

# 107年度公用動物設施 教育訓練課程



日期: 107/08/23(星期四)

時間: 13:00 ~ 17:00

地點: 生物醫學研究所 B1C 演講廳

時間	課程名稱	講員
13:00-13:30	報到	
13:30-14:20	動物實驗規劃，設計及IACUC protocol撰寫	王毓權博士
14:20-14:30	休息	
14:30-15:20	實驗動物基本操作之相關認識及技術	楊東一
15:20-15:30	休息	
15:30-16:20	實驗動物福祉於動物房內之落實與應用	陳昱卉獸醫師
16:20-16:40	綜合討論Q&A	

# 動物實驗設計與動物實驗計畫撰寫

公用動物設施管理師

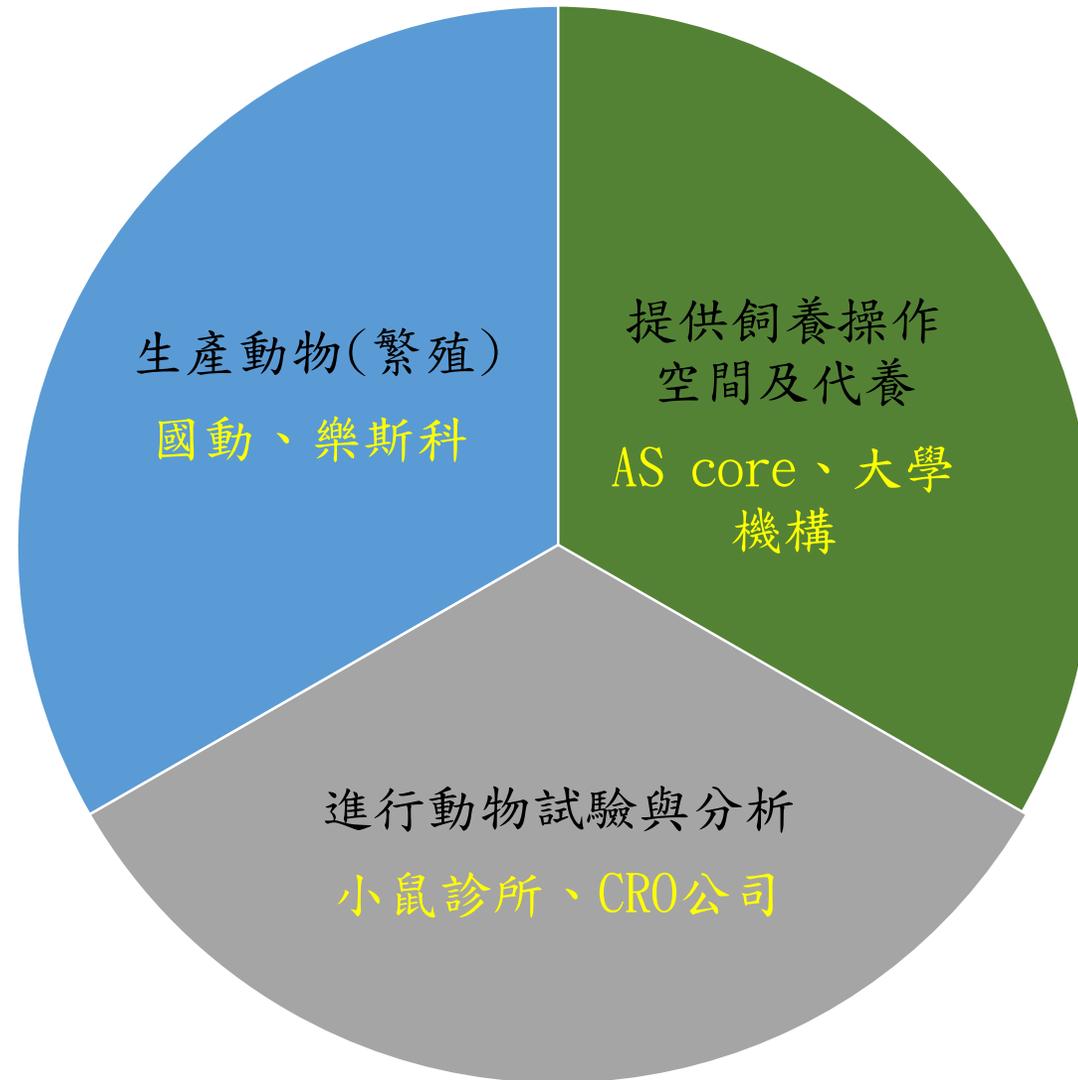
王毓權

2018/08/23

# outline

- 動物設施的角色
- 實驗目的
- 動物選擇與條件
- 材料方法
- 動物實驗計畫撰寫與注意事項

# 實驗動物設施依功能屬性區分



基本功能: 提供動物維持生命與生活所需物質與環境

# 實驗目的: 要問甚麼樣的問題?

- 生理、生化、細胞、腫瘤、發育、行為、藥理、毒理

# 動物選擇與條件

- 動物種類
- 品系
- 性別: 公鼠、母鼠
- 年齡: 成鼠、小鼠、胚胎、實驗進行時間(日、夜、間隔)
- **Normal、Transgene、Knockout**
- 用多少數量、養多久、生多少可以拿到多少?
- 特殊的食物、飲水、給藥
- 手術模式、**inducible 模式(Challenge)**

# 小鼠基本生理特性

成年公鼠體重	20-40 g
成年母鼠體重	25-40 g
出生體重	0.5-1.5 g
體溫	36.5-38.0°C
染色體數	40
壽命	1.5-3 yr
食量	15 g/100g/day (#成鼠一天約1.5顆飼料)
飲水量	15 ml/100g/day (#水瓶200ml 可供5隻成鼠8天)

