实验动物学总论

一 实验动物和实验用动物

（一）实验动物(Laboratory animals)

是指经人工培育或人工改造，对其携带的微生物实行控制；遗传背景明确，来源清楚，用于科学实验、药品、生物制品的生产和检定及其他科学实验的动物。

（二）实验用动物(Animals for research ；Experimental animals）

所有用于科学实验的动物统称为实验动物。包括实验动物，野生动物，经济动物和观赏动物。

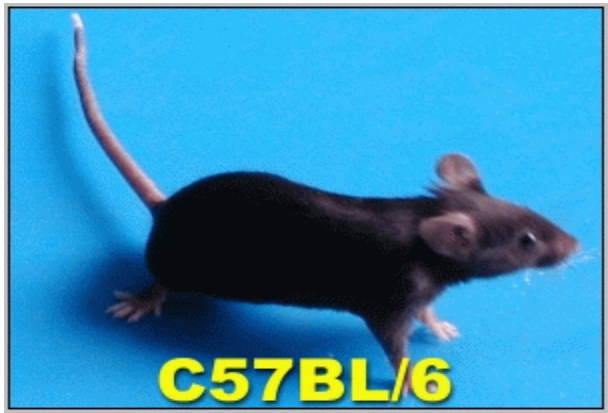
二 实验动物学的定义和范围

（一）定义

实验动物学（Laboratory animal science）是研究实验动物和动物实验的科学。

（二）研究范围

1. 实验动物遗传育种学 （Laboratory animal genetic breeding science）
2. 实验动物微生物学和寄生虫学 （Laboratory animal microbiology and parasitology）
3. 实验动物环境生态学 （Laboratory animal environmental ecology）
4. 实验动物营养学（Laboratory animal nutriology ）



（二）研究范围(续)

5. 实验动物饲养管理（Laboratory animal husbandry）

6. 实验动物医学（Laboratory animal medicine）

7. 比较医学（Comparative medicine）

8. 动物实验（Animal experimental techniques）

三 实验动物的重要性

（一）实验动物是生命科学研究的支撑条件之一

生命科学实验研究的四个支撑条件----AEIR要素

A：Animal：实验动物；

E：Equipment：仪器设备；

I： Information：信息；

R：Reagent：试剂；

（二）实验动物在生命科学研究中被广泛应用，很多重要的科研成果来源于实验动物

（三）实验动物是人类的替身，起着“活的天秤”和“活的化学试剂”的作用

（四）实验动物工作实行法制化管理

四 实验动物的分类

（一）传统的动物学分类方法

依据自然分类法，把整个生物，通常是用界(kingdom)、门(phylum)、纲(class)、目(order)、科(family)、属(genus)、种(species)等划分分类等级。以大家鼠为例，它属于：

脊椎动物门(phylum vertebrata)

哺乳动物纲(class mammalia)

啮齿目(order rodentea)

鼠科(family murinae)

大家鼠属(genus rattus)

大家鼠种(species *rattus norvegicus*)

学名：褐家鼠（大家鼠）(*Rattus norvegicus*)

多数情况下，根据不同目的进行种下分类， 把实验动物划分为不同品系。

（二）按实际用途分类

1、实验动物

2、经济动物（Economical animals），或称家畜、家禽

3、野生动物（Wild animals）

4、观赏动物（Exihibiting animals）

（三）按遗传学控制分类

根据基因的纯合程度，把实验动物分成下列四类：

1、近交系动物（Inbred strain animals）

2、突变系动物（Mutant strain animals）

3、杂交群动物（Hybrid colony animals）

（杂交一代，F1代动物）

4、封闭群动物(Closed colony animals)

1、近交系动物（Inbred strain animals）

又叫纯系动物。是采用同胞兄妹或亲子交配，连续繁殖20代以上所培育出来的遗传上达到高度一致的动物群。

基因纯合程度可达99.8%。

① 主要指啮齿动物；可出现近亲交配衰退。

② 亲子交配与兄妹交配不能混用。

③ 亲子交配时必须采用年轻的双亲同其子女交配。

④ 较大动物纯种培育很难获得成功，因为世代间隔较长，费用较大，所以成功率低。

⑤ 禽类和兔的血缘关系达到80%以上（相当于兄妹交配四代）时，即可称为近交系。

2、突变系动物（Mutant strain animals）

具有特殊突变基因的品系动物，正常染色体基因发生突变，并具有各种遗传缺陷的动物。在长期繁殖过程中，动物的子代突然发生变异，变异的基因位点又可遗传下去，或者即使没有明确的基因位点，经淘汰和选育后，仍能维持其稳定的遗传性状。这种变异并能继续保持遗传基因特性的品系动物，称为突变系动物。如无胸腺裸鼠、无K细胞、或无K、无B、无巨噬细胞等裸鼠。用于免疫研究、移植实验等。

3、杂交群动物（Hybrid colony animals）

（杂交一代，F1代动物）

两个近交品系动物之间进行有计划交配所获得的第一代动物。

例如：C57BL/6J×DBA/2→B6D2F1

（B6为 C57BL/6J的缩写，D2 为 DBA/2的缩写。）

4、封闭群动物(Closed colony animals)

以非近亲交配方式进行繁殖生产的一个种群，在不从外部引入新的血缘条件，至少连续繁殖四代以上称封闭群。

封闭群又称远交群。

（四）按微生物学控制分类

1、无菌动物（Germ free animals，GF）

体内、外无任何可检测出的活的微生物和寄生虫的动物。来源于无菌手术剖腹取胎，饲养在无菌隔离器内，人工喂乳或保姆代养培育而成。

悉生动物(Gnotobiotes animals，GA)

体内携带有已知微生物的动物。这种动物来源于无菌动物，人为的投给已知的单菌、双菌、三菌或多菌。这些均为已知菌，与无菌动物一样，饲养在隔离器中。

2、无特定病原体动物(Specefic pathogen free animals，SPF）

体内不存在特定病原微生物和寄生虫的的动物，简称SPF动物。是指无传染病的健康动物。这种动物都是来自无菌动物或悉生动物，转移到屏障系统中饲养。要在屏障系统环境设施中饲育繁殖和进行实验，要进行严格消毒、检疫、隔离并定期剖腹净化。

3、清洁动物(Clean animals，CL)

又称最低限度疾病动物(Ginimal disease animals)，体内外不携带人畜共患的病原体或动物传染病病原的动物，不能带有体外寄生虫和大部分体内寄生虫。

