HHS Public Access

Author manuscript

Cold Spring Harb Protoc. Author manuscript; available in PMC 2015 April 06.

Published in final edited form as:

Cold Spring Harb Protoc. ; 2013(4): 312–318. doi:10.1101/pdb.emo071357.

Octodon degus (Molina 1782): A Model in Comparative Biology and Biomedicine

Alvaro Ardiles[1], **John Ewer**[1], **Monica L. Acosta**[2], **Alfredo Kirkwood**[3], **Agustin Martinez**[1], **Luis Ebensperger**[4], **Francisco Bozinovic**[4], **Theresa Lee**[5], and **Adrian G. Palacios**[1,6]

[1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso, 2360102 Valparaíso, Chile [2]Department of Optometry and Vision Science, University of Auckland, Auckland 1142, New Zealand [3]Mind/Brain Institute and Department of Neurosciences, Johns Hopkins University, Baltimore, MD 21218, USA [4]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago 6513677, Chile [5]Department of Psychology & Neuroscience Program, University of Michigan, Ann Arbor, MI, 48109, USA

Abstract

One major goal of integrative and comparative biology is to understand and explain the interaction between the performance and behavior of animals in their natural environment. The Caviomorph, *Octodon degus*, is a native rodent species from Chile, and represents a unique model to study physiological and behavioral traits, including cognitive and sensory abilities. Degus live in colonies and have a well-structured social organization, with a mostly diurnal–crepuscular circadian activity pattern. More notable is the fact that in captivity, they reproduce and live for between 5 and 7 years and exhibit hallmarks of neurodegenerative diseases (including Alzheimer's disease), diabetes, and cancer.

BACKGROUND

The Octodontidae family (Rodentia) is endemic to South America and exhibits a wide range of diversity, from its genes to its communities. Octodontidae fossil records go back to the last Eocene, around 40 million years ago. Currently, they are dispersed in north and central Chile from sea level to approximately 3500 m altitude, with microhabitats in matorral (bush) with evergreen sclerophyllous shrubs over a seasonal herbaceous layer. This environment forms a characteristic South American scrub ecosystem with diverse flora and fauna. The Octodontidae includes nine species (Spotorno et al. 1995), with a unique morphological gradient ranging from cursorial/generalist to subterranean. The number of chromosomes varies among Octodontidae species from 38 (2N) to 102 and the phylogenetic relationship of Octodontidae has been established by cladistics analysis (Honeycutt et al. 2003). The monophyletic *Octodon* genus has three species: the common *O. degus*, *O. lunatus*, and *O. bridgesi*. All are endemic to Chile and related to the Chinchilloidea and Cavioidea families

[6]Correspondence: adrian.palacios@uv.cl.

(Opazo et al. 2005). *Octodon degu* is a small, diurnal, herbivorous rodent that lives in social groups (see Fig. 1).

SOURCES AND HUSBANDRY

The accompanying protocol, Husbandry and Breeding in the *Octodon degus* (Molina1782) (Palacios and Lee 2013), describes successful husbandry and breeding practices based on the experience of the University of Michigan degu colony.

USES OF THE DEGU AS AN ANIMAL MODEL

Eye and Vision

Octodon degus is a diurnal–crepuscular rodent with dichromatic vision. The ratio and distribution of retinal rods and cones varies substantially depending on habitat and life style (Peichl et al. 2005). Degus' retina presents M-cones with green sensitivity (λ_{max} = 510 nm) and S-cones with ultraviolet (UV) sensitivity (λ_{max} = 370 nm), which is unique for a diurnal rodent. In the majority of rodent taxa, S-cones have blue sensitivity, depending on the amino acids present at a few key positions. Degus' UV cones were confirmed by electroretinography (ERG) (Chavez et al. 2003), behavior, immunocytochemistry (Jacobs et al. 2003), and partial opsin sequences (Schleich et al. 2010). Why some rodents have UV versus violet-sensitive cones is not known, but it is speculated to be useful for sexual selection, navigation, foraging, object, and urine detection (Chavez et al. 2003; Goldsmith 1994). The degu is a social rodent and uses common trails, scent marked with urine and feces, to move in their territory. Furthermore, fresh urine in degus has a strong UV reflectance whereas old dry urine does not, and their complementary set of cones could reliably distinguish between both types of urine, creating a critical communicative role of scent marking with UV reflecting urine (Chavez et al. 2003).