\*不同品系、個體將有所差異

#以AS core為例

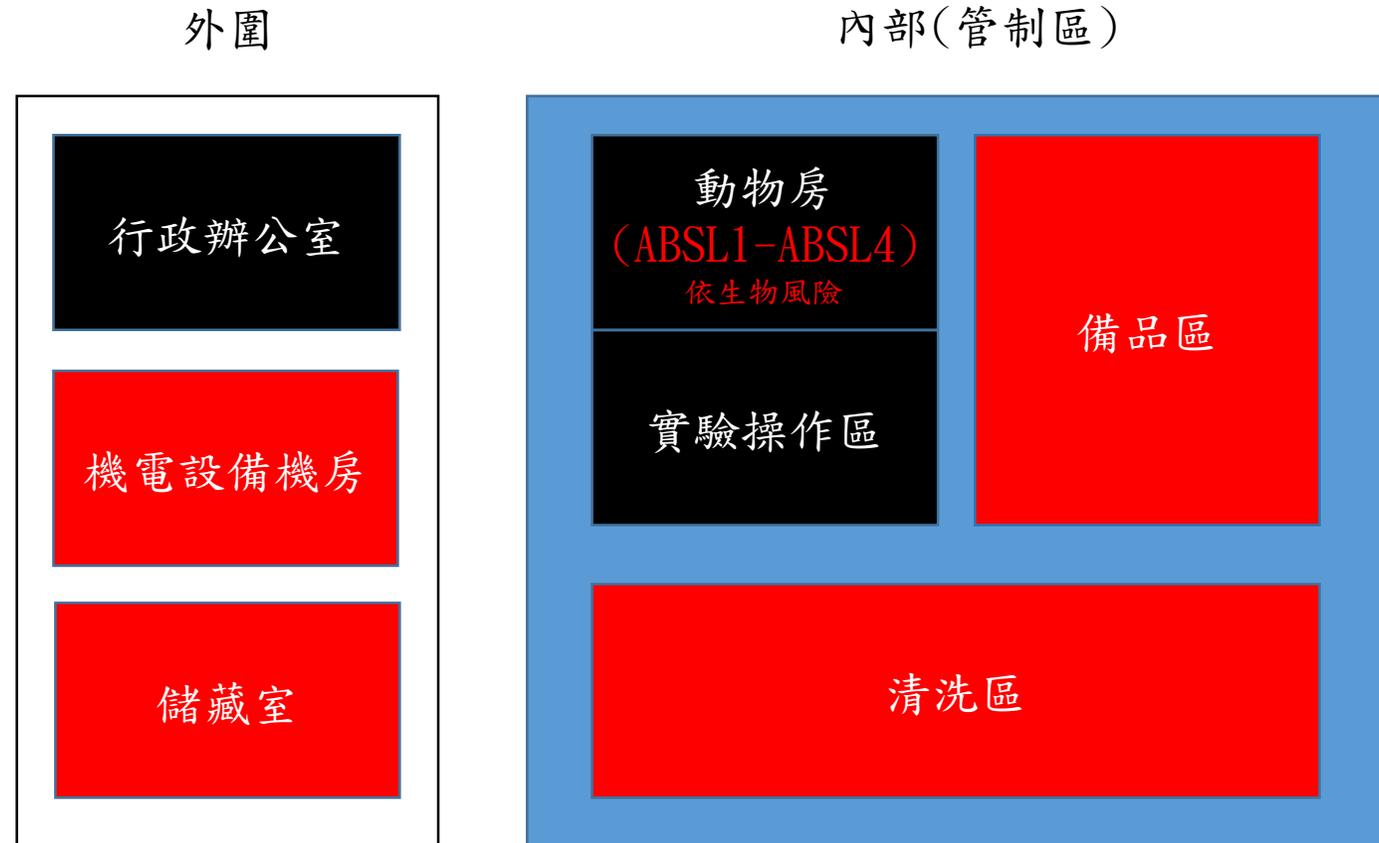
# 材料方法 (1): 繁殖管理策略

- 實驗室使用者繁殖管理方式: (1) 使用者各自飼養繁殖 (2) 統一由實驗室專人繁殖分配，或由一管理者統籌 (3) 不繁殖
- 使用小鼠類別: (1) 胚胎 (2) 仔鼠 (3) 成鼠 (4) 懷孕鼠或代理孕母 (5) 特定性別(公or母鼠) (6) 特殊基因型
- 繁殖策略考量: (1) 基因型 (2) 時間 (3) 數量

# 實驗動物依微生物等級分類

- Germfree (GF) 無菌動物 (isolator)
- Gnotobiotics (GN、DF) 確菌動物 (isolator)
- Specific pathogen free (SPF) 無特定病原動物 (IVC)
- Conventional (C) 一般動物 (open cage)

# 材料方法: (2)飼養空間選擇



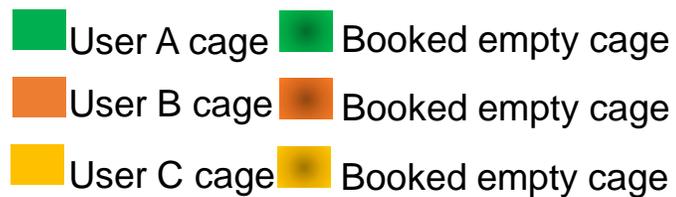
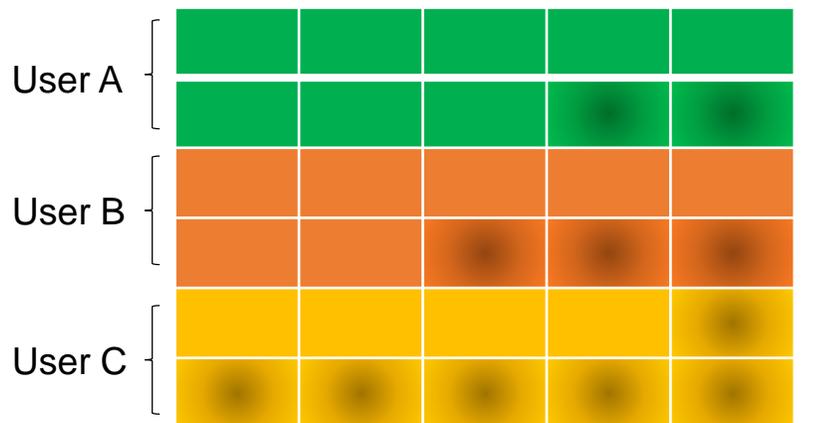
依用途區分：行政區、操作飼養區、機電設備區、備料區

# 材料方法: (3)繁殖注意事項

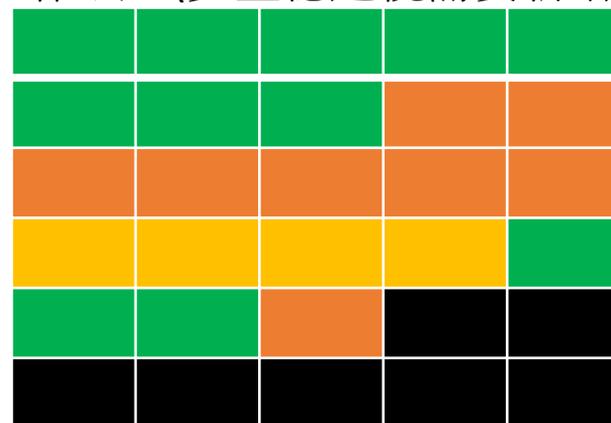
- 小鼠每胎平均約6-10隻(視品系) 動情週期4-6天，懷孕週期19.5天，哺乳期間可受孕(受精卵著床會延遲)，出生後18-21天離乳
- 每一代老鼠週期從胚胎受精成長到性成熟約8週(公母鼠略有差異，公鼠較晚)，最佳繁殖期6週~9個月
- 小鼠的出生是有目的的，被安排的，並且user需能完全掌握
- AS core規定小鼠離乳分籠期限為28天，此亦代表小鼠出生後申請籠位至少有25天操作時間(扣除三天申請作業時間)
- 分籠原則每籠<5隻，公母分離，若公母不分離就會進入下個繁殖週期
- Check point: (1) mating plug (2) mating 後14天 (3) 出生 (4) 出生後14天

# 籠位使用與安排

作法 1 (流動性高，保留緩衝籠位)



作法 2 (少量穩定視需要新增)



(新增籠位未必在同架)



