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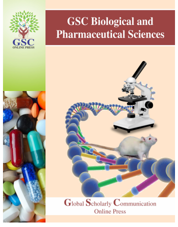

(REVIEW ARTICLE)

Overview of African naked mole-rat *Heterocephalus glaber* for bioprospecting and access and benefit sharing in Ethiopia

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Abstract

Biodiversity in developing countries such as Ethiopia has been accessed for a long time, for various purposes, by outside researchers and private companies with little or no returns to conservation activities and with no equitable sharing of the benefits resulting from the commercial use of genetic resources. Ethiopia now aims to conserve, sustainably use and share the benefits from bioprospecting of its richer biodiversity by developing legislations which practically put in place the contents of basic principles of the international treaties such as the Convention on Biological Diversity and the Nagoya Protocol. Bioprospecting of potentially valuable genetic resources from the country's biodiversity-rich regions can bring monetary and non-monetary benefits from users, bioprospectors and investors. This review also aims to have an overview of the really bizarre looking, little explored and economically important rodent animal, the East African naked mole-rat, *Heterocephalus glaber*, from the Horn of Africa, for Bioprospecting and Access and Benefit Sharing in Ethiopia. It reveals that this animal has lots of peculiar morphological, physiological, ecological and environmental adaptations, which attract the attention of outside researchers to conduct analgesic, anti-cancer and anti-aging and various other innovative scientific researches, or invite bioprospectors to undergo medicinal, pharmaceutical and industrial bioprospecting on the animal genetic resource. However, any research and development studies related with animal bioprospecting in Ethiopia should be complemented by the conservation, sustainable utilization of biodiversity, and the access and benefit sharing of this animal genetic resource.

Keywords: Access and Benefit Sharing; African naked mole-rat; Bioprospecting; Ethiopia; *Heterocephalus glaber*

1. Introduction

For millennia, people around the world have studied nature as part of humanity's never-ending search for new ways to improve crops for food production, to combat disease and other maladies, and to make other discoveries that might enhance the overall quality of life on Earth. Our early ancestors explored biodiversity and learned how to derive benefits from nature. Nowadays, biodiversity or biological diversity is defined as the variability among living organisms from all sources including, *inter alia*, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity or variability within species, between species and of ecosystems [1]. The Convention on Biological Diversity (CBD) defines biological resources to include genetic resources, organisms or parts thereof, populations, or any other biotic component of ecosystems with actual or potential use or value for humanity. It also defines genetic resources to mean genetic material of actual or potential value [1].

Bioprospecting denotes an activity that involves the search of biodiversity for valuable genetic or biochemical resources or information or both for purely scientific research or commercial purposes [2, 3]. It aims at the search for

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identification, collection, extraction, screening and procuring any biological or genetic resource samples that have actual or potential use or value for humanity [4]. Bioprospecting uses biological and genetic resources of any organism (plant, animal or microbe) for scientific research or commercial development. In recent years bioprospecting has acquired increased attention as countries inquire about to conserve their biodiversity and share the benefits from bioprospecting [5]. Agreements are taken as a means of improving national capacities of developing countries to add value to natural resources and share benefits with developed countries at the same time ensuring that these resources are protected and used sustainably [6].

This review aims to examine first the developments made over years in bioprospecting to meet with the objectives of international treaties such as the CBD so as to conserve and sustainably use biodiversity and share the benefits resulting from the commercial use of genetic resources. It also indicates how the access and benefit sharing provisions have been implemented into the national laws of Ethiopia so that a range of possible kinds of benefits could be derived from the utilization of the country's wide range of potentially valuable genetic resources. The review then deals with an overview of the really bizarre looking and economically important rodent animal from the Horn of Africa, the East African naked mole-rat, *Heterocephalus glaber*, which is to be called for bioprospecting and access and benefit sharing in Ethiopia.