Chronobiology

The degu has attracted the attention of chronobiologists because it displays a variable chronotype. *Chronotype* refers to the time of day when animals are active. For example, most humans express a diurnal chronotype, as they are normally active during the day. In general, the chronotype is a feature of the genus and is relatively invariant. Degus are an exception: they can display a diurnal chronotype, unlike the majority of rodents, which are nocturnal. Furthermore, this chronotype can vary among animals of the same colony and even in a given animal depending on environmental conditions. Thus, within a colony some animals may be preferentially diurnal, whereas others may be nocturnal or even crepuscular (i.e., mostly active during the start and/or the end of the day) (Kas and Edgar 1999; Vivanco et al. 2007). In field studies, degus forage above ground mostly during the day when temperatures are low (and days are short), whereas they become crepuscular as ambient temperatures rise (and days lengthen) (Bozinovic et al. 2004). This switch can be induced in the laboratory by increasing daytime temperatures (Vivanco et al. 2010), suggesting that degus' temporal niche is very sensitive to environmental temperature. Further plasticity of the degu chronotype can be observed in a laboratory setting: in the presence of a running wheel, diurnal degus can, paradoxically, switch to a strictly nocturnal chronotype in one

cycle, a phase preference that is then maintained under conditions of constant darkness and temperature, which suggests that it is not simply caused by masking (Kas and Edgar 1999).

The chronotypic plasticity of degus is unusual and is of interest because the basis of an animal's chronotype is unknown. In particular, it appears that the phase of the central pacemaker in the suprachiasmatic nucleus (SCN) is very similar in diurnal and nocturnal animals, raising the question of where and how the chronotype is encoded. In this regard, studies on *per2* clock gene expression show that *per2* cycling outside of the SCN is in the opposite phase compared to that of a nocturnal rodent (*Rattus norvegicus*), suggesting that the chronotype is set “downstream’ of the SCN (Vosko et al. 2009). The existence of diverse chronotypes and plasticity within a given colony raises the possibility of determining the genetic bases of this diversity using methods similar to those originally used to identify the hamster *clock* gene, which do not rely on the existence of a sequenced genome (Lowrey et al. 2000). (However, sequencing of the degu's genome is in progress; see below). See Lee (2004) for a discussion of other interesting aspects of degu circadian rhythms not discussed here.

Ecological Physiology

The balance between acquisition and expenditure of energy depends on the interplay between intake, processing, and allocation to alternative functions such as thermoregulation, reproduction, and others. The ecological physiology of degus populations, in the seasonal Mediterranean and semiarid environment of Chile, indicates that degus’ thermal opportunities for activity shift seasonally/spatially along with the habitat's biotic and abiotic conditions (Bozinovic and Vásquez 1999). Seasonal changes in the availability and quality of food affect foraging, digestion, and nutritional ecology (Bozinovic 1995), as well as the level of seasonal and spatial metabolic expenditure (Bozinovic et al. 2009). Such flexibility in the timing of activity allows degus to maintain a thermal homeostasis and energy balance throughout the year and in different localities (Kenagy et al. 2002). Bozinovic et al. (2004) showed that field metabolism in free-living degus varied seasonally but was lower in summer (non-breeding season). This indicates that degus show physiological flexibility and can shift between various categories of energy expenditure (Naya et al. 2004) that allow them to manage their overall energy balance by minimizing total expenditure, recycling micronutrients through coprophagy (Kenagy et al. 1999), and saving water. In a seasonal field and integrative study at cellular and organismal levels, Bozinovic et al.. (2003) found that rates of water fluxes were significantly lower in summer than winter. Overall, the high phenotypic flexibility of degus may allow them to adjust to changing biotic and abiotic environmental conditions in time and space.