# 動物標記方式

夾耳標：常用方法之一（21天後）

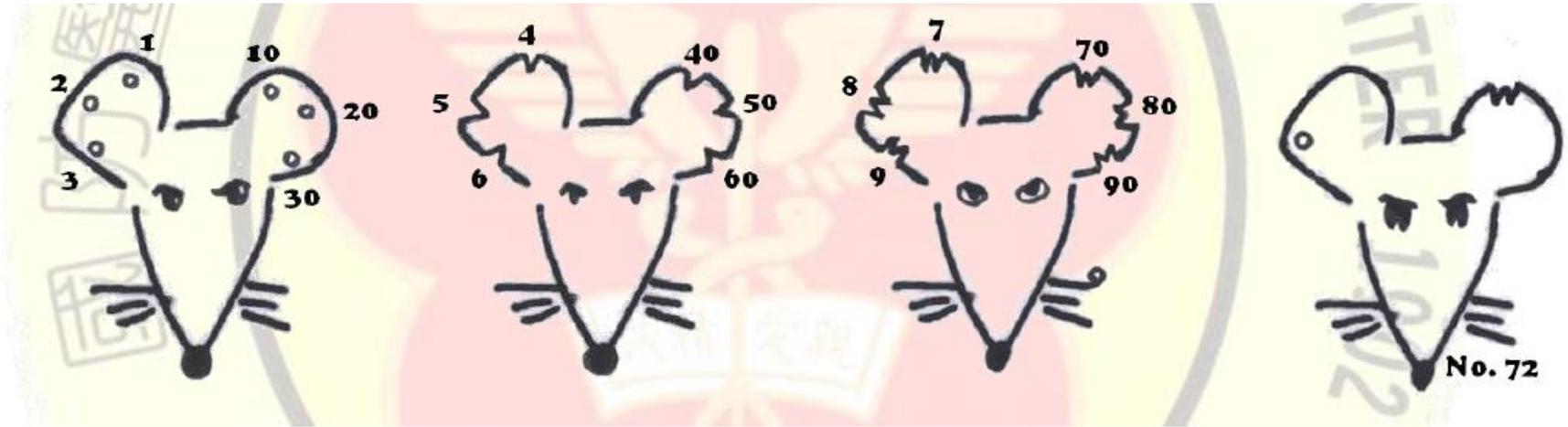
耳號：目前最常用方法之一（21天後）

奇異筆：以油性奇異筆塗寫在大鼠與小鼠之尾巴，可暫時作記，僅能維持12-24小時，尤以紅色奇異筆最不持久。（任意時候）

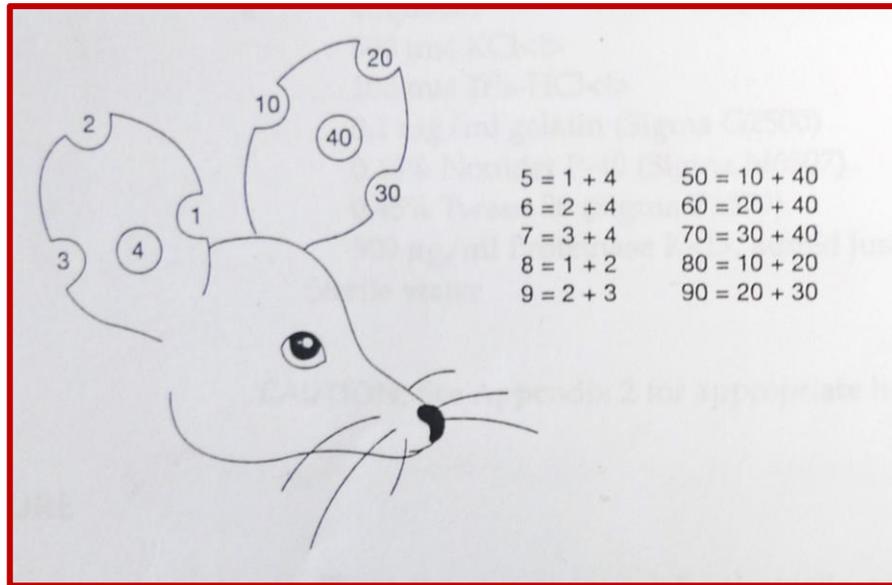
刺青：此法常應用於必須長期飼養的動物。動物須先鎮靜或麻醉使用刺青工具標記。此法常用於標示於兔耳之內側，以及大鼠與小鼠之尾巴。

趾號：常用方法之一（14天前）小鼠失去一節腳趾時，會影響攀爬及抓取食物的能力。由於此法對小鼠會造成嚴重的緊迫，所以兩週齡以上的小鼠剪趾時需對小鼠進行局部或全身性的麻醉。標記時僅能剪去第一指節，且每隻腳僅能剪去其中一隻腳趾。