2. Developments in bioprospecting

2.1. Conceptual framework of bioprospecting

Today's bioprospecting" was developed from a concept of "chemical prospecting" originally introduced in 1989 [7] and redefined in 1993 as "bioprospecting" or "biodiversity prospecting" - a term which applies to the exploration and utilization of the biological diversity or the potentially valuable genetic resources and biochemical compounds in nature for commercial purposes, either within the context of indigenous as well as traditional medical knowledge or without [7, 8]. It embraces systematic field explorations of biodiversity to seek and document indigenous/traditional medical knowledge and/or the biodiversity with which the indigenous/traditional medical knowledge is attached, and its conversion into a commercialized product [9]. Getachew Mengiste [4] defined bioprospecting as the search for, identification, collection, extraction and screening of biological resource samples that have commercial value that can directly be sold or developed for eventual sale.

Bioprospecting has gained prominence over the centuries due to technological advances in pharmaceutical, biotechnological and agricultural sectors. When the activity of bioprospecting is performed by non-scientists as well as scientists and it involves a large-scale effort to search and commercialize the biological diversity, indigenous as well as traditional medical knowledge, it is called "mass bioprospecting" [9].

2.2. Bioprospecting and international treaties

At earlier times, bioprospecting was considered natural and justified, because the outcome benefits the scientific and general communities, locally and globally. At that time that the world's biodiversity, especially the plant genetic resources with which indigenous as well as traditional medical knowledge is attached, represents a common heritage of mankind and should be available without restriction [9, 10].

Biodiversity in developing countries has been accessed for a long time, for various purposes, by outside researchers and private companies with little or no returns to conservation activities and with no equitable sharing of the benefits resulting from the commercial use of genetic resources. Bioprospecting is carried out by a wide range of established industries such as pharmaceuticals, manufacturing and agriculture, aquaculture, bioremediation, biomining, biomimetic engineering, nanotechnology, construction [11]. For instance, pharmaceutical bioprospecting has been sharply criticized for 'biopiracy', which is unauthorized and uncompensated taking/stealing of genetic or biological resources. This biopiracy also occurs when the bioprospecting is pursued without the knowledge and free prior consent of the owners of the biological resources and without benefit sharing [12, 13]; in which large international pharmaceutical corporations make use of local medicinal knowledge without acknowledging that it is indigenous intellectual property. Profits have accrued solely to the pharmaceutical companies and indigenous people received little or nothing in return [14].

Excessive bioprospecting and biopiracy lead to reduction and loss of floral and faunal biodiversity throughout the world. To alleviate this biodiversity loss and preserve the world's valuable biodiversity, an international treaty known as the Convention on Biological Diversity (CBD) was opened for signature on June 5, 1992 at the UN Earth Summit in Rio de Janeiro, Brazil. In that year, the recognition of ownership of traditional knowledge and the biodiversity to which the knowledge is attached, and the sharing of the benefits that may arise as a result of their utilization was enforced in the form of the United Nations Convention on Biodiversity [5]. The three objectives of the CBD, which are to be met through bioprospecting, are (i) the conservation of biodiversity, (ii) the sustainable use of its components, and (iii) the equitable sharing of the benefits resulting from the commercial use of genetic resources.

After the CBD, the biological resources i.e. the plant, animal and microbial genetic resources are no more considered common heritages. The biodiversity-rich countries have sovereignty rights over their biological or genetic resources as the CBD treaty recognizes their right to regulate and charge outsiders for access to their biodiversity. The CBD [1] also clarified the rights of indigenous people and local communities, and a variety of treaties and national laws have been enacted worldwide to control the use of intellectual property and to establish equitable benefit sharing [14, 15]. Another international treaty, the Nagoya Protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilization to the convention on biological diversity was adopted at the tenth meeting of the conference of the parties on 29 October 2010, in Nagoya, Japan [16]. This Protocol significantly advances the CBD's third objective by providing a strong basis for greater legal certainty and transparency for both providers and users of genetic resources. This Protocol is the instrument for the implementation of the access and benefit-sharing provisions of the convention.

2.3. Benefits of bioprospecting

Bioprospecting can create a venue of revenue generation from potentially valuable genetic resources situated in the South (money-poor, biodiversity-rich countries). In the presence of well-designed laws and contracts, it can generate benefits which can be used for a range of purposes such as improving livelihoods of indigenous and local communities, biodiversity conservation programmes and biotechnological capacity building [7, 17, 18]. The benefits arising from the use of potentially valuable genetic resources could be monetary and/or non-monetary.

