if no toxicity was found in lower doses, as shown in Table 1. In the cases of mice, rats, dogs (beagle dogs), and regular minipigs, amounts of test article for one regular study are 480 – 960 mg, 4.8 – 9.6 g, 288 – 336 g, and 1440 – 1920 g, respectively. On the other hand, in the case of Microminipigs, only 180 g test article is needed. It may be less than that needed for beagle dogs that are often used as a non-rodent experimental animal in pre-clinical toxicity studies. In
In general, the cost of the test article in discovery research and the early development stage, in other words, the cost of drug substance produced under Good Manufacturing Practice toward clinical study, is extremely expensive. Therefore, it may be more economical to choose the Microminipig as a non-rodent animal (Table 1).

One might think that the small size of the Microminipig is due to food restriction. As shown in Fig. 4, however, the Microminipig never grows up in terms of body length even if it was given much sufficient food. Microminipig just develops fat and body weight with enough diet. Furthermore, Murayama et al. have recently reported that...
Microminipigs could be used as a possible new animal model for humans in the non-clinical pharmacological/toxicological research area, like the predecessor minipigs (3). In September 2010, legislation by the European Parliament has broadly banned the use of great apes such as chimpanzees, bonobos, gorillas, and orangutans for scientific testing. The Commission’s draft law would also have in principle restricted the use of other non-human primates such as ouistitis and macaques. Therefore, substitute animals will be required hereafter, and the Microminipig will be one of the promising candidates.

Thus, the Microminipig is a non-rodent experimental animal optimized for life science research including pharmacology, toxicology, and pharmacokinetics, and so on. In this series of reviews, some of the latest data that were already obtained will be shown (4, 5). This Forum Minireview series is based on the symposium at the 83rd Annual Meeting of The Japanese Pharmacological Society held on March 17, 2010, in Osaka, Japan.

Table 1. Comparison of cost/benefit of the Microminipig with other species of experimental animals

<table>
<thead>
<tr>
<th>Species (body weight)</th>
<th>Dose/Animal</th>
<th>n = 4 (control + 3 doses)</th>
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<tbody>
<tr>
<td>Mouse (20 – 40 g)</td>
<td>40 – 80 mg</td>
<td>480 – 960 mg</td>
</tr>
<tr>
<td>Rat (200 – 300 g)</td>
<td>400 – 600 mg</td>
<td>4.8 – 9.6 g</td>
</tr>
<tr>
<td>Dog (12 – 14 kg)</td>
<td>24 – 28 g</td>
<td>288 – 336 g</td>
</tr>
<tr>
<td>Minipig (30 – 80 kg)</td>
<td>60 – 160 g</td>
<td>720 – 1920 g</td>
</tr>
<tr>
<td>Microminipig (7.5 kg at 5 months old)</td>
<td>15 g</td>
<td>180 g</td>
</tr>
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Maximum dose generally administered in a toxicology study is around 2,000 mg/kg.

References