4、普通动物（Conventional animals）

未经积极的微生物学控制，饲养在开放卫生环境里的动物。垫料和饲料和饮水一般不消毒，饮用普通自来水。

所谓普通动物也并不是对微生物没有一定控制的一般动物，而是要求不带能够感染人的微生物和体外寄生虫。这种动物只能供教学和一般实验用。

根据新修订的国家实验动物微生物、寄生虫质量标准，我国将实验大、小鼠分为三类即清洁级、无特定病原体级、无菌级（包括悉生动物）。其它品种实验动物仍然分为普通级、清洁级、无特定病原体级、无菌级（包括悉生动物）四级。即从2002年5月1日起取消了普通级大、小鼠标准。

The Jackson Laboratory

In 1929, Harvard-trained geneticist Clarence Cook Little founded The Jackson Laboratory, based on the then-radical idea that mice were key to understanding the genetic basis of human development, diseases and disorders. Throughout the 1900s, that idea would become increasingly central to the progress of biomedical research, reaching ultimate confirmation when the mouse and human genomes were sequenced at the turn of the century and proved definitively that the two species share the vast majority of their genes.

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【国家啮齿类实验动物种子中心上海分中心】

Animal Care and Use

Laboratory animals are used in biomedical research as models for humans. Observed behavioral or physiological changes exhibited by these animals, when they are used in the protocol, are assumed to be responses to the experimental procedures. If non-experimental variables caused by inadequate housing, disease, or stress from improper handling are inadvertently introduced into the study they can elicit similar responses which could skew the data or totally confound the experiment. The safe and effective use of animals in a laboratory setting is an essential element of your research activities.

The Animal Welfare Act (AWA), and PHS Policy require that all Animal Users complete training on the laws, regulations, and procedures associated with animal care and use. This course is designed to fulfill that requirement, providing a quick overview of the relevant laws and regulations covering use of animals in a laboratory setting, and the recommended procedures for working with specific animals. The course includes practical and essential information that will guide you in the everyday care and use of animals in your laboratory environment.

Importance of Proper Animal Care

Your primary responsibility when working with laboratory animals is to treat them humanely. With that in mind, the major challenge is to manage the animals in a way that minimizes their exposure to pain and distress and maintains the integrity of their physiological functions to facilitate the generation of reliable research data. This course will teach you how the proper treatment of animals carries the added benefit of minimizing the introduction of unwanted variables into the research process.

Importance of Proper Animal Care

Your care and treatment of animals must also comply with the appropriate laws, regulations, and with NIH policy. Many of these laws, regulations and policies were enacted in response to public concern about the treatment of animals in the research setting. Consequently, your objective should be to treat your animals in a manner that complies with the ethical and legal imperatives prescribed for the humane treatment of laboratory animals that will reflect positively on NIH as a research institution.

Laws and Regulations:

The main regulations, policies and guidelines that apply to animal use at NIH are:

The Animal Welfare Act (AWA)

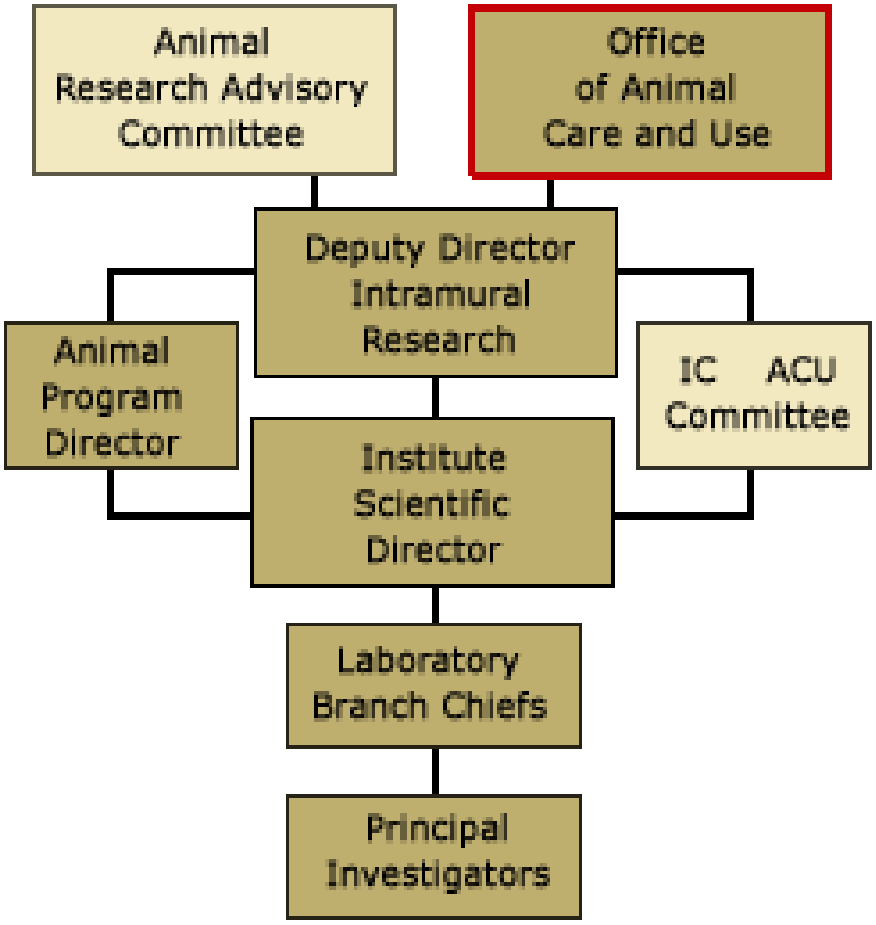
The Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy)

U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (Government Principles)

Guide for the Care and Use of Laboratory Animals (Guide)

NIH Manual 3040-2: Animal Care and Use in the Intramural Program

Structure and Accreditation



The DDIR delegates to the Director of the Office of Animal Care and Use (OACU) overall responsibility for ensuring that the ACU program complies with applicable policies and regulations.

Pain and Distress

There is also a pragmatic point of scientific logic that supports minimizing the exposure of research animals to experimental pain or distress. Animals respond to pain and distress with changes in their normal physiology which can skew data being collected.

Alleviating Pain and Distress

Animals, like humans, can be expected to generate a stress response to novel stimuli. Handling animals very early in life, even as new-borns, to "gentle them" is a procedure that has been widely used on a variety of species to familiarize the animals with the handling process. When animals are trained this way to associate handling with pleasant circumstances they are much less likely to generate a stress response later in life when they are handled.