2.3.1. Non-monetary benefits from bioprospecting

A range of potential non-monetary benefits could be negotiated in return for access to a particular biological or genetic resource such as: institutional capacity-building; increased connectivity and sharing of research and development results between research entities; joint ownership of intellectual property rights; contributions to the local economy such as employment opportunity, personnel training; facilities and equipment transfer; increased scientific capacity by building a technology infrastructure; increased scientific and public knowledge of the natural environment such as taxonomic information; and the acknowledgment of contributions in publications or joint authorship and joint research [4, 19]. The non-monetary benefits also include, *inter alia*, collaboration, cooperation and contribution in scientific research and development programmes; participation in product development; collaboration, cooperation and contribution in education and training; training related to genetic resources with the full participation of countries providing genetic resources; access to scientific information relevant to conservation and sustainable use of biological diversity, biological inventories and taxonomic studies; institutional and professional relationships that can arise from an access and benefit-sharing agreement and subsequent collaborative activities [16, 20]. Bioprospecting firm often provides free access to its technology, equipment, products, and research results [21].

2.3.2. Monetary benefits from bioprospecting

Monetary benefits may include, *inter alia*, access fees for each sample of genetic resource obtained; up-front payments; royalties; negotiated advance payment; milestone payments; license fees in case of commercialization; special fees to be paid to trust funds supporting conservation and sustainable use of biodiversity; research funding; and joint ownership of relevant intellectual property rights [13, 20, 22]. Monetary benefits can be applied to fund conservation programs, to promote sustainable use of biodiversity, and to develop alternative income-generating schemes.

2.4. Bioprospecting and national laws of Ethiopia

Ethiopia has acceded and ratified the two international treaties related with biodiversity, the CBD in 1994 [23] and its supplementary protocol, Nagoya Protocol on access and benefit sharing in 2012 [24], which could help to obtain benefits from bioprospecting activities. After ratifying those treaties, Ethiopia enacted the proclamation on Access to Genetic Resources and Community Knowledge and Community Rights Proclamation No. 482/2006 [22] and its supplementary Regulation No.169/2009 [25]. These legislations practically put in place the contents of basic principles of the CBD. Although the CBD and Nagoya Protocol do not clearly define what constitutes access, the Ethiopian Proclamation on Access to Genetic Resources and Community Knowledge and Community Rights Proclamation No. 482/2006 [22] defines the term access as the collection, acquisition, transfer or use of genetic resources and/or community knowledge. Since the ratification of the above-stated international treaties, the Ethiopian Biodiversity Institute (EBI) which had been established with the objectives of conservation, sustainable utilization and access and benefit sharing [26] was designated as a National Focal Point and Competent National Authority on access and benefit sharing issues [ABSCH, https://absch.cbd.int/countries/ET, Last accessed on 25/05/2018].

Since 2012, the EBI had an access and benefit sharing (ABS) directorate, named as Genetic Resources Access and Benefit Sharing Directorate, which plays a major role in the implementation of the Nagoya Protocol on the access to genetic resources and associated traditional knowledge, and the fair and equitable sharing of benefits arising from their utilization to the CBD. The EBI has the authority to grant access permits in accordance with the access law, and follow up their implementation [26]. It grants two different types of access permits: non-commercial access permit for basic research and studies to higher learning institutions and research organizations; and commercial access permit for bioprospecting companies.

Plants, animals and microbes are the basis of many bioprospecting opportunities around the world. The Genetic Resources ABS Directorate of the Ethiopian Biodiversity Institute has started reviewing potential genetic resources of plants, animals and microbes of Ethiopia for bioprospecting and access and benefit sharing since 2012 [Ethiopian Biodiversity Institute website, http://www.ebi.gov.et/identification, Last accessed on 24/05/2018]. Ethiopia can be benefited from its rich biodiversity by providing its potential genetic resources to bioprospecting companies and outside researchers. Though bioprospecting potential of animals has been little explored, compared to plants, studies show that animal genetic resources such as the African naked mole-rats are highly promising in the search for new drugs of medical or pharmaceutical interest [27].