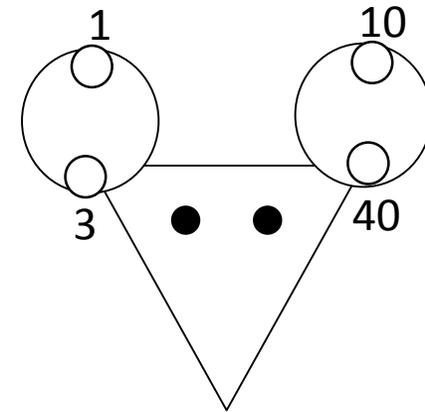
耳號A：



耳號B：



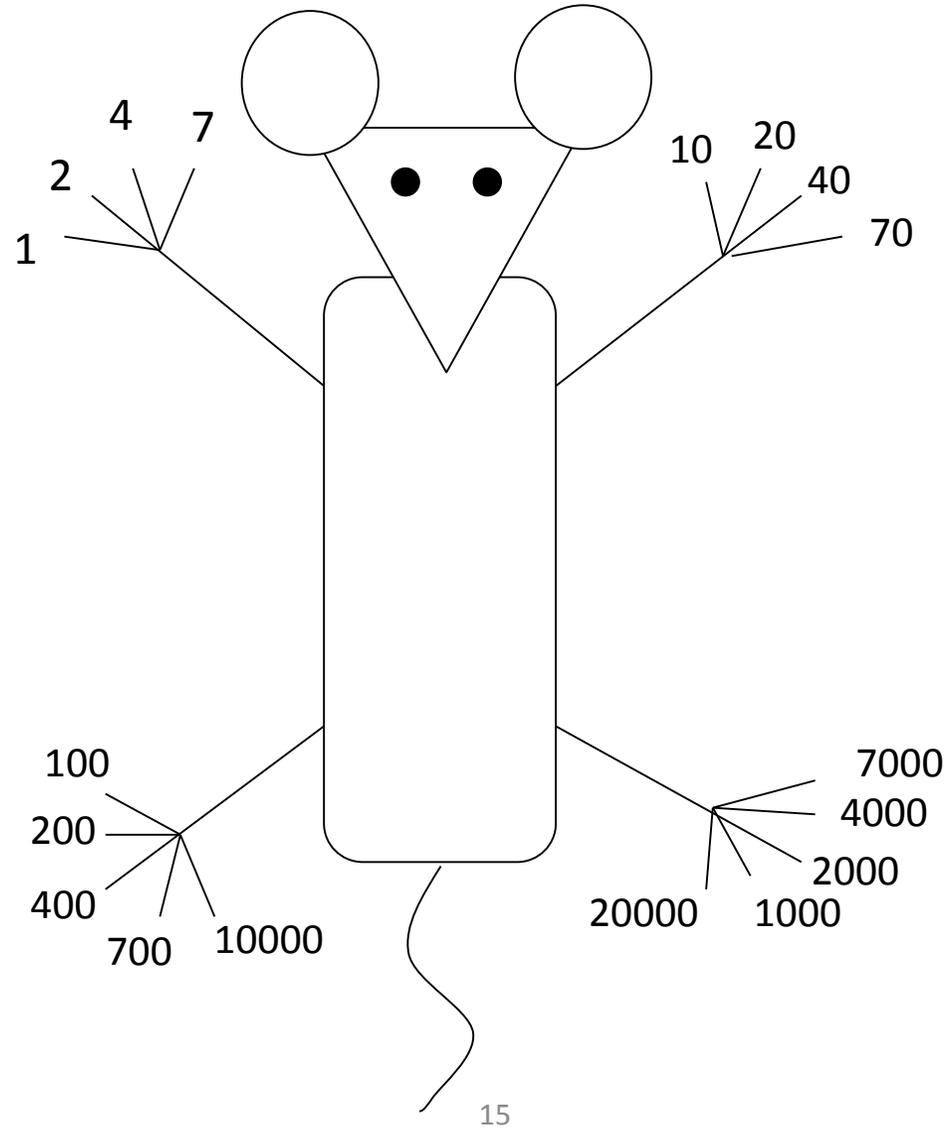
耳號C：



0、1、3、10、40、4、50、11、13  
14、41、43、44、51、53、54

耳標+耳號（左右及位置）or 指號

趾號:標示法(一) 不建議

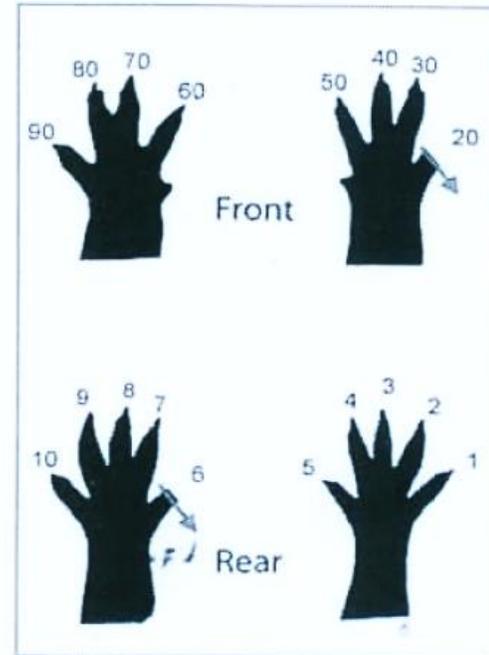


趾號:標示法(二)

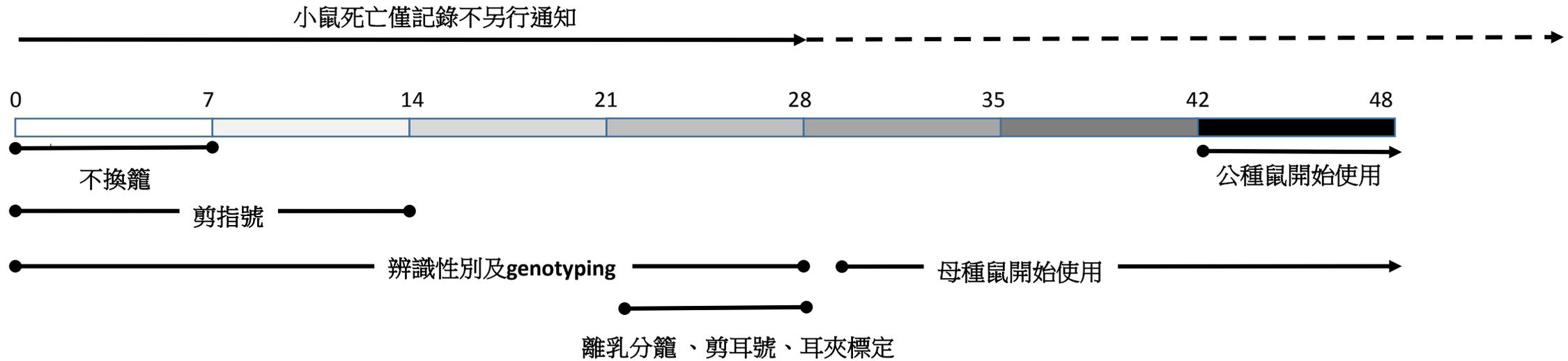
趾號圖示:



Example : mouse no.26



# 小鼠飼育操作基本schedule (AS core)



## 表單紀錄管理

- (1) 動物基本資料清單
- (2) 座標籠位內容紀錄表
- (3) 繁殖紀錄表
- (4) 行事曆 (Calendar)
- (5) 系譜圖 (pedigree)
- (6) 小鼠使用數量、死亡記錄表
- (7) 飼養卡



## (2)座標籠位紀錄表

S4籠架

	1	2	3	4	5	6	7
A	WT (M)	WT (M)	A <sup>-/-</sup> (M)	A <sup>-/-</sup> (M)	A <sup>+/-</sup> (M)	B <sup>-/-</sup> (M)	B <sup>+/-</sup> (M)
B	WT (F) X3	WT (F) x2	A <sup>-/-</sup> (F) X3	A <sup>-/-</sup> (F)X1	A <sup>+/-</sup> (F)X3 A <sup>-/-</sup> (F)X2	B <sup>-/-</sup> (F)X2	B <sup>+/-</sup> (F)X3

## 座標籠位內容紀錄表 (詳實記錄特徵編號)

WT (M) 公種鼠 #1	WT (M) 公種鼠 #2	A <sup>-/-</sup> (M) 公種鼠 #1	A <sup>-/-</sup> (M) 公種鼠 #2	A <sup>+/-</sup> (M) 公種鼠 #2	B <sup>-/-</sup> (M) 公種鼠 #1	B <sup>+/-</sup> (M) 公種鼠 #1
WT (F) X3 (耳標掛左 耳，右耳作 記) WT#1 WT#2 WT#3	WT (F) x 2	A <sup>-/-</sup> (F) X3 A <sup>-/-</sup> #1 A <sup>-/-</sup> #2 A <sup>-/-</sup> #3	A <sup>-/-</sup> (F)X1 A <sup>-/-</sup> #4	A <sup>+/-</sup> (F)X3 耳標掛左耳 A <sup>+/-</sup> #1 A <sup>+/-</sup> #2 A <sup>+/-</sup> #3  A <sup>-/-</sup> (F)X2 耳標掛右耳 A <sup>-/-</sup> #5 A <sup>-/-</sup> #6	B <sup>-/-</sup> (F)X2 B <sup>-/-</sup> #1 B <sup>-/-</sup> #2	B <sup>+/-</sup> (F)X3 B <sup>+/-</sup> #1 B <sup>+/-</sup> #2 B <sup>+/-</sup> #3

