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Abstract: Since the publication of the landmark study by O'Brien *et al*. on the lack of genetic variation in cheetahs, a flurry of reports have questioned this work. This skepticism is due, in part, to the acceptance of reciprocal skin grafts between unrelated cheetahs reported by O'Brien *et al*., a phenomenon not previously observed in wild mammals. We performed skin-graft experiments in *Thomomys bottae*, the pocket gopher, in order to repeat this test on an other wild species. Our results indicate that individuals from populations with low levels of genetic variation can have similar major histocompatibility complex (MHC) genotypes, and we believe that the earlier cheetah results, because of their concordance with our work, were real phenomena.

Skin grafts and cheetahs

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SIR — Since the publication of the landmark study by O'Brien *et al.*[1] on the lack of genetic variation in cheetahs, a flurry of reports have questioned this work[2–6]. This scepticism is due, in part, to the acceptance of reciprocal skin grafts between unrelated cheetahs reported by O'Brien *et al.*, a phenomenon not previously observed in wild mammals. Such allogeneic graft acceptance suggests unusual monomorphism at the major histocompatibility complex (MHC), a group of loci responsible for many immune functions. These skin-graft results, a cornerstone of O'Brien *et al.*'s hypothesis on genetic vulnerability, have been criticized for problematic methodology and inconsistencies[3]. Recently, in *Nature*, May[6] and Laurenson *et al.*[7] characterized these trials as "dodgy" and "suspect", respectively, citing concerns first raised by Caughley[3]. Surprisingly, no attempts have been made to repeat this test on other wild species[3].

We performed skin-graft experiments in *Thomomys bottae*, the pocket gopher. The populations of this species together span the range of mean heterozygosities (H) found in all mammals (H = 0.01–0.24)[8]. We trapped individuals from two low-variation populations (Patricks J and Patricks F, $H \approx 0.02$) and one high-variation population (Hastings, $H \approx 0.16$), and performed reciprocal skin grafts on within-population pairs of animals. Each animal received one allograft in addition to an autograft as a control. We monitored grafts for 3 months for signs of rejection. Accepted allografts became indistinguishable from autografts typically within 2 weeks after surgery. The few technical failures caused through graft injury were excluded from our analyses.

Multi-locus DNA fingerprinting analyses were performed on all individuals and band sharing was assessed[9]. Hastings animals showed low band sharing (0.55, $n = 16$), whereas the Patricks J and Patricks F animals showed extreme sharing of bands within populations (0.97, $n = 21$; 0.98, $n = 7$, respectively) but low band sharing between populations (0.31). We used a subset of these animals for skin grafting. Essentially all Patricks J ($n = 14$) and Patricks F ($n = 6$) individuals accepted within-population allografts, whereas Hastings animals ($n = 12$) rejected all such grafts. The difference in acceptance between high- and low-variation populations was highly significant ($\chi^2 = 30$, $P < 0.0001$). To test immunocompetence in the low-variation populations, we gave allografts from Hastings animals to each of three Patricks J and two Patricks F animals that accepted within-population allografts; these grafts were rejected.

Skin graft acceptance is an indicator of genetic near-identity, at least at the MHC. Our results indicate that individuals from populations with low levels of genetic variation can have similar MHC genotypes, and we believe that the earlier cheetah results[1], because of their concordance with our work, were indeed real phenomena. A consequence of such extreme homozygosity could be a loss of fitness caused by a reduction in immune-system pliancy[1,10]. Patricks J and Patricks F gophers, like many endangered species, appear to be highly homozygous, but are not immunocompromised and manage to persist in the wild. Such populations, however, assuming a concordance between MHC variability and disease susceptibility, may be equally vulnerable (or resistant) to particular pathogens.

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