3. Description of the animal genetic resource

There are approximately 30 different kinds of mole-rats. The best known naked mole-rat, the East African naked mole-rat (*Heterocephalus glaber*), which Science Authors [28] named it as the "Vertebrate of the Year 2013", belongs to the Mammalian Order Rodentia and the Family Bathyergidae [29]. According to recent molecular-based phylogenetic analysis, the bathyergids can be divided into six main genera: *Bathyergus, Georychus, Heliophobius, Fukomys, Cryptomys* and *Heterocephalus* [30, 31]. Species among these genera can be split into solitary species, social species and eusocial species. The eusocial taxa consist of the naked mole-rat (*Heterocephalus glaber*) and the Damaraland mole-rat (*Fukomys damarensis*) [32, 33, 34, 35]. The naked mole-rat (*Heterocephalus glaber*) also known as the sand puppy or desert mole-rat, is a burrowing rodent native to parts of East Africa and is the only species currently classified in the Genus *Heterocephalus* [29].

As shown in Figure 1, naked mole-rats have little or no body hair (hence the common name, naked mole-rat). The only hairs that can be found are touch-sensitive hairs like a cat's whiskers, which are used for feeling their way through their tunnels and sensing the space around them. Naked mole-rats have cylindrical bodies with short limbs and purplish brown back and tail. Their skin is wrinkled and loose, which helps them to turn in compact spaces or squeeze through the tiniest of tunnels, and allowing them to maneuver around confined spaces [36, 37].

Figure 1 Dorsal view of East African naked mole-rat (*Heterocephalus glaber*) [38]

The naked mole-rat's cylindrical body is 8 to 10 cm long. Its skinny tail adds 3 to 5 cm of length. It weighs 30 to 35 grams but the queens are larger and may weigh well over 50 grams, the largest reaching 80 grams [37].

They have small eyes and small holes for ears. Their legs are thin and short, but highly adept at moving underground, and moving backward as fast as moving forward through tunnels. Their large incisors protrude or stick out beyond its mouth, which are used to dig. Their lips are sealed just behind the teeth, preventing soil from filling their mouths while digging [36, 37].

4. Food habits

Like many subterranean mammals, naked mole-rats chiefly feed on roots, tubers, and corms of various geophyte plant species [39]. They dig randomly for food with their constantly growing long incisors, in order to find food - roots and tubers from above ground plants. They eat the underground parts, particularly the succulent tubers of the arid growing plant species. They have adapted to survive in the desert by extracting their liquid needs solely from plants. In the wild, they survive on long roots and fat tubers from the grassland plants above and vegetation [36]. Naked mole-rats have high densities of gut fauna that aid in digestion of their indigestible higher cellulose diet. They also regularly practice coprophagy, the reingestion of feces, which allows them to maximize their uptake of nutrients from their food [37].

5. Geographic range

African naked mole-rat has a wider range of distribution. It is found throughout most of Somalia, central Ethiopia, and much of northern and eastern Kenya as shown [40]. The species has also been recorded from Djibouti of an altitudinal range of 400 to 1,500 m above sea level [41, 42].

The naked mole-rat is native to the drier parts of the tropical grasslands of East Africa, predominantly southern and central Ethiopia, Kenya, and Somalia [40, 43]. Clusters averaging 75 to 80 individuals live together in complex systems of burrows in arid African deserts. Mengistu Wale *et al.* [38] reported the distribution of African naked mole-rats in the Oromia Region of Mizan Teferi, Babille and Fadis of Eastern Hararghe, and Somali Region of Ethiopia as shown in Figure 2.