Alternatives

The Three Rs:

Reduction: Reductions in the numbers of animals used to obtain information of a certain amount and precision.

Refinement: Decrease in the incidence or severity of pain and distress in those animals that are used.

Replacement: Substitution of insentient material for animals or substitution of a lower species, which might be less sensitive to pain and distress, for a higher species.

Minimizing Exposure to Disease when Working with Animals

Standard laboratory protective clothing includes:

Uniforms - Uniforms are clothing, such as surgical scrub suits and coveralls, dedicated for wear during work in the animal facility. A uniform should not be worn outside of the animal facility or research setting. For example, uniforms should not be worn in public cafeterias, lecture halls, and medical patient care areas.

Gloves - Lightweight vinyl or latex gloves prevent contamination of the skin with pathogens that may be on animals' bodies or on surfaces soiled by their excreta.

Lab coats - Disposable lab coats and coveralls protect street clothes from contamination with animal pathogens. Lab coats should not be worn outside of the animal facility or research setting. For long term work in the animal facility, a uniform may be substituted for these types of covering garments.

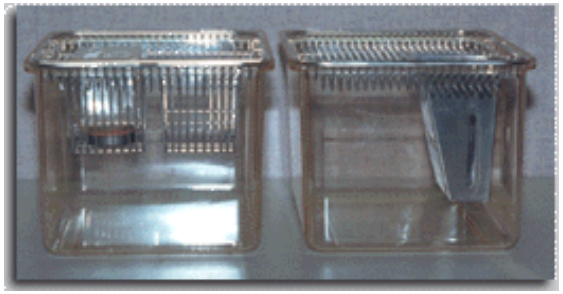
Mucous Membrane Protection –

A device or a combination of devices such as face shields or surgical face masks combined with protective glasses or goggles, worn to protect the mouth, nose, and eyes from splash or droplet contamination. The degree of protection needed varies with the specific procedure being conducted and should be adjusted to the level of the anticipated risk. Full face shields provide splash protection for all of the facial mucus membranes. Partial mucous membrane protection is provided by using only a face mask and may be appropriate when the fecal oral route of contamination is the only concern.

Shoe Covering - Stretch booties, usually made of paper or plastic, are worn over street shoes to prevent the transfer of pathogenic organisms. Booties should not be worn outside of the animal facility. Dedicated footwear can be substituted for shoe coverings during long-term activities. If dedicated shoes are worn, shoe coverings may be used to cover the shoes when outside the animal facility, but the shoe covers must be removed on return to the facility.

Cage Systems

Cage systems that meet the general requirements for maintenance of normal body functions and provide moderate protection from exposure to pathogens are described as "conventional" cages. Conventional cages, however, do not adequately protect rats and mice from airborne diseases to which they are highly susceptible so cage systems that are specially designed to provide extra protection from these pathogens are used.Rodent viruses and other airborne pathogens may be transported by clinging to dust particles and other particulate matter suspended in the air inside and above the animal cage. The risk of exposure to these organisms is reduced by increasing fresh air circulating around the cages, or filtering the air.

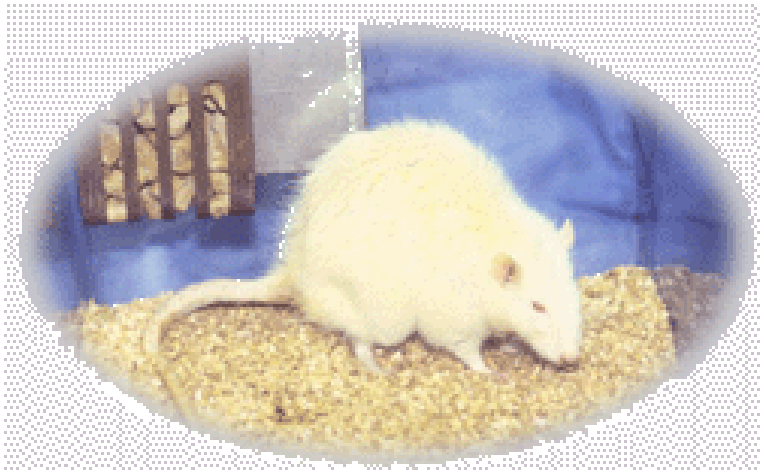


water
Sanitation
Filtered Air Unit

Observing and Reporting Problems with Animals

While animal health is the charge of the veterinarians, you will have a responsibility to observe and report changes in an animal's health and to inform the veterinarian or animal facility manager so that the animal can be treated. Immediate identification of sick or injured animals is critically important in a research setting because the animals are closely confined, and housing space is frequently shared by several investigators. Infectious disease in one group of animals could jeopardize all of the animals in the room or building.

Signs of Illness and Injury:

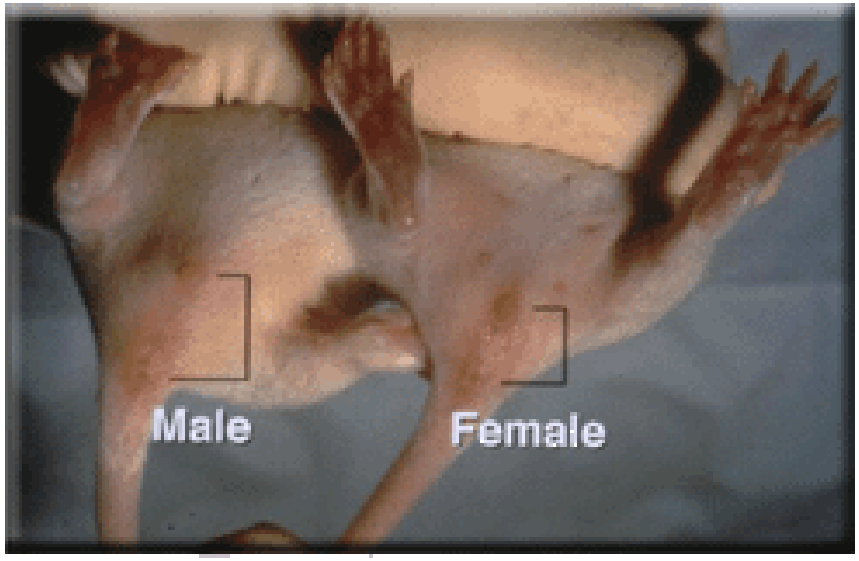


Picking up mice.

