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Novel Husbandry Techniques Support Survival of Naked Mole Rat (*Heterocephalus glaber*) Pups

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The naked mole rat (NMR) is a small eusocial rodent. Because of its remarkable longevity (maximal lifespan, 32 y) and resistance to cancer, the NMR has emerged as a valuable model for aging and cancer research. However, breeding NMR can be difficult. Here, we report the successful introduction and acceptance of pups into a foreign colony with existing pups of different ages. Among the 7 NMR colonies in our satellite facility, one had a consistently poor record of pup viability, with nearly 100% preweaning mortality in multiple litters born over the course of 2 y. The queen of this colony gave birth to 18 pups in January 2013; by 2 d after parturition, it was evident that the pups were not receiving sufficient nourishment. To salvage the litter, the most vigorous pups were cross-fostered to another queen that had recently given birth. On postparturition day 1 (PD1), two pups from the poorly nourished donor litter were bathed with warm water, rolled in recipient colony bedding, and transferred to the recipient colony, which included 8 PD14 pups. The new pups were accepted by the recipient queen, who continued to produce milk in response to suckling by the donor pups well past the weaning of her own litter. This case report provides evidence of successful cross-fostering of NMR pups despite age differences between donor pups and those in the recipient litter; this technique may prove beneficial to researchers struggling with NMR breeding issues.

Abbreviations: NMR, naked mole rat; PD, postparturition day.

The naked mole rat (NMR; *Heterocephalus glaber*) is the longest-lived rodent, with a maximal lifespan of 32 y.[2] NMR also are characterized by their extreme resistance to cancer.[1,4,8] These unique qualities make the NMR a valuable model for aging and cancer research. Although multiple NMR colonies have been established at research universities, breeding NMR in captivity is challenging, because this rodent is a true eusocial species, with cooperative brood care and division of labor between reproductive and nonreproductive animals.[6] NMR colonies are based on a hierarchical arrangement, with a single, dominant breeding queen, one or more breeding males, and several workers.[5,6] In addition, with the exception of dispersive morphs,[7] NMR tend to be philopatric, remaining in their natal groups throughout life.[3] Here we describe a case in which NMR pups born to a queen with lactation problems were fostered successfully by another colony with pups of older age.

Case Report

The animal research facility at the University of Rochester is accredited by AAALAC. All of the animal work described was done in accordance with guidelines established by the US Department of Agriculture and University of Rochester Committee on Animal Resources and approved by the University of Rochester IACUC.

Among the 7 NMR colonies at the University of Rochester, one queen (queen 5) was discovered to have severe lactation problems, resulting in nearly 100% mortality of all her litters by postparturition day 5 (PD5). Currently 5.9 y old, queen 5 was born in the lab of Kenneth Catania (Vanderbilt University, Nashville, TN). Prior to the cross-fostering event, she gave birth to a total of 15 litters, of which only 5 litters yielded any pups that survived past weaning (Table 1). Queen 5 gave birth to 18 pups on 8 January 2013. Examination of the colony on PD0 (the day on which the pups were born) revealed that her mammary tissue was not fully milk-laden; similar deficiencies had been noted during previous instances in which preweaning mortality of litters reached 100%. On PD1, we found that the pups could not successfully find nipples to suckle, suggesting that queen 5 was unable to secrete sufficient milk or did not emit a characteristic odor to attract pups to suckle. Pups suckled occasionally but soon stopped, even without perturbation, and sought other nipples, further indicating that queen 5 had lactation problems.

By chance, another colony had a litter born 14 d prior to the one in colony 5. This other queen (queen 6) had successfully raised 8 of 11 pups to 14 d of age. The mammary glands of queen 6 were fully developed, and plenty of milk was visible through her skin. The surviving 8 pups were healthy and nursing well.

Given the impending death of queen 5's litter and the abundance of milk produced by queen 6, we decided to intervene by transferring pups from colony 5 to colony 6. On PD1, 2 of the strongest pups from colony 5 were bathed in warm water, dried with gauze, rubbed with soiled bedding from colony 6, and then transferred to colony 6. Members of colony 6 responded by initially smelling these 2 foreign pups and then shoving them. However, after approximately 5 min, the worker NMR began cleaning the pups and carried them to the sleeping chamber. Once there, the pups sensed the queen's odor and started seeking her nipples. Queen 6 did not reject the donor pups but instead lifted her forefeet to gather them under her foreleg and let them suckle. The pups immediately latched on and were nursed successfully thereafter. Milk spots were visible in the fostered pups when they were checked the same night. On PD2, we performed a similar transfer of 2 additional pups from colony 5, but these 2 were already very weak and

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Table 1. Reproductive history of queen 5

Litter	Date of birth	Age (y) of queen at birth of litter	No. of pups born	No. of pups weaned	Preweaning mortality (%)
1	7/30/2008	0.96	6	0	100
2	10/15/2008	1.17	9	0	100
3	12/30/2008	1.38	10	2	80
4	6/21/2009	1.85	13	0	100
5	11/25/2009	2.28	NA	0	100
6	2/17/2010	2.51	10	7	30
7[a]	11/22/2010	3.27	15	0	100
8	2/8/2011	3.48	15	0	100
9	7/11/2011	3.91	15	0	100
10	9/27/2011	4.12	10	0	100
11	12/13/2011	4.33	9	0	100
12	2/29/2012	4.54	10	2	80
13	5/19/2012	4.76	2	0	100
14	8/4/2012	4.97	14	0	100
15	10/21/2012	5.18	18	1	94
16[b]	1/8/2013	5.40	18	2	89

Queen 5 was born on 8/15/2007; her current age is 5.9 y, and current average weight is 63 g.
[a]Colony 5 arrived at the University of Rochester on 9/27/2010.
[b]2 pups were cross-fostered to colony 6.

dehydrated. Although colony 6 accepted these PD2 pups, they failed to survive past PD4.

Since the transfer, the 2 fostered pups have been accepted by colony 6. They have been nursed and reared past weaning age. Eventually and alongside of the 8 pups native to colony 6, the 2 fostered pups began eating solid food and begging for feces from older colony members. Although initially smaller than the native pups, the fostered pups became indistinguishable from the native ones by day 44 after fostering (Figure 1). Observations of our NMR colonies demonstrate that most NMR queens have a reduction in milk production 3 wk after parturition. However, queen 6 continued to produce milk until PD32, well past the weaning of her original litter, in response to suckling by the 2 fostered pups.

Discussion

Experimental successful introduction of foreign NMR pups into colonies with pups of the same age has previously been reported.[9] However, the current case is the first instance of the successful introduction and acceptance of NMR pups into a foreign colony wherein the existing pups were of a different age (that is, 14 d older). Our observations indicate that foreign NMR pups can be fostered successfully even though they are younger than pups in the existing colony. Furthermore, the suckling stimulus provided by the younger foreign pups may be sufficient to stimulate milk production in the recipient queen even after her native litter has passed weaning age. In counteracting problems associated with NMR reproduction in captivity, this case can be used as an example of cross-fostering NMR pups to a foreign colony, despite age differences among the pups.

Figure 1. (A) On day 27 after fostering, the younger fostered pups are visibly smaller than their adoptive siblings. (B) By day 44 after fostering, the 2 fostered pups had become indistinguishable from the 8 native pups.

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