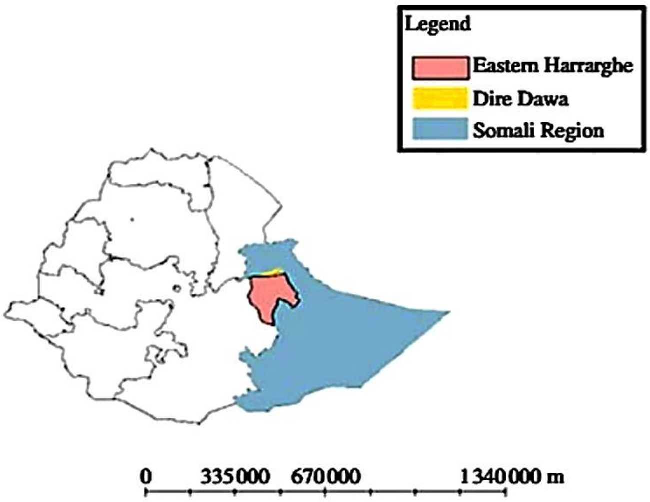

Figure 2 Distribution of African naked mole-rat in Ethiopia [38]

Heterocephalus glaber was identified as a widely distributed pest rodent in the study sites of Dire Dawa Administration, Eastern Ethiopia [44]. Mengistu Wale *et al.* [38] found out that 92% of the Eastern Ethiopian communities in the Eastern Hararghe Zone and Dire Dawa City Administration considered the naked mole-rat as a pest.

6. Habitat and ecology

African naked mole-rats, like other mole-rats species, are obligatory subterranean hystricognath rodents endemic to the Afro-tropical Region i.e. they live underground in arid regions. They occupy dry grasslands and savannas in Ethiopia, Kenya, Djibouti, and Somalia. These naked mole-rats live in arid habitats, characterized by high temperatures and low and irregular rainfall, which generally average 200-400 mm/year. They are found most frequently in hard, consolidated, lateritic loams, but they also live in fine sand, pure gypsum, and laterite [36, 40]. The subterranean habitat provides stable climatic conditions, allowing for an ambient temperature and humidity levels to be maintained in the burrows. Temperature varies from 28 ˚C to 32 ˚C depending upon burrow depth with little seasonal change, while humidity is uniformly high [45, 46]. The burrow temperature and humidity is very stable because there is very little air exchange with the surface, with the burrow air remaining between 30 and 32^{0}C year round [Data Sciences International portal, http://www.datasci.com/solutions/thermoregulation/uncovering-the-secretsof-the-naked-mole-rat, Last accessed on

25/05/2018]. Naked mole-rats live in mazes of tunnels, which can extend for up to 3-5 kilometers, depending on the food availability and the number of individuals composing the colony [47].

7. Behavior

Naked mole-rats are the first and only mammals known to have a colony structure similar to that of social insects such as ants, termites, bees and wasps. This behavior is known as eusociality or eusocial. Naked mole-rats are extremely social and they are the only known eusocial mammals along with its close relative, the Damaraland mole-rat. They live in colonies comprising one breeding female, one to three breeding males, and hormonally-suppressed, non-reproducing workers [32, 36, Data Sciences International, http://www.datasci.com/solutions/thermoregulation/uncovering-the-secretsof-the-naked-mole-rat, Last accessed on 25/05/2018].

These eusocial species live in large colonies averaging between 75 and 80 animals per colony and yet some have up to 300 animals [32, 33, 46]. The colonies are extended family groups, with overlapping generations. The queen rules the land of the large colony. Workers care for the queen and her young; find food for the entire colony; and expand the tunnel system. Large, strong soldiers protect the colony and threaten invaders and predators [34, 35].

8. Reproduction and life span

Reproduction of naked mole-rat is restricted to a single reproductive female i.e. the queen that produces all the young in the colony with two or three breeding males. The species has a gestation length of 66 to 74 days, after which between one and 28 young or pups are born. Females can bear litters every 76 to 84 days, and wild females regularly bear more than 50 pups per year in 4 or 5 litters [32, 36, 40]. The other colony members, non-breeding animals (which are sociologically suppressed by aggressive behaviour of the dominant female) help care for and defend the reproductive animals and young, maintain the colony burrow system and do the digging and other duties, such as colony defense [40]. African naked mole-rat (*Heterocephalus glaber*) is a relatively long-lived species in captivity. They have been reported to live from 23 up to 30/31 years [36, 48].

