建立裸鼠模型研究鹿茸发育（Development of a Nude Mouse Model for Studying Antlerogenesis）

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摘要 鹿茸生长发育的研究常因所需试验材料只有在特定季节才能获取，以及昂贵的动物饲养管理费用而受到影响。为此我们建立了一个裸鼠模型来解决这一问题。裸鼠为一种免疫缺陷型动物，其可以接受异体移植物。生茸骨膜（AP）和非生茸额骨骨膜（对照）取于三头6到8月龄的仔公赤鹿，然后被分割成小块（4×5mm²）。这些小块骨膜组织，被移植到25到60天龄的公裸鼠头上额部的皮下（一块/鼠，n=24）。裸鼠被饲养在无菌笼中。为刺激实验鼠的睾酮分泌，在每个笼中放入一只母鼠。高水平的睾酮能刺激移植的AP的组织发生。实验鼠每周观察两次，连续观察28周。在屠宰取样前的4小时，腹腔注射Brdu（5'—溴—z'—脱氧尿苷）以定位快速分裂细胞。

形态观察结果表明，只有AP移植的鼠生长了角柄形组织柱。其中有三只鼠还生长了鹿角样（裸露的骨质）组织。与此相反，非生茸骨膜移植鼠只生长了盘状组织隆起。这些隆起远远小于角柄形组织柱。而且在这些组织隆起上没有形成任何鹿角样组织。组织学研究表明，由这些移植AP而形成的组织柱的组织构成（骨，软骨和骨软骨组织）和鹿角柄发育过程中形成的组织一致。Brdu定位的结果显示，绝大多数快速分裂细胞都位于移植AP的细胞层的内层，这正好与角柄、鹿茸形成过程中的研究结果一致。鉴于一头供体鹿能提供AP移植物（具有生成角柄，甚至鹿茸样组织潜力的）给20只裸鼠，我们结论，裸鼠模型是一种除鹿模型本身之外的研究鹿茸发育的既有用又经济的补充，同时也具有开展快速相关鹿茸发育活体研究的潜力。

ABSTRACT Antler studies in deer are limited by the seasonal availability of appropriate tissue，the cost of the animals and the facilities required to keep the numbers needed to carry out satisfactory experiments. We have therefore developed a system for studying antlerogenesis in nude mice. These are an immune－deficient host system，which accepts xenografts. Antlerogenic（AP）and non－antlerogenic frontal periosteum（control）were biopsied from

three 6—or 8—month—old red deer stag calves and cut into small pieces ($4\times5mm^2$). The pieces of periosteum were then transplanted subcutaneously on to the heads of 25—or 60—day old male nude mice (1 piece/mouse, n=24). The mice were kept in cages with one female to maximise testosterone levels, thereby supporting the growth of the deer AP. The mice were observed twice weekly for 28 weeks, then they were injected with BrdU (5'—bromo—2'—deoxyuridine)and killed four bours later, The BrdU is localised in mitotically active cells.

Morphological studies revealed that only AP—grafted mice formed pedicle—shaped protuberances. In three of the mice, antler—like tissue (bane bone) was formed on the top of each pedicle—shaped protuberance after traumatisation. In contrast, the mice implanted with control periosteum formed dish—shaped protuberances, which were much smaller than those implanted with AP, and did not produce antler like tissues. Histological studies confirmed that the tissue components (bone, cartilage and osseocartilaginous tissue) derived from the AP were comparable to those formed during deer pedicle development. BrdU localisation showed that the majority of mitotic cells were located in the inner part of the AP cellular layer, which is the same as during pedicle growth. In view of the fact that one donor deer can supply AP explants with sufficient potential to form pedicle or even antler—like tissue in up to 20 recipient nude mice, we conclude that the nude mouse model is a useful economic alternative for the deer model for studying antlerogenesis in vivo with the potential to carry out rapid, relevant studies.