

# Introduction

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By definition, any study of the mouse anatomy should take into consideration the structure, disposition and shape of the organs that constitute the body of the mouse. Etymologically, the word «anatomy» comes from the Greek, meaning «to cut up». Currently, the dissection procedure is just one of the many that morphologists employ. From its origins, as gross and descriptive anatomy, the concept of anatomy has been enriched with other meanings and approaches, such as functional, comparative, microscopic or applied. In addition, thanks to technological advances in the methods of imaging, we can also talk about other specializations of anatomy, such as radiological anatomy, ultrasound anatomy, etc.

In accordance with the modern definition of anatomy, this book attempts to provide an overview of the different levels of morphology of the mouse. It ranges from gross anatomy and topographical anatomy, to explain the relative position of the organs and structures of a particular body region, down to the microscopic anatomy. In addition, we have also introduced the latest imaging technologies applicable to the study of mouse anatomy, including computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography and angiography.

## ■ ORIGIN OF THE LABORATORY MOUSE

The mouse belongs to the order of rodents and, within this, to the murine family. More specifically, the mouse belongs to the genus *Mus*, which comprises at least a dozen species quite homogeneous in appearance. The origin of the genus *Mus* goes back five million years to Southeast Asia. In fact, the word mouse comes from the Sanskrit word «mush». Later, in Roman times with improved communications and changes in agricultural practices, the mouse spread across Europe and Africa. Within the genus *Mus*, the laboratory mouse belongs to the *Mus musculus* species. Within this species there are four subspecies or populations: *Mus musculus musculus*, which was the first to be described and occupies most of northern Europe and Asia; *Mus musculus domesticus*, which occupies Western Europe, North Africa, the Arabian Peninsula and the Middle East; *Mus musculus castaneus*, which is located in Southeast Asia; and *Mus musculus bactrianus*, which predominates in Iran, Pakistan and India. The subspecies *domesticus* was transported by man to America, Australia and South Pacific countries. There is some controversy about the existence of a fifth subspecies, *Mus musculus*

*molossinus*, which are proposed to inhabit the islands of Japan, although they are generally considered to be a hybrid between *musculus* and *castaneus*.

Mice commonly used in laboratories are mainly derived from the *domesticus* subspecies and to a lesser extent from the *musculus* and *castaneus* subspecies. These lines were created from albino mice, which were used as pets in Egypt. It has been shown that all inbred albino lines carry the same mutation, which occurs very rarely in nature, and they thus represent in a certain way a totally artificial mouse population.

One of the known origins for the use of the mouse as a laboratory animal took place in 1664, when English scientist Robert Hooke used them in his studies of the properties of air. However, it was not until 1902 when their use becomes widespread in genetic studies. It was in this year that Lucien Cuénot first crossed mice carrying recessive mutations related to coat color and showed that Mendel's laws could be applied to animals. At the same time, William Castle began his studies on inheritance in mice, thanks to the generosity of Mrs. Abbie Lathrop, a retired teacher, who kept as an entertainment and small business a mouse breeding farm in Massachusetts. Many of the current laboratory mouse lines were originally derived in her farm. In 1909 C. C. Little and William Castle created the first inbred line for use in cancer research, which today is known as the DBA (Dilute, Brown and non-Agouti) line. It was Little, who went on to found the «Jackson Laboratory» in 1929, who first published crucial data linking genetic inheritance with resistance to growth of certain tumors using these mice. In 1913, J. Hasley Bagg used albino mice for behavioral studies, whereas in 1920, Leonell C. Strong crossed the DBA line with Bagg's albino mice to form hybrids. From these hybrids he developed a series of inbred lines that includes the C3H line. In 1921, Strong further crossed Bagg's albino mice with Little's mice to produce the line A, characterized by a high incidence of breast and lung tumors. In the same year, and operating from Bussey Institute for Research in Applied Biology at Harvard, Little crossed female 57 with male 52 from the farm of Mrs. Lathrop. The mice obtained were segregated into two populations, one black and one brown, thereby creating the respective C57BR and C57BL lines. Subsequently, E. Carleton MacDowell received from C. C. Little the descendants of Lathrop's mice and created the line C58. MacDowell also raised Bagg's albinos and sent some of them to George D. Snell in 1932. Snell used the letter «c» to indicate that the

animals were white and henceforward this albino strain was called BALB/c and is still commonly used today. Swiss albino mice were maintained in colonies that were not inbred (cosanguineous) and are derived from mice that were originally acquired in 1926 by Clara J. Lynch at the Rockefeller Institute from A. Coulon of Lausanne in Switzerland. Descendants of these mice were spread across different laboratories and other lines were created including the SWR/J and SJL/J lines during the 50s. Also in the 50s, to assess the risk of the use of nuclear energy on genetic inheritance, millions of mice were irradiated at the Oak Ridge Centre (Tennessee) and at Harwell (Great Britain). Here they found hundreds of new mutations, which permitted a very precise study of the mouse genome.

