

# A queen odour mediates reproductive suppression in a eusocial mammal

<https://doi.org/10.1038/s41586-026-10772-5>

Received: 17 September 2025

Accepted: 5 June 2026

Published online: 15 July 2026

Open access

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Eusociality is exceptionally rare in mammals, and its proximate mechanisms remain poorly understood. Naked mole-rats provide a striking example, with reproduction restricted to a single queen, while all other females remain infertile<sup>1</sup>. Here we identify a chemical signal in queens that can regulate this reproductive hierarchy. Isopropyl myristate is a low-volatility ester that is enriched in queens and nearly absent from non-breeding animals. Isopropyl myristate is detected by peripheral and central olfactory neurons and elicits avoidance in high-ranking animals. Exposure alters levels of prolactin and progesterone in non-breeders to suppress reproduction. Daily addition of isopropyl myristate to a queenless colony prevented queen succession, whereas withdrawal triggered aggression and reproductive competition. Isopropyl myristate was also detected in breeding females of several *Fukomys* mole-rat species, but reaches higher levels in naked mole-rats, paralleling their extreme reproductive skew. These findings reveal a chemical cue that can mediate reproductive suppression in a mammal, linking insect and mammalian eusociality.

Naked mole-rats (*Heterocephalus glaber*) are remarkable for their eusocial lifestyle, a rare social structure that is more commonly found in invertebrates such as bees, termites and ants<sup>1,2</sup>. Eusociality is characterized by cooperative care of offspring, overlapping generations and extreme reproductive skew, with reproduction typically monopolized by a dominant breeding female, the queen, who is normally the sole reproducing female in the colony<sup>3–5</sup>. Indeed, naked mole-rats are at the extreme end of a mammalian eusociality spectrum<sup>2</sup>. An essential feature of this complex social organization is the suppression of reproduction among colony members, a process that is primarily regulated by the queen<sup>6</sup>. Despite decades of research following the discovery of eusociality in mammals<sup>1</sup>, the precise mechanism by which queens govern colony structure and suppress reproduction has remained unknown.

Reproductive suppression through chemical communication, particularly via olfactory cues, is a common mechanism by which dominant individuals influence the reproductive physiology of conspecifics<sup>7</sup>. In mammals, olfactory cues can trigger profound reproductive consequences, including pregnancy disruption (the Bruce effect)<sup>8</sup>, suppression of ovulation in subordinates in conjunction with other social cues<sup>9</sup>, and the concealment of oestrus in social carnivores<sup>10</sup>. In eusocial

insects, queen pheromones maintain colony harmony by inhibiting worker reproduction<sup>11,12</sup>, suggesting an evolutionary precedent for chemically mediated reproductive control. In naked mole-rats, reproductive suppression depends on the presence of the queen<sup>1</sup> and is rapidly reversed upon her death or removal<sup>13</sup>. Colonies possess distinct odour signatures that facilitate recognition of nestmates versus outsiders<sup>14,15</sup>, and queen scent correlates with changes in cooperative task performance, suggesting a ‘social organizer’ role<sup>16</sup>. These observations indicate that olfactory communication is central to social cohesion, cooperative behaviour and probably to reproductive suppression, yet the identity and function of a chemical signal produced by queens remained unknown.

Here we combine behavioural, chemical and neuroendocrine analyses to identify and functionally characterize a queen-derived chemical signal in naked mole-rats. We show that olfactory cues underlie social recognition and modulate aggression, and that the long-chain ester isopropyl myristate (IPM) is uniquely present in queens and peaks in vaginal secretions during reproductive readiness. This compound is detected by olfaction, alters prolactin and progesterone levels in non-breeding females, and can prevent reproduction and maintain social stability even after queen removal. These findings reveal a

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