9. Special adaptations

9.1. Morphological adaptation

Unlike Mammals, which are typically characterized as furry, naked mole-rats have morphologic characteristics such as thick, hairless skin (with little or no body hair), and little subcutaneous fat [49]. Like mammals, they possess brown adipose tissue which is a similar characteristic of homoeothermic species [50]. African naked mole-rats have a good sense of smell, hearing and touch to survive. As they are well-adapted to their underground existence, their eyes are quite small, and thus they are with poor eyesight. They use their whiskers in the dark, and they use face and tail whiskers to feel tunnel walls and while turning. Their thin, hairless skin allows them to cool quickly. They possess long incisors for digging [36, 37].

9.2. Thermoregulatory adaptation

Unlike Mammals, which are typically characterized as homeothermic or warm-blooded, the African naked mole-rat (*Heterocephalus glaber*) is cold-blooded, and thus it is known to be the only poikilotherm mammal. As they live in a very controlled underground environment and being surrounded by hundreds of their members, they have lost the ability to regulate their body temperature physiologically [36]. The high constant ambient temperature maintained in the burrows of the very controlled underground environment is a critical factor for naked mole-rats, as they have a poor thermoregulatory capacity and with a surprisingly low body temperature (approximately 32 °C) in comparison to other fossorial mammals [45]. Consequently, when they get cold, they huddle together [37, 51].

Naked mole-rats are termed thermoconformers rather than thermoregulators in that, unlike other mammals, their body temperature tracks ambient temperatures [Data Sciences International, http://www.datasci.com/solutions/thermoregulation/uncovering-the-secretsof-the-naked-mole-rat, Last accessed on 25/05/2018]. When exposed to temperatures outside their thermoneutral zone (31°C to 34°C), naked mole-rats do not maintain their body temperature, and thus their body temperature follows the ambient temperature [45, 52]. Buffenstein *et al.* [53] suggested this poor thermoregulatory capacity of naked mole-rats as might be due to their low thyroid hormone levels. Some scientists claimed that the naked mole-rats have a distinct temperature and activity rhythm that is not coupled to environmental conditions [Data Sciences International, http://www.datasci.com/solutions/thermoregulation/uncovering-the-secretsof-the-naked-mole-rat, Last accessed on 25/05/2018].

9.3. Adaptation to oxygen availability

The naked mole-rat, as a subterranean species, is well-adapted for the limited availability of oxygen within the tunnels and thus known for its extreme resistance (tolerance) to hypoxia or low oxygen level [54, 55]. Naked mole-rats likely encounter oxygen levels as low as 6% [55] due to a combination of their subterranean, poorly ventilated habitat, and large colony size [31]. The naked mole-rat's ability to deal with sustained low levels of oxygen is aided by blood haemoglobin with higher oxygen affinity than mice [56] thus increasing the efficiency of oxygen uptake and securing oxygen delivery under low oxygen conditions. Moreover, naked mole-rat's hypoxia-tolerance can also be explained by its surprisingly low basal metabolic rate [52, 54, 57], its very small lung and very low respiration, thus using oxygen minimally [37].

10. Scientific research on *Heterocephalus glaber*

10.1. Pain sensitivity

Kanui and Hole [58] reported that opioids such as morphine induce hyperactivity and aggressive behavior but not analgesia in naked mole-rats. The peculiar skin of naked mole-rats does not become hypersensitive when inflamed or exposed to unpleasantly hot objects, even though they react to excessive heat in the same way that other mammals do [59]. Recent studies using the naked mole-rats as a novel model in nociception research have helped to identify some of the molecular mechanisms that drive pain [60].

The skin (cutaneous C-fibers) of naked mole-rats lacks a key neurotransmitter called substance P and calcitonin gene-related peptide that are responsible in mammals for sending pain signals to the central nervous system [61, 62]. However, when naked mole-rats are injected with substance P, the pain signaling works as it does in other mammals, which is suggested as an adaptation to the animal living in high levels of carbon dioxide due to poorly ventilated living spaces, which would cause acid to build up in their body tissues [62]. Naked mole-rats are behaviorally insensitive to histamine-induced itch, which are known to activate peptidergic C-fibers in other mammals. Lack or deficiency of substance P in naked mole-rats has been tied to their lack of the histamine-induced itching and scratching behavior of typical of rodents [63].