Social and Cognitive Behavior

Degus may form kin-related or unrelated social groups consisting, on average, of 1 male and 1–3 females (Ebensperger et al. 2004). Degus are plurally breeding rodents with communal care, meaning that multiple lactating females share underground nests and rear their litters communally (Ebensperger et al. 2002, 2007). Thus, suppression of reproduction does not seem to occur, given that all members of a female group exhibit signs of pregnancy and lactation (Ebensperger et al. 2011). Laboratory studies indicate that females provide

communal care to their offspring and transfer immunoglobulin to their young during pregnancy and lactation (Becker et al. 2007). Degus also engage in other forms of communal care, including huddling and retrieving of non-descendent offspring (Ebensperger et al. 2010). Natural populations are located throughout central Chile where females typically breed once per year in late autumn (May–June) and after a relatively long gestation (2–3 mo) give birth to litters of precocious offspring in late winter to early spring (September–October) (Ebensperger and Hurtado 2005). This breeding schedule is surprising, given the observation that 85–90% of female and male adults do not survive to their second year of age (Ebensperger et al. 2009), a finding that contrasts with the several years of life reported for these animals under laboratory conditions. Most likely, this difference reflects major negative effects of environmental conditions, including predators and temporal variation in critical resources such as food availability.

When it comes to drivers of sociality, several benefits have been identified as ecological causes of degu group living, including decreased predation risk, decreased costs of thermoregulation, and decreased costs of burrow excavation (Canals et al. 1989; Ebensperger and Bozinovic 2000). However, field and laboratory studies have revealed that direct fitness either decreases or does not change with increasing group size in degus (Hayes et al. 2009). Thus, potential benefits thought to help degus from group living do not translate into fitness gains in current day populations. Current research is aimed at examining how attributes of social groups (such as membership stability, kinship) and individual variation within groups predict fitness effects of sociality (L.A. Ebensperger and L.D. Hayes, personal communication).

Because of their highly evolved social organization, which many times resembles that of humans, degus have been proposed as a new behavioral model to study social-affective neuroscience (Colonnello et al. 2011). In this regard, Braun (2011), through a series of studies using infant degus, demonstrated that repeated parental separation or deprivation of paternal care impairs neuronal connections and produces a set of neurochemical and neuroanatomical modifications in the limbic system. In fact, both infant and juvenile degus exhibit strong social bonds and attachments, and develop robust distress responses, decreased social motivation, and impaired emotional behavior to maternal separation and deprivation of interactions with peers (Colonnello et al. 2011). Together these findings support the degu as a model for the study of social and emotional behavior under stressful conditions, and offer the opportunity to investigate human psychopathologies, such as attention deficit hyperactivity disorder, depression, schizophrenia, and anxiety disorders. In this context, Popovic et al. (2009) found an age effect on the behavioral performance using tests to evaluate anxiety, recognition, and fear memory. Accordingly, degus show a reduction in recognition and spatial memory as they age, indicating a reduction of cognitive function with aging (Braidy et al. 2012; Ardiles et al. 2012). Finally, degus can be trained to manipulate objects and learn to use tools (Tokimoto and Okanoya 2004; Okanoya et al. 2008), and show cognitive capacities observed in higher animals, thereby providing an animal model to evaluate complex tasks and extrapolate to the higher mental capacities of humans. Taken together, degus remain an intriguing animal model that challenges life history and animal sociality theories.

Pathobiology of Diseases

Diabetes—Molecular and histological evidence suggests that in these rodents, there is a natural resistance to insulin due to their lower metabolic activity and their reduced insulin receptor binding affinity. In captured degus, glucose levels are similar to other mammals (Opazo et al. 2004) and the glucose intolerance of the species stems from the different physiological activity of insulin and the general failure of their pancreas (Spear et al. 1984). The degu certainly has a strong predisposition to diabetes as a result of this insulin-reduced activity, but reports on Langerhans islet amyloidosis (Nishi and Steiner 1990) and cytomegalovirus associated insulitis (Fox and Murphy 1979) suggest that pancreatic activity in general is compromised in this species. In their natural environment, the degus do not always develop diabetes. This is likely to be the result of a diet of natural pastures rich in proteins and low in carbohydrates. In the laboratory environment, a slight change in carbohydrate intake leads to development of persistent hyperglycemia and glycosuria (Murphy et al. 1978). Animals fed a diet of simple fruit sugars can readily develop diabetes mellitus along with kidney damage and cataracts (Edwards 2009). The high susceptibility of this animal to develop diabetes shortly after streptozotocin injections, or secondary to minimal changes in its diet, makes it an attractive animal model for the study of the pathophysiology of diabetes mellitus.

On the other hand, recent evidence reported by Homan et al. (2010) indicates that degus may develop atherosclerosis when they are fed a cholesterol-rich diet. Indeed, degus display a similar lipoprotein metabolism to humans, and remarkably also develop hyperglycemia. These studies confirm that *degus* are a suitable natural animal model to study human diseases. This strong similarity between degus and humans provides a unique comparative model when researching strategies and therapies.