When picking up mice, always hold the mouse by the base of the tail. This can be done with either forceps or your fingers. DO NOT pick mice up by the tip of the tail. If you pick a mouse up by the tip of its tail, the mouse may spin in tight circles when its feet lose contact with the cage surface. If this happens, the tip of tail can be pulled off. Additionally, a mouse held by the tip of its tail can "climb up its tail" and bite you!

Separating mice/rats by gender.

Separating mice/rats by gender can be difficult, especially when they are young and males' testicles have not descended into the scrotum. Compare the relative distance between anus and urinary papilla. The distance between the anus and the urinary papilla is greater in the male. This photograph illustrates that the mouse on the right has the lesser (shorter) distance between the anus and the urinary papilla, so it is the female.



Restraining Rats.

Rats can be caught and lifted by the base of their tail, or you can grasp them around their body as illustrated in this photograph. If you grasp the rat around its body you can prevent it from biting you by placing your index finger snugly under the jaw against the point of the shoulder ahead of the right front leg. Your thumb is placed behind the left front leg which pushes it forward against the left side of the neck. This grip secures the head, and the rat cannot reach around to bite. For large rats, keeping a good grasp on the tail will give you additional control.

Guinea Pigs.

Guinea Pigs have no tail and must be caught by grasping them around their body. They are very inclined to avoid being caught by scurrying around the cage and whistling loudly. When they are caught they rarely attempt to bite but may reach forward with their hind feet and scratch with their long toe nails.

Rabbits.

Rabbits are characterized by their thin bones, fragile skeleton, and heavy muscles on their back and hind legs. When restraining and lifting a rabbit, the most important thing to remember is to support the rabbits rump as you pick it up. If the rabbit kicks, even one time, when its back feet leave the cage floor it can break its back, be permanently paralyzed and have to be euthanized. The correct technique is to approach the rabbit with your hand held high over the back, grasp the skin over the shoulders and slide your other hand between the back legs to support the rump before you lift the animal off of the cage floor.

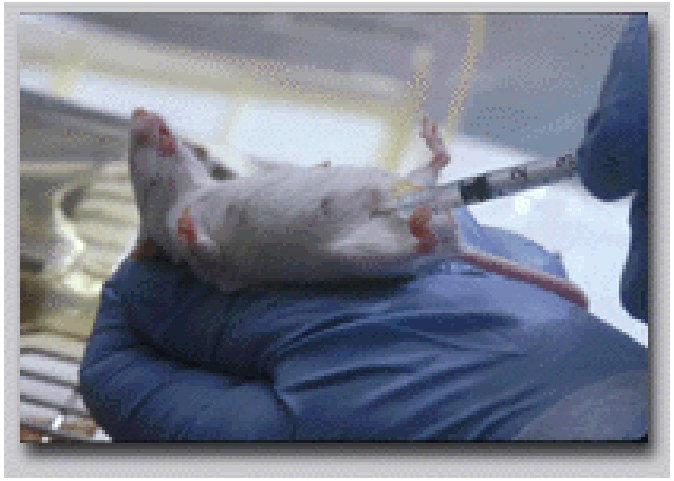
Intra-peritoneal injection.

1. Restrain the mouse by grasping the skin along its back with your left hand (if right-handed).

2. Clamp the tail between your ring finger and little finger for additional control.

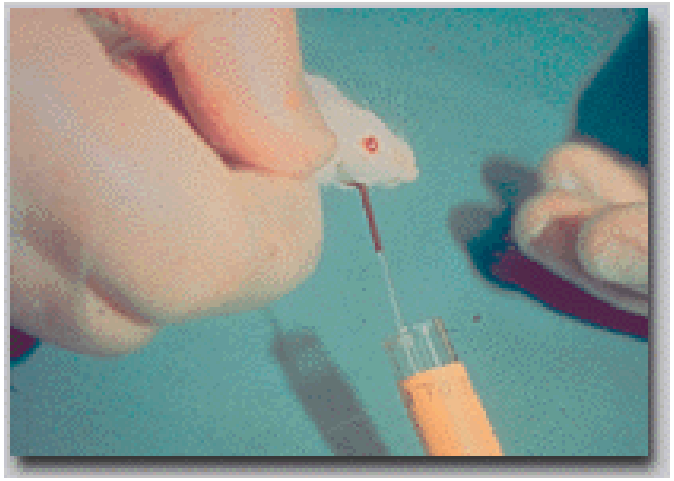
3. Position the mouse so that it's head is down. (Intestines, stomach, etc. should fall forward and create a small space in the posterior portion of the peritoneal cavity.)

4. Insert the needle a little off to the side of the center line (to miss the bladder).



Collecting a blood sample.

1. Give general anesthesia.
2. Use capillary tube treated with heparin inside so that the blood doesn't clot.
3. Introduce the tube into the medial canthus of the rodent's eye, directed toward the back of the orbit.
4. Rotate the tube to cut into the venous sinus in the back of the orbit. Samples may be more difficult to collect from rats because they have a venous plexus rather than a venous sinus at the back of their orbit and the vessels can be hard to locate.
5. Blood flows down into the capillary tube.
6. Remove tube and apply gentle pressure against the eye with a gauze sponge to stop the bleeding.
7. Watch the animal closely to prevent cagemates from injuring it during its recovery from the anesthesia.



Giving Injections/Taking Samples

Rabbits: Rabbits are frequently used to produce antibodies to an injected antigen and large (50 ml) blood samples are collected for harvesting antibodies.

Drawing a sample.

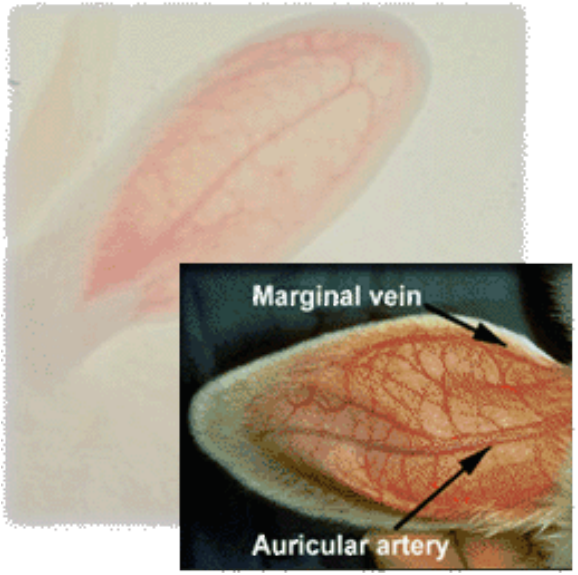
1. Blood is usually collected from the auricular artery (dark line) that lies along the middle of the top surface of the ear.
2. A large bore (18 guage) needle is most frequently used to draw samples.