(3)繁殖紀錄(操作)表 (日期, 籠位, 編號)

Mating date	Male	Female	Plug date	Harvest date	Note
2018/06/03	A <sup>+/-</sup> #1 S4 -A3	WT#1 S4 -B1	2018/06/05 E0.5	2018/06/24 P0	母鼠mating 後留在S4-A3



# (4) 行事曆 (Calendar)

日曆 今天 < > 2014年9月 農曆八月~九月 天 週 月 4天 待辦事項 更多 設定

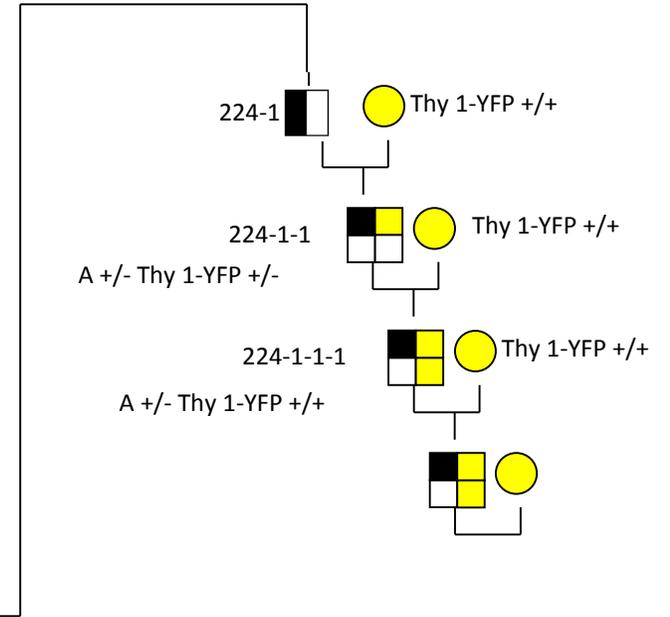
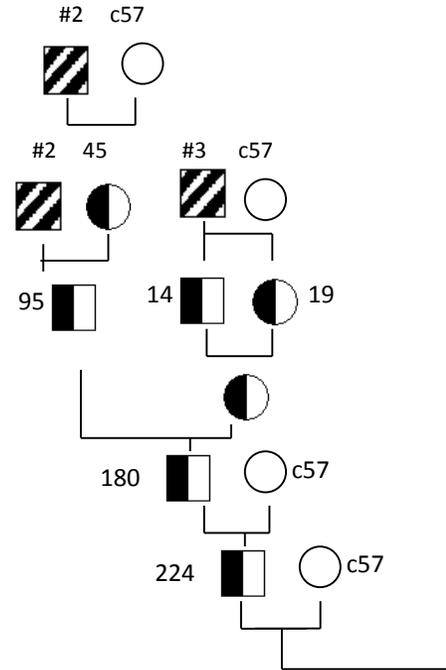
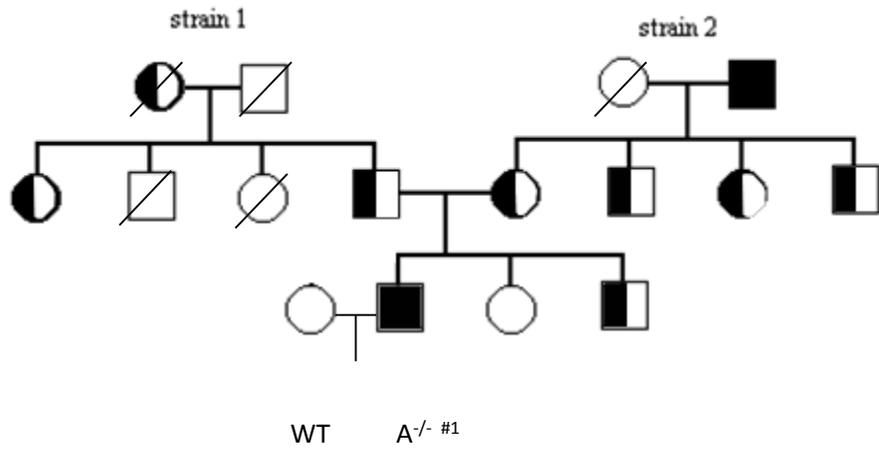
建立

2014年9月 < >

週一	週二	週三	週四	週五	週六	週日
9月1日 初八	2 初九	3 初十	4 十一	5 十二	6 十三	7 十四
8 白露	9 十六	10 十七	11 十八	12 十九	13 二十	14 廿一
15 廿二 A <sup>-/-</sup> #1 S4-A3 WT#1 S4-B1 Set mating	16 廿三 A <sup>-/-</sup> #1 S4-A3 WT#1 S4-B1 Plug E0.5	17 廿四	18 廿五 S4-H5 genotyping P7	19 廿六	20 廿七	21 廿八
22 廿九	23 秋分	24 九月	25 初二	26 初三 A <sup>-/-</sup> #1 S4-A3 WT#1 S4-B1 取E10 embryo	27 初四	28 初五 S4-H5 提出籠位申請
29 初六	30 初七	10月1日 初八 S4-H5 分籠	2 初九	3 初十	4 十一	5 十二

我的日曆  
其他日曆

# (5) 系譜圖 (pedigree)



- male
- female

Genotyping 後再給正式編號，編入pedigree



# 鼠籠卡牌填寫務必詳實，隨時更新

## 一般記錄卡

**Stock Cage**

Rack :      —  
Cage :     

IACUC:

Inst. :		Date:
PI:		User:
Phone:		Source:
Sex	_____ ♂	DOB:
	_____ ♀	DOB:
Strain:		
Comment:		

## 繁殖卡

**Breeding Cage**

Rack :      —  
Cage :     

IACUC:

Inst. :		Date:			
PI:		User:			
Phone:		Source:			
Sex	_____ ♂	DOB:			
	_____ ♀	DOB:			
Strain:					
PG	DOB	NO.	DOW	♂	♀



雙槽飼養務必詳註  
左槽 (L)  
右槽 (R)

# Conclusion

- 公母鼠分開飼養（隻數務必控制在每籠5隻以下，密度過高會抑制繁殖能力）
- 除非是同littermate，8週以上公鼠需分開飼養，避免打鬥，分開飼養後就不再合併
- 只留下要用的老鼠，並給予編號
- 建議使用年齡：繁殖用公鼠2~10個月齡，繁殖用母鼠2~8個月齡
- 小鼠平均發情週期為4-6天，平均夜晚發情期為12個小時，懷孕周期為19天，哺乳期間可再受孕，但著床時間會延後，產期亦會延後
- 操作定義：檢查到陰道栓(plug)當日為E0.5，出生日為P0
- 表單，卡牌填寫確實並搭配實驗記錄本及calendar，有利於管理追蹤及他人檢查
- Genotype不明的老鼠或是不確定的老鼠若未能明確確認，不要使用
- 繁殖策略：每三個月為一代，擬定使用量及代與代間之銜接
- 動物的生與死都是實驗的一部分，是data還是只需要記錄？
- 多久進一次動物房？