Lens—It has been proposed that degus are particularly well suited as an animal model for the study of lens opacities, which develop naturally in laboratory bred animals. Worgul and Rothstein (1975) found that degus have an increased susceptibility to cataract development where there is significant disorganization of the lens epithelium, even before opacity. In this study the authors did not identify the cause of the cataracts, although they did note that the degus were diabetic. Other studies have also indicated that cataracts develop in the degu secondarily to diabetes mellitus (Brown and Donnelly 2001). In fact, the development of cataracts in this species may be related to the disruption of glucose metabolism. It is known that glucose transport into the lens is insulin-independent, regulated by glucose transporters and metabolically processed through the glycolytic and pentose phosphate pathways. A third pathway for glucose metabolism, the polyol or sorbitol pathway, is found in the lens in degus and humans (Barker et al. 1983), and may account for 5% of glucose processing. One possible cause of the increased susceptibility of these animals to develop cataracts is the increased aldose reductase activity within the lens, comparable to humans (Varma et al. 1977). The inhibition of this enzyme, via administration of quercitrin, caused a delay in cataract formation in the degu. In addition, high levels of alditol observed in 6-mo-old degu lens (Barker et al. 1983) are also found in the human lens. The fact that these animals develop cataracts shortly after being made diabetic by injection of streptozotocin, suggests that the degu is a natural model for the study of diabetic cataracts.

Alzheimer's Disease—Recently, the interest in degus as a model has expanded to the study of brain alterations that occur during aging and, in particular, the neurodegeneration that occurs in Alzheimer's disease (AD). In 2005, Inestrosa et al. reported that degus exhibit pathological hallmarks of AD, based on the high homology (97.5%) between human and degus amyloid-β-peptide (Aβ) sequences. They showed that aged degus display both intracellular and extracellular deposits of Aβ, intracellular accumulations of tau-protein and ubiquitin, a strong astrocytic response and acetylcholinesterase-rich pyramidal neurons, suggesting that degus could represent a new natural model for sporadic AD. Supporting these findings, van Groen et al. (2011) found that 6-year-old degus develop Aβ and tau deposits in the hippocampus, preceded by Aβ deposits in blood vessel walls at 3 years of age. This indicates that the pathology of the brain parenchyma was preceded by cerebral amyloid angiopathy. We have recently demonstrated that degu develop synaptic changes related to AD, which explains the early cognitive and neural plasticity impairments observed before the appearance of fibrillar deposition (Ardiles et al. 2012). We found a selective postsynaptic deficiency in those degus who showed elevated amyloid oligomers and tau phosphorylation levels, predominantly in aged, but not in young degus. Interestingly, these data are in agreement with those obtained using transgenic mice models bearing mutations related to familial AD, in which the overexpression of human amyloid precursor protein leads to the early accumulation of soluble Aβ oligomers and memory failures.

GENETICS AND GENOMICS RESOURCES

Some of the particularities of *Octodon degus* discussed above may have a genetic basis and access to the sequence of its genome could be very informative. This line of inquiry will soon be rewarded, thanks to an ongoing effort from the Broad Institute (Cambridge, MA, USA) to sequence this rodent's genome (see http://www.ncbi.nlm.nih.gov). Currently only a draft genome exists and only trace sequences are available, but one can assume that the assembly of the complete genomic sequence will occur soon. Analysis of these sequences may provide unique insights into the genetic bases of diseases and phenotypes discussed above, and produce specific hypotheses to guide future research.

ACKNOWLEDGMENTS

We thank Leo Peichl for joint collaboration and discussion of degus vision. This work was partially supported by grants from NIH-FIRCA, FONDECYT # 1110292, CINV-UV ICM-P09-022-F.

REFERENCES

Ardiles AO, Tapia-Rojas CC, Mandal M, Alexandre F, Kirkwood A, Inestrosa NC, Palacios AG. Post-synaptic dysfunction is associated with spatial and object recognition memory loss in a natural model of Alzheimer's disease. Proceedings of the National Academy of Science. 2012; 109:13835–13840.