Giving Injections/Taking Samples

Rabbits: Rabbits are frequently used to produce antibodies to an injected antigen and large (50 ml) blood samples are collected for harvesting antibodies.

Intravenous injection.

1. Use marginal ear vein, the dark structure along the lower margin of ear.
2. Shave the hair over the vessel to be used.
3. Use small bore (23-27 guage) needle with a syringe or insert a similar gauge scalp vein set (needle with catheter).



Anesthesia / Analgesia

Pentobarbital [Somnifer].

Delivered intravenously (IV) because it is chemically formulated for that route of injection

If it's delivered outside of vein, irritates and can damage tissue

Can be diluted with saline and used intraperitoneally for rodent anesthesia

This is a Drug Enforcement Agency (DEA), Class-II drug, requires a license and special record keeping

Survival Surgery

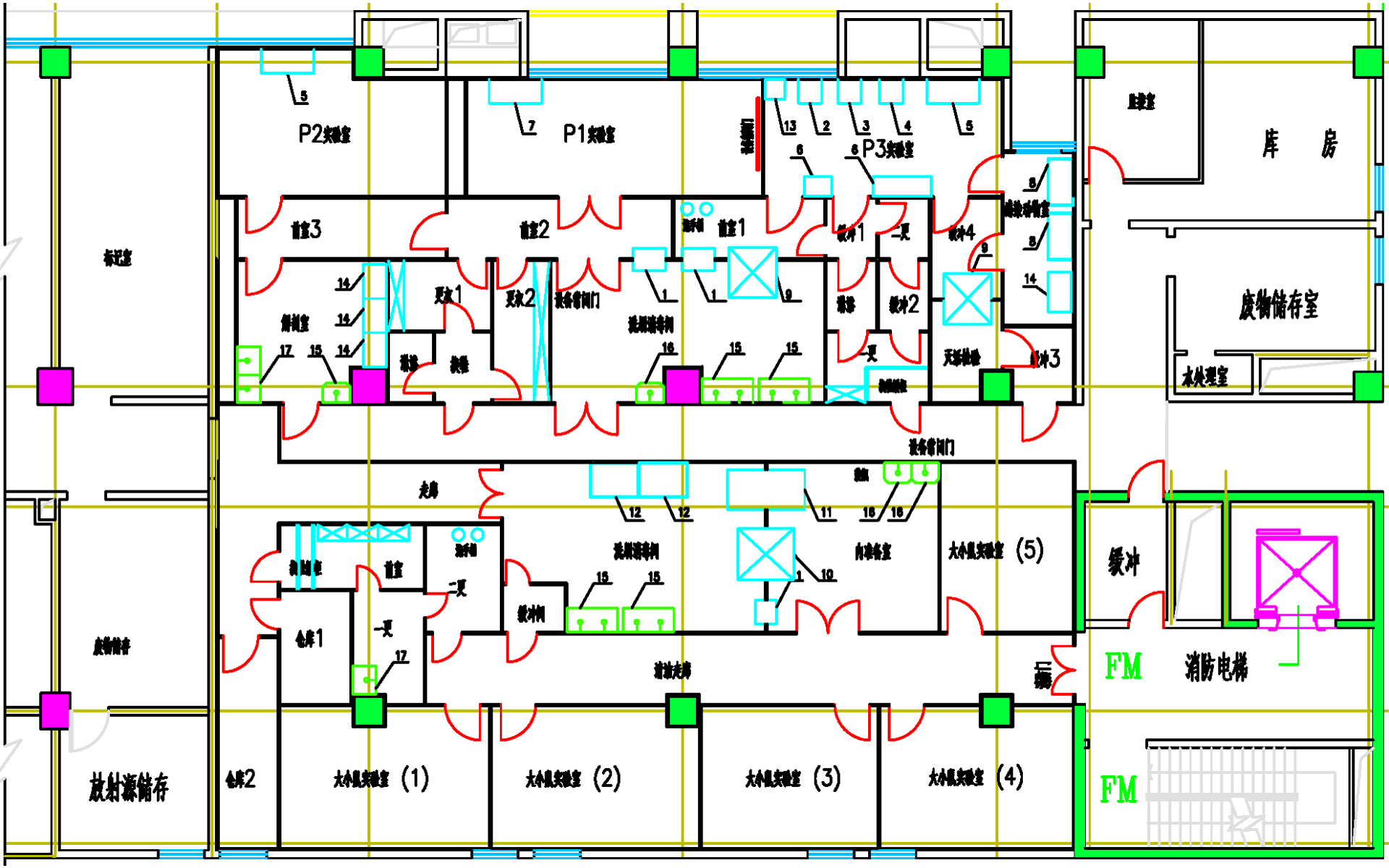
Anesthetize the animal

Remove hair by clipping, shaving, (or plucking, mice)

Thoroughly clean the operative site with a germicidal soap to remove surface debris and bacteria

Secure the animal on the surgery site (ensure airways are clear)