# 動物實驗申請與操作之相關規定

institutional animal care and use committee (IACUC)

# 動物實驗計畫撰寫

- 計畫主持人基本資料
- 實驗操作人員基本資料
- 實驗動物資料
- 危險性實驗說明
- 經費來源
- 實驗緣由
- 實驗步驟
- 附件
- [201808\\_workshop\IACUC\\_17-10-1115\\_王毓權.pdf](#)

# 動物使用計畫書審查(IACUC)3R/5R原則

- 實驗操作
- 人員教育訓練與資格
- 動物疼痛與緊迫評估
- 人道終止/安樂死
- 止痛/麻醉/手術
- 計畫評估
- 有無替代方案
- 活體動物使用情形
- 實驗設計
- 統計方法 (使用數量)

- Replacement 取代
- Reduction 減量
- Refinement 精緻化
- Respect 尊重生命
- Responsibility 負責

世界上最危險的動物

所有的錯都是人的錯

# 資料來源

- 慈濟大學 動物中心 <http://www.lac.tcu.edu.tw/detail.php?recordID=1>
- 成功大學 動物中心 [http://www.ncku.edu.tw/~animal/ch/m\\_weight.html](http://www.ncku.edu.tw/~animal/ch/m_weight.html)
- 屏科大 [018實驗動物飼養管理實習](#)  
<http://openinfo.npust.edu.tw/agriculture/npus12/m18/018/018%E5%AF%A6%E9%A9%97%E5%8B%95%E7%89%A9%E9%A3%BC%E9%A4%8A%E7%AE%A1%E7%90%86%E5%AF%A6%E7%BF%92--%E5%85%A8.pdf>
- 國防大學講義 <http://www.ndmctsgh.edu.tw/mediafile/18580030/news/39/2012-7/42012-7-23-16-53-17-nf1.pdf>
- 飼養育種  
[http://animal.coa.gov.tw/download/labaratory/110524/39\\_download\\_all.pdf](http://animal.coa.gov.tw/download/labaratory/110524/39_download_all.pdf)



# 實驗動物技術操作 教育訓練課程

楊東一

8/23/2018

1. 實驗小鼠基本生理認知
2. 實驗動物(小鼠)操作技術

# 實驗小鼠基本生理認知

## 實驗動物

指為科學應用目的而飼養或管領之動物(行政院農委會「動物保護法」第一章-第3條 )

- Experimental animal – 指動物被用於試驗，教學或研究。
- Laboratory animal - 指動物以人工方式飼養管理，提供作為研究應用並具有特殊遺傳及品系特性之動物。

## 為何小鼠？

**Pennisi E. (2000) A mouse chronology, Science 288:248-257**報導中：

1. >90%哺乳類動物的科學應用
2. 品系與族群最多
3. 成功的基因工程動物模式

其他優點：

體型小，繁殖能力強，壽命短，基因遺傳特性與人類相似度高，育種及操作方便與飼養空間考量。

# 基本生理認知 (I)

## 小鼠

綱：哺乳動物綱

目：齧齒目

科：鼠科

屬：小鼠屬

種：小鼠種



<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0090570>

## 攝食量

- 一般消耗4-5g
- 吃、喝皆在晚上

## 水量消耗

- 每天飲水量2 ml，可到4-6 ml
- 平均代謝水製造2 ml/day，所以每日需4 ml
- 尿1 ml/day，可到4-6 ml
- 小鼠沒有汗腺，亦不會喘氣
- 小鼠表面積較大，藉由蒸散作用降溫
- 水分保留藉由尿液濃縮及冷卻呼出空氣

# 基本生理認知 (II)

## 體溫

- 36.5-38.0°C
- 體溫耐受範圍小 (29.6-30.5°C) , 37°C 造成死亡
- 溫度 > 30°C 雄鼠造成不孕
- 21-25°C 生長速率快

## 壽命

- 一般在2-3年，視品系有不同，
- 小鼠成年重量20-40g

## 生殖生理

- 性成熟35日齡，陰道在24-28日齡已張開
- 公鼠性成熟較母鼠晚兩週
- 動情週期約4-5天，發情期9-20 hr，通常夜間10點-凌晨一點
- 懷孕期19-31天，平均21天

## 基本生理認知 (III)

- 全年可配種，多次發情期動物，飼養過度會抑制發情
- 雜交品系懷孕期較近親品系短
- 每窩仔鼠數依品系及母鼠年齡而異
- 胎次1-12胎，平均每年3-6胎，2-8胎為最佳狀態(10-12頭)，近親品系生產頭數少
- 排卵時間在發情期開始後2-3小時，可配種
- 產後發情期分娩後20-24小時
- 仔鼠移走2-4天內(哺乳)，動情週期重新啟動

# 費洛蒙

- Lee-Boot effect :

當性成熟之雌鼠密集飼育於飼育籠，而飼育室中無性成熟雄鼠，則雌鼠之動情週期將延長從4-5天至10-14天。 Lee, S. van der; Boot, L.M (1956). "Spontaneous Pseudopregnancy in Mice". *Acta Physiol. Pharmacol. Neer.* **5** (213).

- Whitten effect :

飼育籠中加入一性成熟之雄鼠，則大多之雌鼠將於3-4天後發情。 Whitten, W.K. (July 1956). "Modification of the oestrous cycle of the mouse by external stimuli associated with the male". *Journal of Endocrinology.* **13** (4): 399–404.

- Vandenberg effect :

未性成熟雌鼠之飼育籠中出現一性成熟之雄鼠(或尿液)時，尚未性成熟之雌鼠的動情週期會被提早啟動。 Vandenbergh JG, Whitsett JM, Lombardi JR (1975). "Partial isolation of a pheromone accelerating puberty in female mice". *Journal of Reproduction and Fertility.* **43** (3): 515–23.

- Bruce effect :

懷孕小鼠受到陌生雄性小鼠干擾致囊胚未能著床，而使懷孕終止之效應

Bruce, Hilda M. (1959). "An Exteroceptive Block to Pregnancy in the Mouse". *Nature.* **184** (4680): 105

<b>Pheromone</b>	<b>Laboratory procedures</b>	<b>Effects on rodents</b>
<b>Bruce effect</b>	Addition of a foreign male	Blocks pregnancy in females
<b>Lee-Boot effect</b>	Females are housed together and isolated from males	Suppresses or prolongs estrus; decreases luteinizing hormone; increase prolactin
<b>Vandenbergh effect</b>	Accidental exposure of prepubescent female mice to male mice/urine	Accelerates female puberty
<b>Whitten effect</b>	Females exposed to male animal or urine	Induces estrus in a group of females

Bind RH., et al. (2013). "The Role of Pheromonal Responses in Rodent Behavior: Future Directions for the Development of Laboratory Protocols", J Am Assoc Lab Anim Sci, Mar; 52(2): 124–129.