Barker SA, Fish FP, Tomana M, Garner LC, Settine RL, Prchal J. Gas chromatographic/mass spectrometric evidence for the identification of a heptitol and an octitol in human and *Octodon degu* eye lenses. Biochem Biophys Res Commun. 1983; 116:988–993. [PubMed: 6651856]

Becker MI, De Ioannes AE, León C, Ebensperger LA. Females of the communally breeding rodent, *Octodon degus*, transfer antibodies to their offspring during pregnancy and lactation. J Reprod Immunol. 2007; 74:68–77. [PubMed: 17276515]

Bozinovic F. Nutritional energetics and digestive responses of an herbivorous rodent (*Octodon degus*) to different levels of dietary fiber. J Mammal. 1995; 76:627–637.

Bozinovic F, Vásquez RA. Patch use in a diurnal rodent: handling and searching under thermoregulatory costs. Funct Ecol. 1999; 13:602–610.

Bozinovic F, Gallardo PA, Visser RH, Cortés A. Seasonal acclimatization in water flux rate, urine osmolality and kidney water channels in free-living degus: molecular mechanisms, physiological processes and ecological implications. J Exp Biol. 2003; 206:2959–2966. [PubMed: 12878664]

Bozinovic F, Bacigalupe LD, Vasquez RA, Visser GR, Veloso C, Kenagy GJ. Cost of living in free-ranging degus (*Octodon degus*): seasonal dynamics of energy expenditure. J Comp Biochem Physiol A. 2004; 137:597–604.

Bozinovic F, Rojas JM, Broitman BR, Vasquez RA. Basal metabolic rate in correlated with habitat productivity among populations of degus (*Octodon degus*). J Comp Biochem Physiol A. 2009; 152:56–564.

Braidy N, Muñoz P, Palacios AG, Castellano-Gonzalez G, Inestrosa NC, Chung RS, Sachdev P, Guillemin GJ. Recent animal models For Alzheimer's disease: Clinical implications and basic research. J Neural Trans. 2012; 119:173–195.

Brown C, Donnelly TM. Cataracts and reduced fertility in degus (*Octodon degus*). contracts secondary to spontaneous diabetes mellitus. Lab Anim (NY). 2001; 30:25–26. [PubMed: 11395944]

Canals M, Rosenmann M, Bozinovic F. Energetics and geometry of huddling in small mammals. J Theoret Biol. 1989; 141:181–189. [PubMed: 2632987]

Chávez AE, Bozinovic F, Peichl L, Palacios AG. Reflectance in the genus *Octodon* (Rodentia): Implications for visual ecology retinal spectral sensitivity, fur coloration and urine. Invest Ophthalmol Vis Sci. 2003; 44:2290–2296. [PubMed: 12714673]

Colonnello V, Iacobucci P, Fuchs T, Newberry RC, Panksepp J. *Octodon degus*. A useful animal model for social-affective neuroscience research: basic description of separation distress, social attachments and play. Neurosci Biobehav Rev. 2011; 35:1854–1863. [PubMed: 21477615]

Ebensperger LA, Bozinovic F. Communal burrowing in the hystricognath rodent, *Octodon degus*: a benefit of sociality? Behav Ecol Sociobiol. 2000; 47:365–369.

Ebensperger LA, Hurtado MJ. Seasonal changes in the time budget of degus, *Octodon degus*. Behaviour. 2005; 142:91–112.

Ebensperger LA, Chesh AS, Castro RA, Ortiz Tolhuysen L, Quirici V, Burger JR, Hayes LD. Instability rules social groups in the communal breeder rodent *Octodon degus*. Ethology. 2009; 15:540–554.

Ebensperger LA, Chesh AS, Castro RA, Ortiz Tolhuysen L, Quirici V, Burger JR, R Sobrero R, Hayes LD. Burrow limitations and group living in the communally rearing rodent, *Octodon degus*. J Mammal. 2011; 92:21–30. [PubMed: 22328789]

Ebensperger LA, Veloso C, Wallem PK. Do female degus communally nest and nurse their pups? J Ethol. 2002; 20:143–146.

Ebensperger LA, Hurtado MJ, León C. An experimental examination of the consequences of communal versus solitary breeding on maternal condition and the early postnatal growth and survival of degu, *Octodon degus*, pups. Anim Behav. 2007; 73:185–194.