Apply surgical drapes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放射源储存
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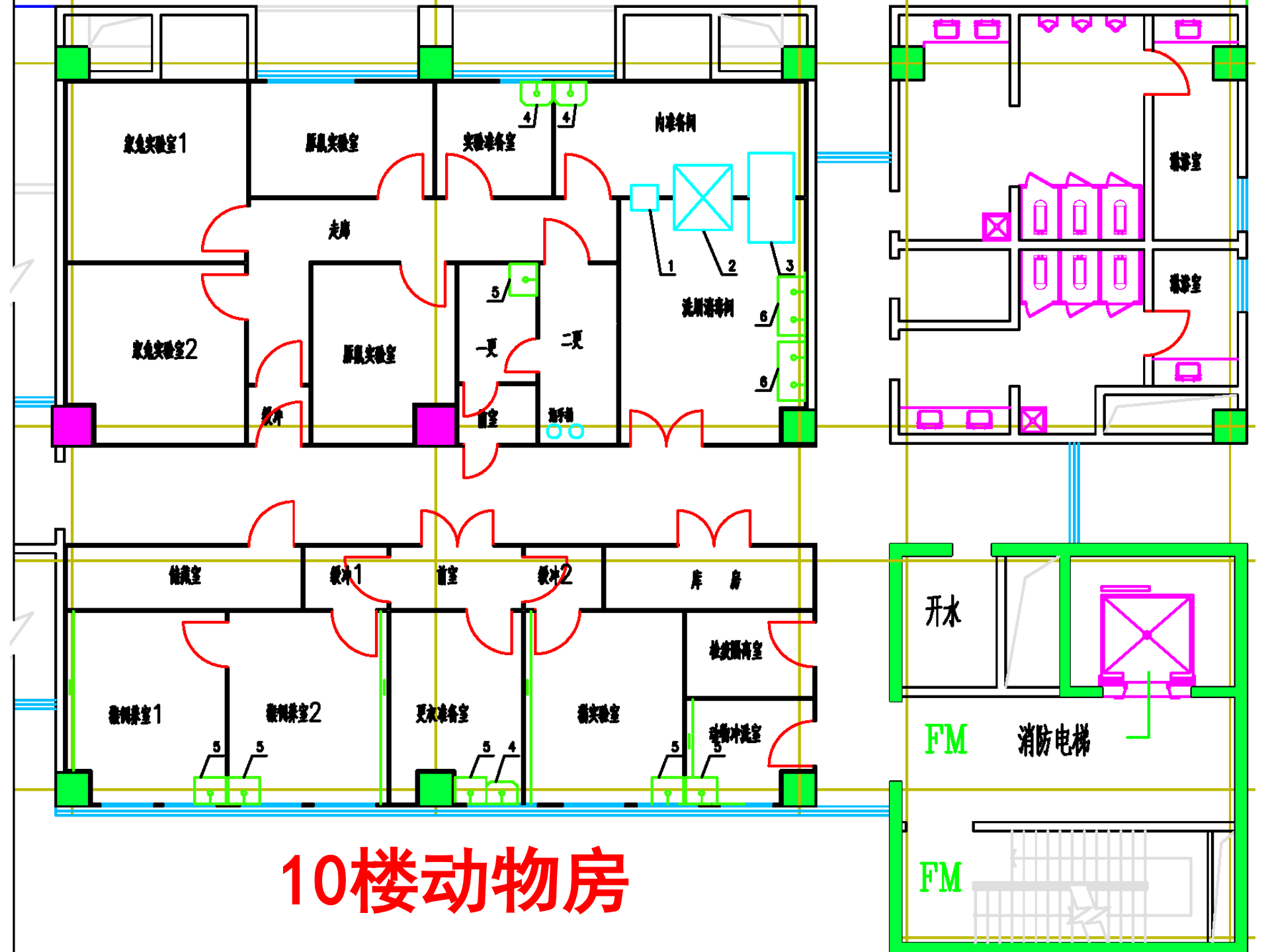
P3实验室(11楼)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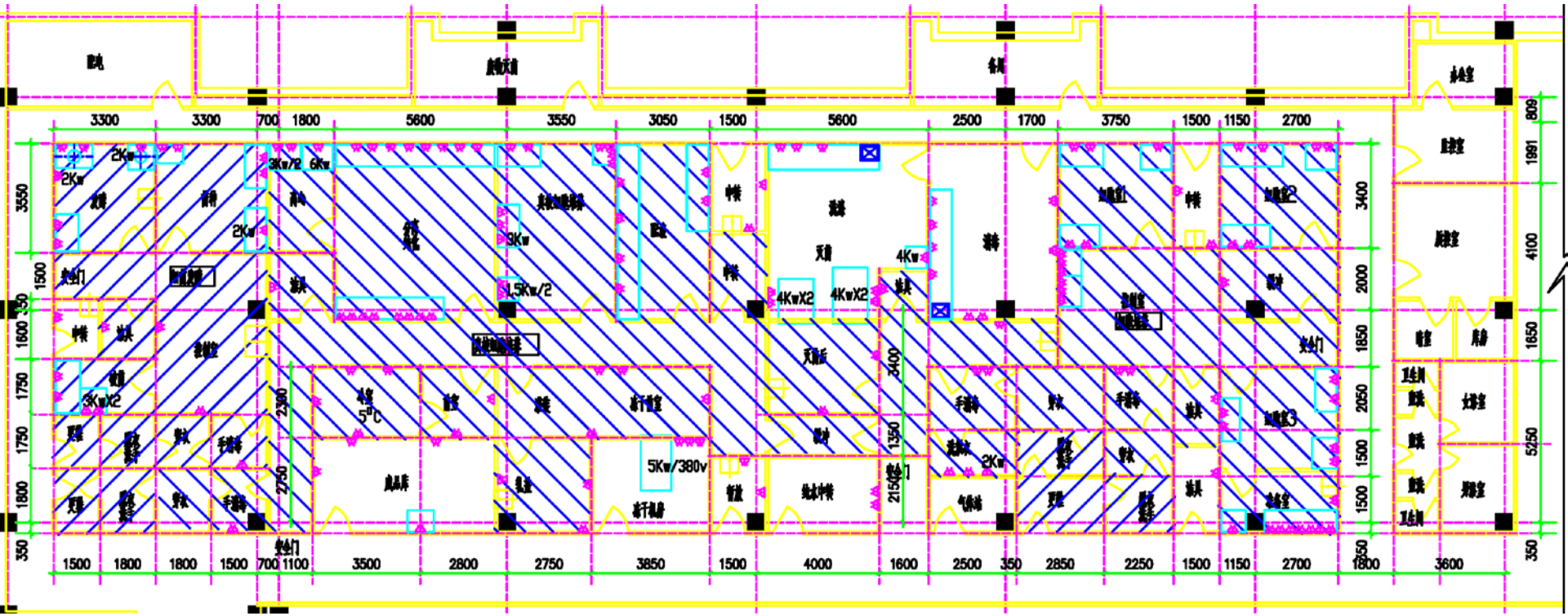
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R&D中试基地