# 實驗動物(小鼠)操作技術

# 動物操作技術

1. 徒手保定
2. 標示與識別技術
3. 投藥技術
4. 採血技術

***“First do no harm”*** –  
**Greek Hippocratic Oath**  
**希波克拉底誓詞**

.....I will use those dietary regimens which will benefit my patients according to my greatest ability and judgement, and I will do no harm or injustice to them.....

# 1. 動物保定

為何要熟練保定技術？

- 能夠減少動物緊迫
- 可減低試驗的操作變因
- 使動物避免人為操作所帶來的危害
- 降低操作人員傷害

# 單手保定

- 輕抓住小鼠尾巴基部，放置於前肢可攀附之鐵網或平面，待其抓住鐵網後將尾巴輕輕向後提拉，此時老鼠會伸展並向前衝。
- 向前衝後，馬上以食指及拇指抓取頸後寬鬆皮膚，其餘指頭固定後背皮膚並將小鼠提起。
- 以小指勾住尾部，確認無晃動。
- 請隨時注意動物呼吸。



# 雙手保定

- 一手抓住小鼠尾巴基部，放置於前肢可攀附之鐵網或平面，待其抓住鐵網後將尾巴輕輕向後拉，此時老鼠會伸展並向前衝。
- 向前衝後，馬上以另一手抓取頸後寬鬆皮膚，其餘指頭固定後背皮膚並將小鼠提起。
- 以小指勾住尾部，確認無晃動。
- 請隨時注意動物呼吸。

1



2



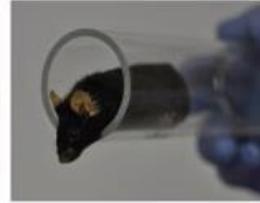
3



# Handling methods used to pick up mice

## Handling with a tunnel

- ▶ Mice guided into tunnel with free hand
- ▶ Lifted above cage without direct contact
- ▶ Tip mice out of the tunnel backwards



- ▶ Smooth clear plastic tunnels are ideal for handling

## Practicalities: cup

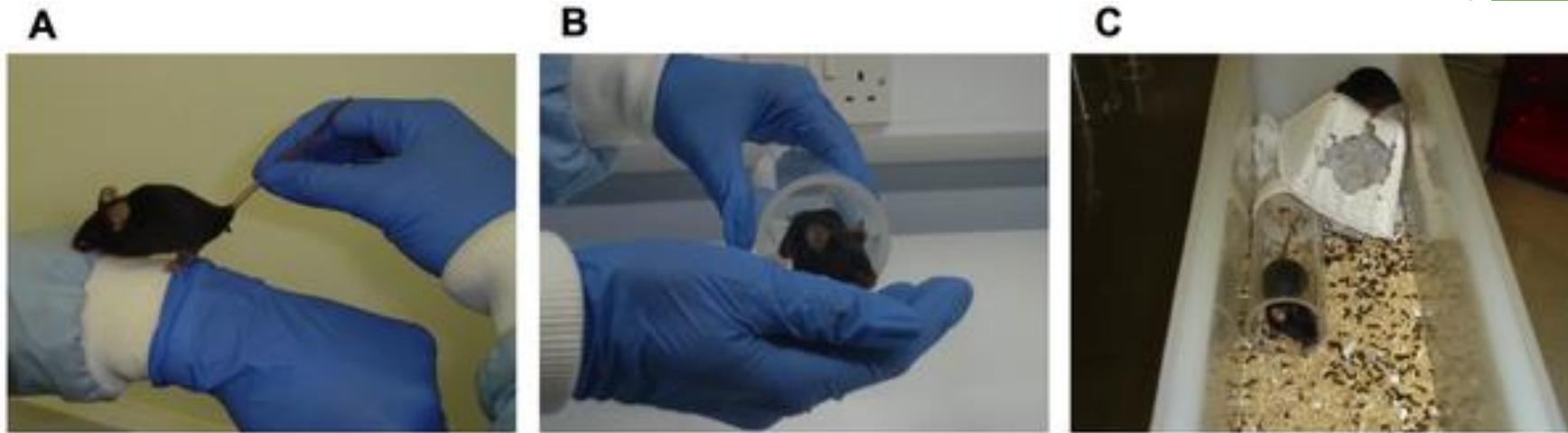
- ▶ Habituation to the hand
  - On first handling, close hands loosely around mouse for up to 20s (5-10s often sufficient)



Can also habituate by

- ▶ holding between closed hands when transferring to clean cages

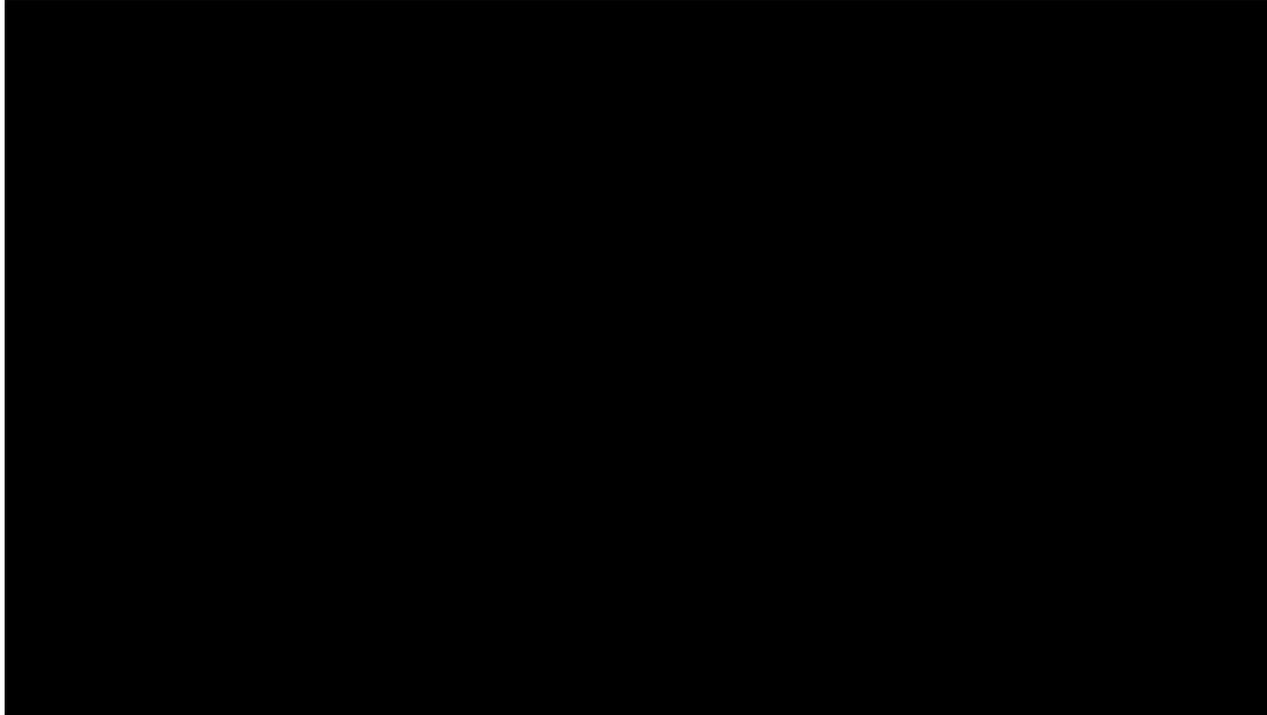
# Handling methods used to pick up mice.