Ebensperger LA, Ramírez-Otarola N, León C, Ortiz ME, Croxatto HB. Early fitness consequences and hormonal correlates of parental behaviour in the social rodent, *Octodon degus*. Physiol Behav. 2010; 101:509–517. [PubMed: 20688088]

Edwards MS. Nutrition and behavior of degus (*Octodon degus*). Vet Clin North Am Exot Anim Pract. 2009; 12:237–53. [PubMed: 19341951]

Fox JG, Murphy JC. Cytomegalic virus-associated insulitis in diabetic octodon degus. Vet Pathol. 1979; 16:625–628. [PubMed: 224559]

Goldsmith TH. Ultraviolet receptors and color vision: evolutionary implications and a dissonance of paradigms. Vision Res. 1994; 34:1479–1487. [PubMed: 8023460]

Hayes LD, Chesh AS, Castro RA, Tolhuysen LO, Burger JR, Bhattacharjee J, Ebensperger LA. Fitness consequences of group living in the degu *Octodon degus*, a plural breeder rodent with communal care. Anim Behav. 2009; 78:131–139.

Homan R, Hanselman JC, Bak-Mueller S, Washburn M, Lester P, Jensen HE, Pinkosky SL, Castle C, Taylor B. Atherosclerosis in *Octodon degus* (degu) as a model for human disease. Atherosclerosis. 2010; 212:48–54. [PubMed: 20630529]

Honeycutt RL, Rowe DL, Gallardo MH. Molecular systematics of the South American caviomorph rodents: relationships among species and genera in the family Octodontidae. Mol Phyl Evol. 2003; 26:476–489.

Inestrosa NC, Reyes AE, Chacon MA, Cerpa W, Villalon A, Montiel J, Merabachvili G, Aldunate R, Bozinovic F, Aboitiz F. Human-like rodent amyloid-beta-peptide determines Alzheimer pathology in aged wild-type Octodon degu. Neurobiol Aging. 2005; 26:1023–1028. [PubMed: 15748782]

Jacobs GH, Calderone JB, Fenwick JA, Krogh K, Williams GA. Visual adaptations in a diurnal rodent, Octodon degus. J Comp Physiol A. 2003; 189:347–361.

Kas MJ, Edgar DM. A nonphotic stimulus inverts the diurnal–nocturnal phase preference in *Octodon degus*. J Neurosci. 1999; 19:328–333. [PubMed: 9870962]

Kenagy GJ, Veloso C, Bozinovic F. Daily rhytms of food intake and feces reingestion in the degu, an herbivorous Chilean rodent: optimizing digestion through coprophagy. Physiol Biochem Zool. 1999; 72:78–86. [PubMed: 9882606]

Lee TM. *Octodon degus*: a diurnal, social, and long-lived rodent. Ilar J. 2004; 45:14–24. [PubMed: 14752204]

Lowrey PL, Shimomura K, Antoch MP, Yamazaki S, Zemenides PD, Ralph MR, Menaker M, Takahashi JS. Positional syntenic cloning and functional characterization of the mammalian circadian mutation *tau*. Science. 2000; 288:483–492. [PubMed: 10775102]

Murphy JC, Niemi SM, Hewes KM, Zink M, Fox JG. Hematologic and serum protein reference values of the octodon degus. Am J Vet Res. 1978; 39:713–715. [PubMed: 646210]

Naya DE, Ebensperger LA, Sabat P, Bozinovic F. Digestive and metabolic flexibility allows female degus to cope with lactation costs. Physiol Biochem Zool. 2008; 81:186–194. [PubMed: 18190284]

Nishi M, Steiner DF. Cloning of complementary DNAs encoding islet amyloid polypeptide, insulin, and glucagon precursors from a new world rodent, the degu, octodon degus. Mol Endocrinol. 1990; 4:1192–1198. [PubMed: 2293024]

Okanoya K, Tokimoto N, Kumazawa N, Hihara S, Iriki A. Tool-use training in a species of rodent: the emergence of an optimal motor strategy and functional understanding. PLoS One. 2008; 3:1860.

Opazo JC. A molecular timescale for caviomorph rodents (Mammalia, Hystricognathi). Mol Phylogenet Evol. 2005; 37:932–937. [PubMed: 16085429]

Opazo JC, Soto-Gamboa M, Bozinovic F. Blood glucose concentration in caviomorph rodents. Comp Biochem Physiol A. 2004; 137:57–64.