重要的科研地位：

中国科学技术大学生命科学学院
生命科学实验中心
安徽省分子医学重点实验室
中心实验室

合肥微尺度物质科学国家实验室
公共技术部
生物技术实验室

有合理的内部机构设置、动物设施。包括软件和硬件条件。


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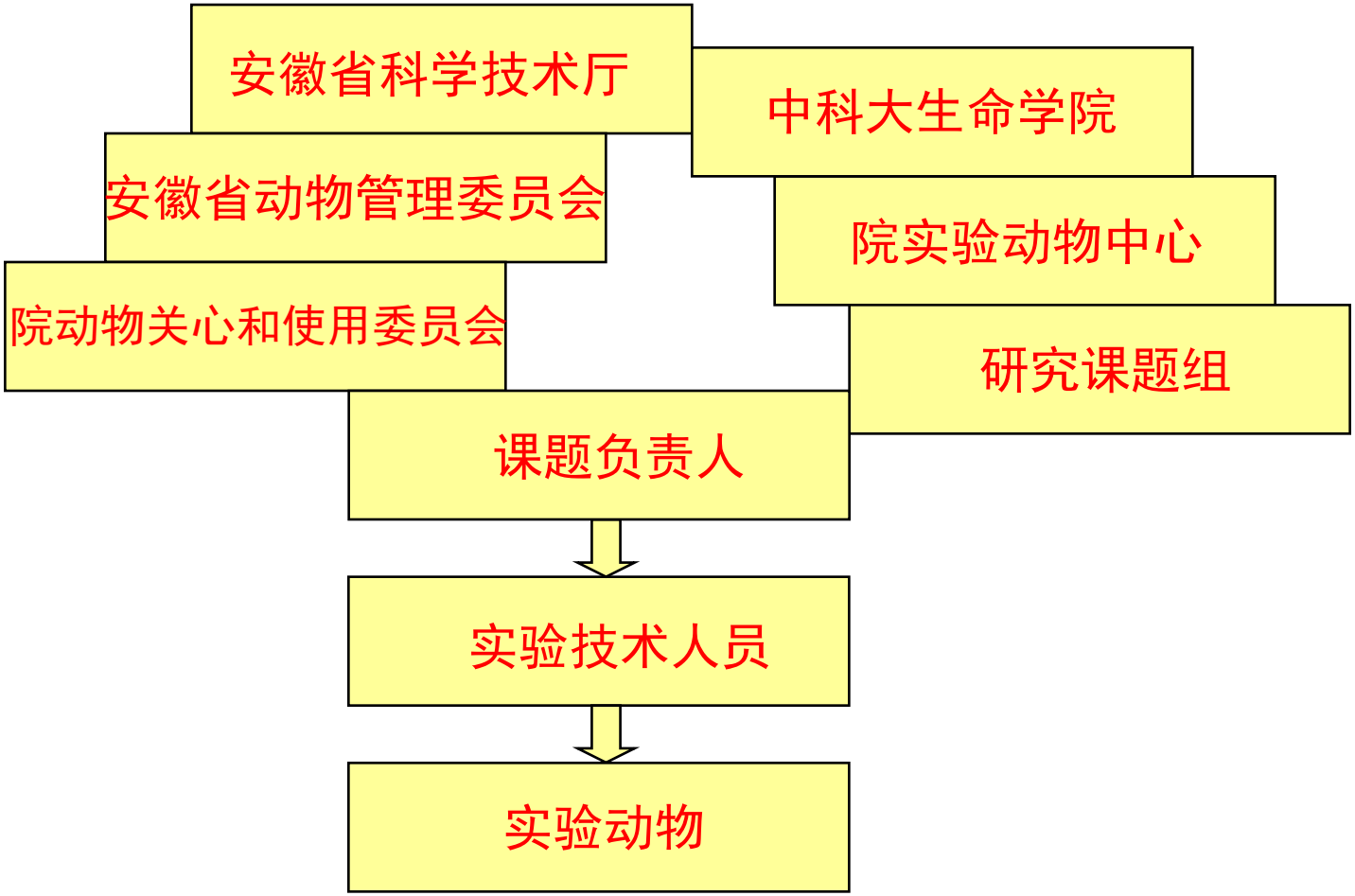
实验动物管理机构


安徽省科学技术厅
中科大生命学院
安徽省动物管理委员会
院实验动物中心
院动物关心和使用委员会
研究课题组
课题负责人
实验技术人员
实验动物

1.3 相关管理技术文件

有健全的管理制度和操作规程(SOP)。

1. 实验动物中心岗位职责
2. 实验动物中心工作人员上岗培训制度
3. 实验动物中心工作人员健康管理制度
4. 实验动物中心工作人员工作时间安排
5. 库房管理制度
6. 屏障动物房日常工作操作规程
7. 动物实验人员须知
8. 动物实验申请书
9. 实验动物中心收费制度
10. 实验动物中心开放时间
11. 屏障动物房人员进出操作规程
12. 屏障动物房物品消毒、传递操作规程
13. 实验动物购买、运输、发放规范
14. 屏障动物房实验动物进出操作规程
15. 实验废物、废弃动物、动物尸体处理规范
16. 传递窗操作规程
17. 屏障动物房启用前净化操作规程
18. 动物试验卡填写说明
19. 屏障动物房中IVC的操作规程
20. 高压灭菌器操作规程
21. 隔离器操作规程
22. 灭菌通道操作规程
23. 自控设备操作规程
24. 空调、通风设备的维护管理规范
25. 饲料管理规范
26. 垫料管理规范