The naked mole-rats feel no pain when they are exposed to acid or capsaicin. Petherick [59] reported that nasty stimuli such as acid and capsaicin, the ingredient in chilli peppers that causes a burning sensation in many animals, did not bother the naked mole-rats. Naked mole-rats are also behaviorally insensitive to capsaicin and ammonia fumes, both of which are known to activate peptidergic C-fibers in other mammals [64]. Naked mole-rats are also insensitive to acid-induced pain and acidic fumes [62, 64]. Park *et al.* [62] reported that acid failed to excite the *in vitro* skin-nerve preparation of naked mole-rats sensory neurons which suggests the lack of nocifensive response to acid and the insensitivity of naked mole-rats neurons to acid.

The African naked mole-rat is being targeted for its resistance to pain inflicted by acid. The immunity to feeling pain on skin of naked mole-rats bears vast implications for analgesic drug research-bringing new hope to chronic pain sufferers. Its protein can also be used as a local anesthetic in dentistry [65].

10.2. Resistance to cancer

Naked mole-rats do not develop cancer throughout their long lives [66, 67]. Buffenstein [68] suggested that the cells of naked mole-rats possess anti-tumour capabilities that are not present in other rodents or in humans, and he put the animals as highly resistant to cancer or tumours [68]. According to Seluanov *et al.* [66], the cells of naked mole-rats undergo contact inhibition via the gene p27 which prevents cellular reproduction at a much higher cell density than an "over-crowding" gene p16, a potential mechanism that averts cancer and prevent cell division once individual cells come into contact. The combination of p16 and p27 in naked mole-rat cells is a double barrier to uncontrolled cell proliferation, one of the hallmarks of cancer. Naked mole-rats cells transplanted into immunodeficient mice exhibit a high incidence of crisis [69, 70]. Liang *et al.* [70] investigated the tumorigenicity of naked mole-rat cells expressing oncogene expression SV40 T antigen (LT) and Ras, which commonly leads to tumor formation in mice and rat cells. It has been proposed that the rapid crisis, acting as a tumor suppressor mechanism, form an important component of cancer resistance in the naked mole-rats.

Recent studies suggested that naked mole-rat as a cancer resistant species, with a plethora of different mechanisms that biomedical research might be able to leverage for the treatment of cancer in patients [31].

10.3. Longevity and anti-ageing

Naked mole-rats are extraordinarily long-lived for rodents of their size, with a maximum lifespan of 30 or 31 years - 5 times longer than expected on the basis of body size [36, 71, An Age: The Animal Ageing and Longevity Database, http://genomics.senescence.info/species/entry.php? species=*Heterocephalus glaber*, Last accessed on 25 /05/2018] and hold the record for the longest living rodents [72, 73] and maintain healthy vascular function longer in their lifespan than shorter-living rats [74].

Their extraordinary longevity makes the scientists to expect to find reduced levels of cell-damage and higher levels of anti-oxidant activity in naked mole-rats [36]. Their longevity is thought to be related to their ability to substantially reduce their metabolism during hard times, and so prevent aging-induced damage from oxidative stress [Science Daily, https://www.sciencedaily.com/releases/2007/10/071015225336.htm, Last accessed on 25/05/2018]. Their longevity has also been attributed to protein stability [75]. Naked mole-rats maintain normal activity, body composition, and reproductive and physiological functions with no obvious age-related increases in morbidity or mortality rate for at least 80% of their lives. The physiological and biochemical processes in this species have evolved to dramatically extend both their good health and lifespan [71].

Healy *et al*. [76] suggested the fossorial lifestyle of naked mole-rats and other long-lived rodents as a contributor to the extended lifespan. The Scientists analyzed the age and body mass data of vertebrates including naked mole-rats, taking into account habitat and ecology, and showed that there is a clear correlation between fossorial lifestyle and longer life. However, Williams and Shattuck [77] argued that a more important driver of longevity is eusociality. Using data that included loosely eusocial species (such as wolf, jackal, and coyote), as well as Naked mole-rats and Damaraland mole-rats, the scientists concluded that body mass accounts for about 30% of the variation in maximum lifespan, sociality for 3.3% and habitat for only 0.01% of the effect.