Palacios AG, Lee TM. Husbandry and breeding in the *Octodon degus* (Molina1782). Cold Spring Harb Protoc. 2013 doi: 10.1101/pdb.prot073577.

Peichl L, Chavez AE, Ocampo A, Mena W, Bozinovic F, Palacios AG. Eye and vision in the subterranean rodent cururo (*Spalacopus Cyanus*, Octodontidae). J Comp Neurol. 2005; 486:197–208. [PubMed: 15844175]

Popovic N, Bano-Otalora B, Rol MA, Caballero-Bleda M, Madrid JA, Popovic M. Aging and time-of-day effects on anxiety in female *Octodon degus*. Behav Brain Res. 2009; 200:117–121. [PubMed: 19162080]

Schleich C, Vielma A, Palacios AG, Peichl L. The retinal photoreceptors of two subterranean tuco–tuco species (Rodentia, Ctenomys): Morphology, topography and spectral sensitivity. J Comp Neurol. 2010; 518:4001–4015. [PubMed: 20737597]

Spear GS, Caple MV, Sutherland LR. The pancreas in the degu. Exp Mol Pathol. 1984; 40:295–310. [PubMed: 6144570]

Spotorno AE, Walter L, Contreras LC, Torres-Mura JC, Fernández-Donoso R, Berríos MS, Pincheira J. Chromosome divergence of *Octodon lunatus* and the origins of Octodontoidea (Rodentia, Hystricognathi). Rev. Chilena Hist Nat. 1995; 68:227–239.

Tokimoto N, Okanoya K. Spontaneous construction of “Chinese boxes” by Degus (Octodon degu): A rudiment of recursive intelligence?1. Japanese Psychol Res. 2004; 46:255–261.

van Groen T, Kadish I, Popovic N, Popovic M, Caballero-Bleda M, Bano-Otalora B, Vivanco P, Rol MA, Madrid JA. Age-related brain pathology in Octodon degu: blood vessel, white matter and Alzheimer-like pathology. Neurobiol Aging. 2011; 32:1651–1661. [PubMed: 19910078]

Varma SD, Mizuno A, Kinoshita JH. Diabetic cataracts and flavonoids. Science. 1977; 195:205–206. [PubMed: 401544]

Vivanco P, Ortiz V, Rol MA, Madrid JA. Looking for the keys to diurnality downstream from the circadian clock: role of melatonin in a dual-phasing rodent, *Octodon degus*. J Pineal Res. 2007; 42:280–290. [PubMed: 17349027]

Vivanco P, Rol MA, Madrid JA. Temperature cycles trigger nocturnalism in the diurnal homeotherm *Octodon degus*. Chronobiol Int. 2010; 27:517–534. [PubMed: 20524798]

Vosko AM, Hagenauer MH, Hummer DL, Lee TM. period gene expression in the diurnal degu (*Octodon degus*) differs from the nocturnal laboratory rat (*Rattus norvegicus*). Am J Physiol Regul Integr Comp Physiol. 2009; 296:R353–R361. [PubMed: 19036829]

Worgul BV, Rothstein H. Congenital cataracts associated with disorganized meridional rows in a new laboratory animal: The degu (*Octodon degus*). Biomedicine. 1975; 23:1–4. [PubMed: 1174633]

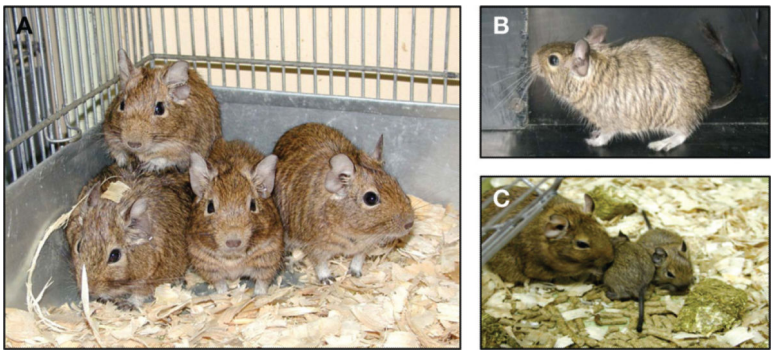

FIGURE 1.

(*A–B*) Adult degus in a house cage in the animal breeding facility. (*C*) Female degus contribute to the rearing of all pups in the communal nest, and closely attend to the pups who remain in the nest until they reach 2 wk of age.