管理人员

技术人员

饲养人员

实验人员

动物实验申请书

课题项目名称：_____

课题承担单位及项目负责人：_____

实验起止时间:_____

在何种实验动物设施内进行实验：

□开放动物房（10楼，仅限猕猴）

□屏障动物房（10楼清洁级动物实验室）

□IVC+屏障动物房（11楼SPF级动物实验室）

□隔离器+屏障动物房（11楼SPF级动物实验室）

所用实验动物资料：

来源_____合格证号_____数量_____

品种_____品系_____微生物级别_____

年龄_____体重 _____性别_____

请声明实验方法及所用材料、试剂对人体和其他课题有无危害，若有危害，请说明拟采用消除危害的方法：

_____

甲方_____乙方_____ _____

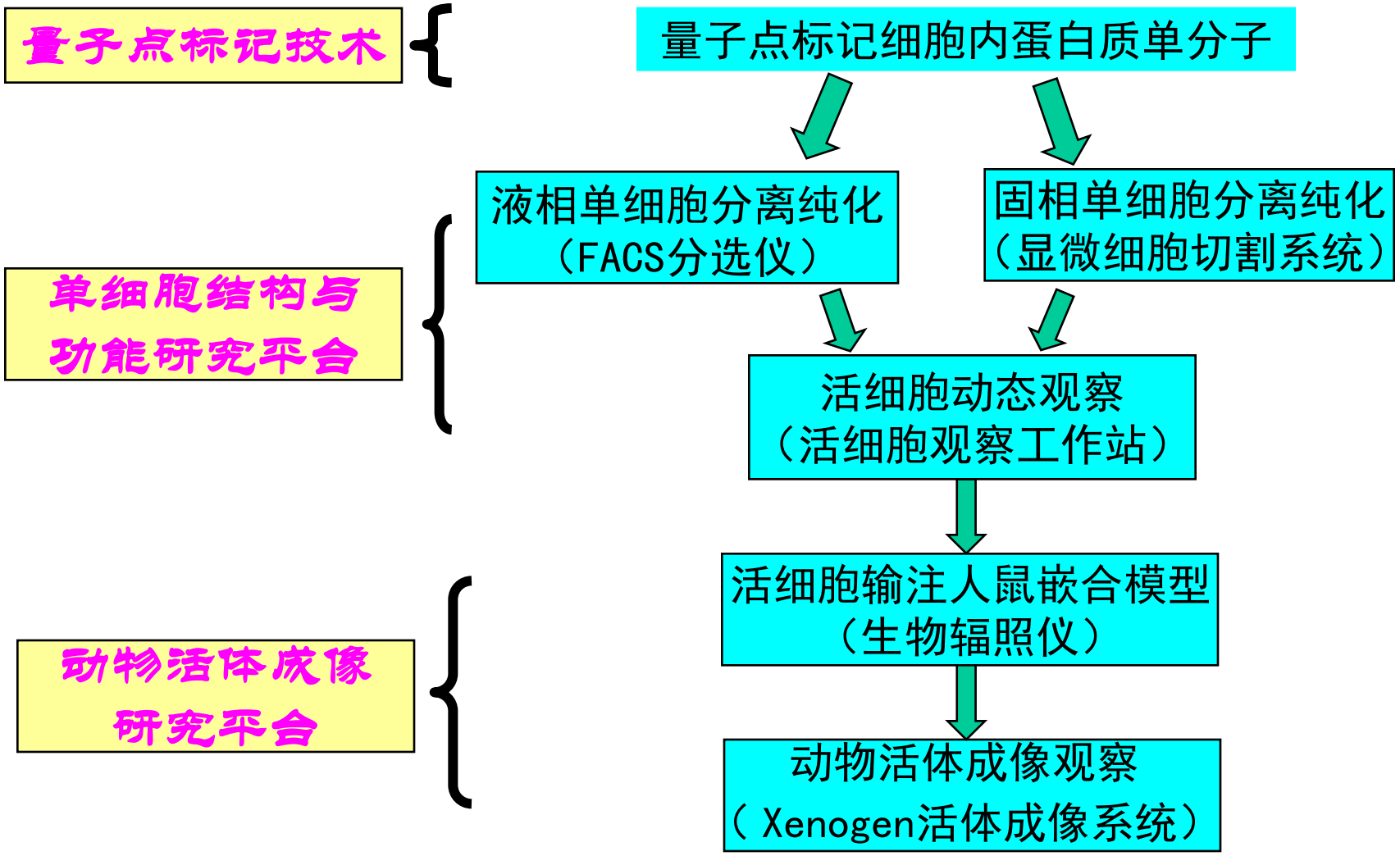
地址_____地址_____

电话 _____电话_____

联系人 _____联系人_____

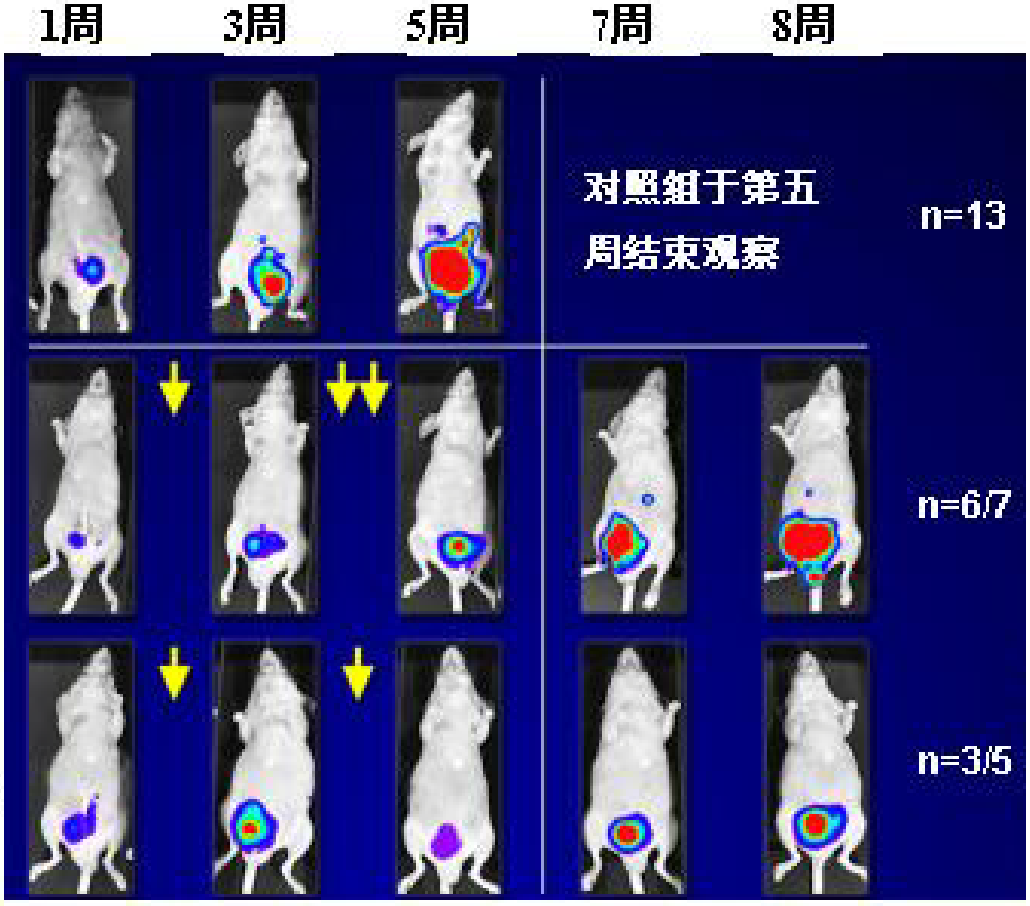
负责人签名_____负责人签名_____

协议签定日期　　年　　月　　日



单细胞结构与功能研究框架

实验动物活体成像技术



利用动物
善待动物