In addition to long life, naked mole-rats also fulfill all criteria associated with negligible senescence: the queen reproduces life-long with fully maintained fecundity, and there is no age-related change in physiological functions or gradual change in mortality rate, as is usually observed in most other species which exhibit a gradual, life-long deterioration [68]. Naked mole-rats also show no age-related changes in basal metabolic rate, body fat, bone mineral density, and only very small changes in cardiovascular and gastrointestinal function and thus exhibit no significant cardiovascular and gastrointestinal aging [78, 79]. Naked mole-rats also show no signs of neurodegeneration [80].

Pérez *et al*. [75] investigated into the molecular adaptations and metabolic changes of naked mole-rats and showed that their resistance to the oxidative stress and dealing with the elevated levels of DNA oxidative damage are determinants of their longevity. Fang *et al*. [81] and MacRae *et al*. [82] suggested that low background mutation rate and low nucleotide diversity of the naked mole-rats genome would point to more efficient DNA damage control.

Owing to their extraordinary longevity and resistance to ageing, scientists have sequenced the genome of the naked mole-rat and used the genomic information to study the mechanisms thought to protect against the causes of ageing, such as DNA repair and genes associated with these processes. Transcriptome sequencing revealed genes related to mitochondria and oxidation reduction processes to have high expression levels in the naked mole-rat when compared to mice, which may contribute to their longevity [83]. Telemetry is also used by scientists as an ideal method to unravel the mystery of naked mole-rats [Data Sciences International, http://www.datasci.com/solutions/thermoregulation/uncovering-the-secretsof-the-naked-mole-rat, Last accessed on 25/05/2018]. Though the naked mole-rats have surprisingly high levels of oxidative stress and relatively short telomeres, they are extremely resilient when subjected to cellular stressors and appear capable of sustaining both their genomic and protein integrity under hostile conditions. Studying these mechanisms will provide useful information for enhancing human life and healthspan, making the naked mole-rat a true “supermodel” for aging research and resistance to chronic age-associated diseases [71].

11. Conservation status and threat

The IUCN Red List of Threatened Species by Maree and Faulkes [42] listed the naked mole-rats as least concern. Currently, naked mole-rats are widespread and numerous in the drier regions of East Africa. In Eastern Ethiopia, they are regarded as pests and are known to eat important agricultural crops such as cassava and sweet potatoes. Naked mole-rats, while they are in their underground network of tunnels, are usually killed by farmers to prevent crop damage.

Mengistu Wale *et al.* [38] identified factors such as agricultural expansion, killing by humans and lack of awareness of this important animal genetic resource as the main threats.

12. Conclusion and recommendation

The East African naked mole-rat, *Heterocephalus glaber*, from the Horn of Africa has a great potential for bioprospecting as well as access and benefit sharing in Ethiopia. Both inside and outside researchers can conduct further analgesic, anti-cancer, anti-aging and various other innovative scientific researches on this animal genetic resource if they apply to the Ethiopian Biodiversity Institute by fulfilling the basic pre-conditions required for non-commercial access application. Bioprospectors, who want to undergo medicinal, pharmaceutical and industrial bioprospecting on the genetic resource, are also highly encouraged to apply to the EBI by fulfilling the basic pre-conditions required for commercial access application. Bioprospecting of this animal is allowed as long as the access to such genetic resources may not cause danger of ecosystem and loss of the biodiversity. Although African naked mole-rats are not threatened at present, they might in the future be experiencing the threat through use and utilization by consumers and bioprospectors. Therefore, any economic development related with bioprospecting of this animal genetic resource can be complemented by conservation and sustainable utilization of its biodiversity. The benefits, either monetary and/or non-monetary, arising from the use of this potentially valuable genetic resource should result in the protection of this animal genetic resource and its habitat, through funding of conservation activities. Moreover, local communities of the region should have the rights to obtain the benefits derived out of the utilization of their genetic resources.

Compliance with ethical standards

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