Most of these mouse lines were developed for use in cancer research, in order to prove or refute the existence of genetic factors involved in this disease. By using inbred crossings, mouse lines were obtained that had a higher frequency of occurrence, whereas others were resistant to the development of tumors. In parallel, it was found that in some of these inbred lines there appeared a high incidence of other diseases, such as anemia, eye and ear defects, neuromuscular disorders, digestive problems, obesity, bone malformations or urinary tract diseases, etc. It was by this manner that many diseases were first linked to genetic factors.

In 1966, A. K. Tarkowski and B. Mintz produced *in vitro* mouse chimeras from four different embryos, and then in 1969 R. Gardner obtained chimeric mice by injecting cells into the embryonic blastocyst cavity of a recipient mouse. In 1976, R. Jaenisch produced the first transgenic mice by infecting embryos with a retrovirus. Later, in 1980 and 1981, five laboratories (Gordon *et al.*, 1980; Brinster *et al.*, 1981; Costantini and Lacy, 1981; Harbers *et al.*, 1981; Wagner *et al.*, 1981) more or less simultaneously produced transgenic mice by injecting a DNA fragment into one of the pronuclei of a fertilized oocyte. The next breakthrough, which launched a wide range of applications, was the possibility of replacing genes in the mouse. Initially total «knockouts» were created by deactivating a gene in the whole body, which subsequently became more tissue specific in the so-called conditional «knockouts». Perhaps the last big step towards the current state of the art occurred in December 5, 2002, when the full sequence of the mouse genome was published in Nature (Waterston *et al.*, 2002). Subsequent studies have shown that 99.5% of mouse genes have a homologous gene in human, making the mouse one of the most important models for studying human diseases.

## ■ ■ ANATOMICAL NOMENCLATURE

The mouse body is divided externally into the head, neck, trunk, tail and the thoracic (fore) and pelvic (hind) limbs. To situate in a precise position the different parts of the body, it is necessary to know a number of descriptive terms and directional planes (Fig. 1-1). Holding the mouse in its **anatomical position**, that is, with all four limbs resting on the ground, the term **dorsal** is used in the trunk to refer to structures located or projecting towards the top of the

trunk. The term **ventral** is used for the structures located or directed towards the belly. By extension, the same terminology is used in the head and tail. The term **cranial** is used for structures that are positioned or projected towards the head (or cranium), whereas **caudal** is used for structures located or directed towards the tail. Within the head itself, structures located toward the nose are considered **rostral**. The mouse body is divided in two halves, the right and left, by the **median plane**. The structures that lie closest to this plane are said to be **medial**, in contrast to the **lateral** structures that are located towards the exterior of the mouse. Planes parallel to the median plane, but that do not pass exactly through the centre of the animal, are called **sagittal planes**. Furthermore, **dorsal planes** are horizontal planes parallel to the back, and the **transversal planes** are perpendicular to the longitudinal axis of the body. A specific nomenclature is also used for the limbs. Structures located near the junction with the trunk are called **proximal**, whereas the more distant structures are said to be **distal**. In the forearm and forepaw (Fig. 1-1), the structures located more cranially are called **dorsal**, while those in the caudal face are called **palmar** in the forearm and **plantar** in the forepaw. Further terms are applied to the fingers, where **axial** and **abaxial** refer to structures located closer or farther from the longitudinal axis of the third finger.

Superficially, the body of the mouse is divided into regions (Figs. 1-2 to 1-5). Firstly there are the **regions of the head**, which are divided into the skull and face. In the trunk are located the **neck regions** (dorsal, lateral and ventral), the **pectoral regions** situated in the thoracic wall, the **abdominal regions** located at the surface of the abdomen, and the **pelvic regions**. Finally, the **thoracic limb regions** and the **pelvic limb regions** are named in according with bones located in deep.

The anatomical terms that have been used here to describe the morphology of the mouse mainly correspond to the «**Nomina Anatomica Veterinaria (NAV)**» (4th edition, 1992). However, there are anatomical structures that exist in the mouse, the clavicle for example, which are very similar to humans, but different from domestic animals. In these situations, we have used the human anatomical nomenclature published in the «**Anatomisches Bildwörterbuch der interantionalen Nomenklatur**» (3rd edition, 1993), by H. Feneis; and the «**International Anatomical Terminology**», by The International Federation of Association of Anatomist (IFAA) and the Federative Committee of Anatomical Terminology (FCAT) (1st edition). For the description of the mouse nervous system, we have also followed the terminology of the book «**The Mouse Nervous System**» (2012), edited by C. Watson, G. Paxinos and L. Puellas. The histological and cellular description used the terms proposed in the «**Nomina Histologica**» (2nd edition, 1992). Finally, we have also taken into account the mouse anatomical and pathological ontologies contained in Pathbase (<http://eulep.pdn.cam.ac.uk>), which have been designed specifically to morphologically phenotype genetically modified mice.