Gouveia K, Hurst JL (2013) Reducing Mouse Anxiety during Handling: Effect of Experience with Handling Tunnels. PLOS ONE 8(6): e66401. doi:10.1371/journal.pone.0066401  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0066401>

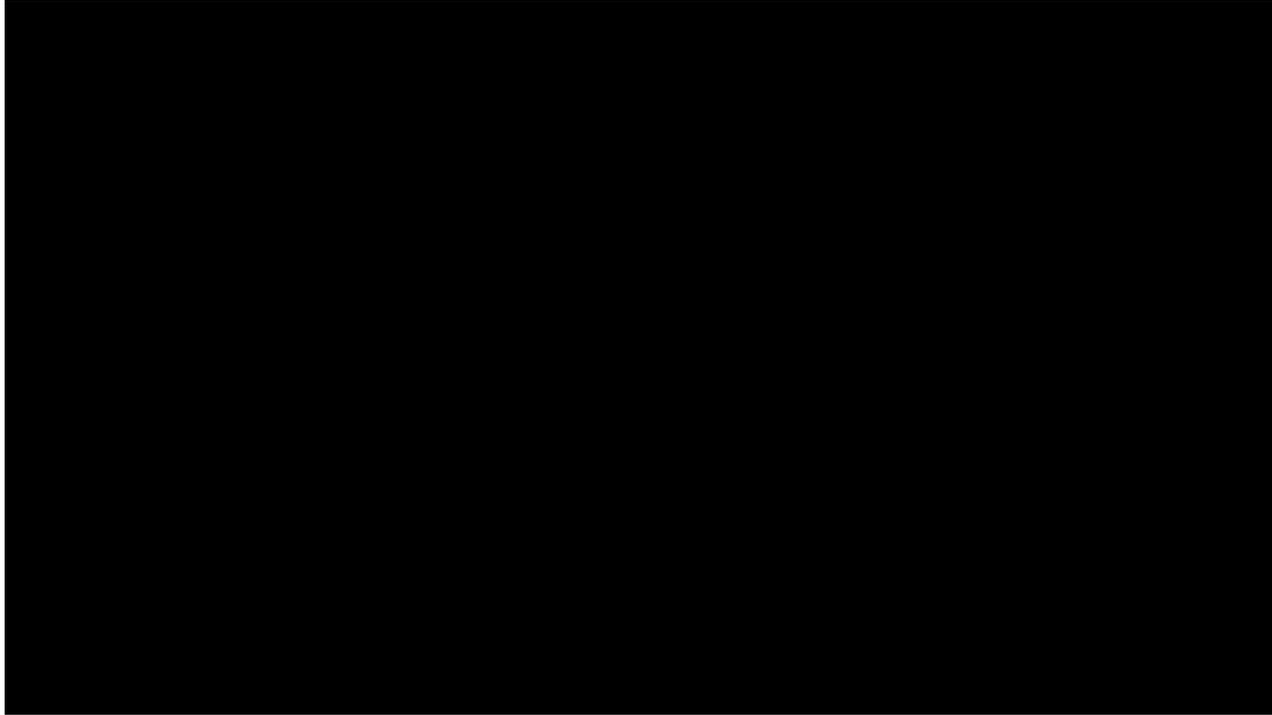
[Video](#)

## Tunnel handling

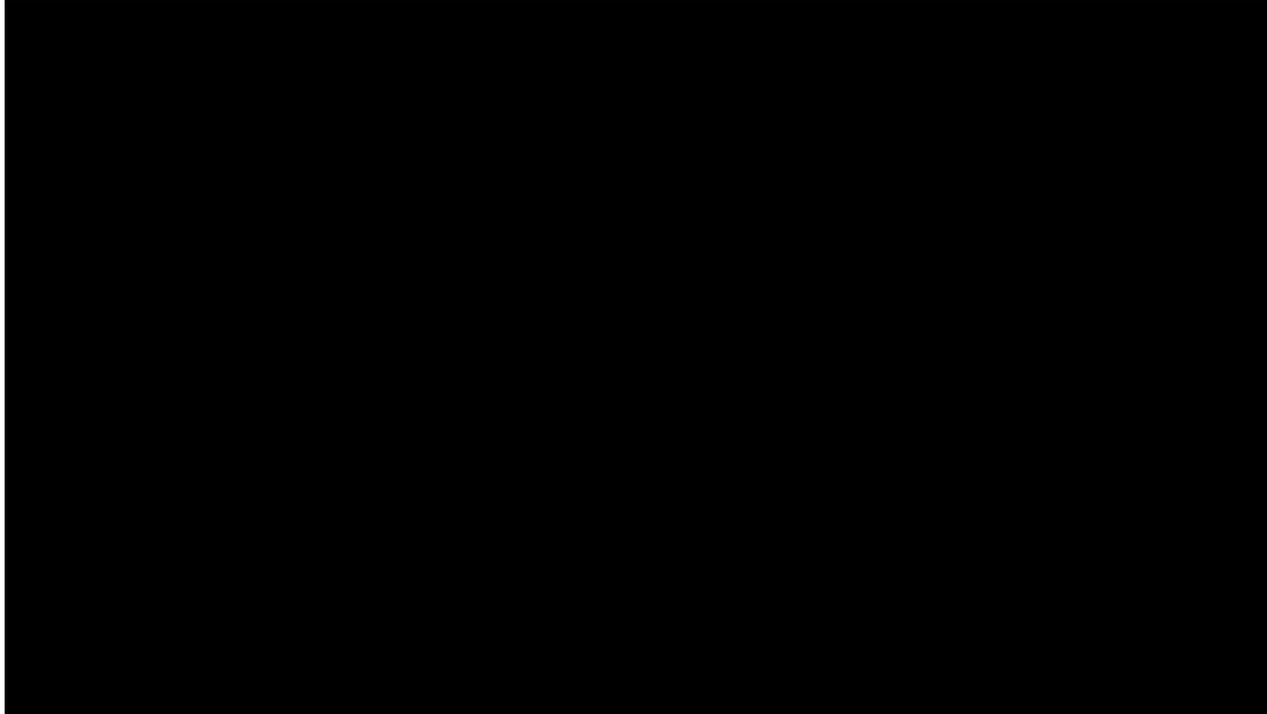


<https://www.nc3rs.org.uk/video-clips>

## Tunnel handling at IVC cage



## Cupping method



<https://www.nc3rs.org.uk/video-clips>

## Radial maze annotation



<https://www.nc3rs.org.uk/video-clips>

## 2. 動物標示與識別技術

分為：暫時性及永久性

暫時性：簽字筆標示、食用色染毛、剃毛



永久性: 耳洞、耳標、剪趾、刺青、microchip



<http://www.somarkinnovations.com/labstamp-gallery-2>

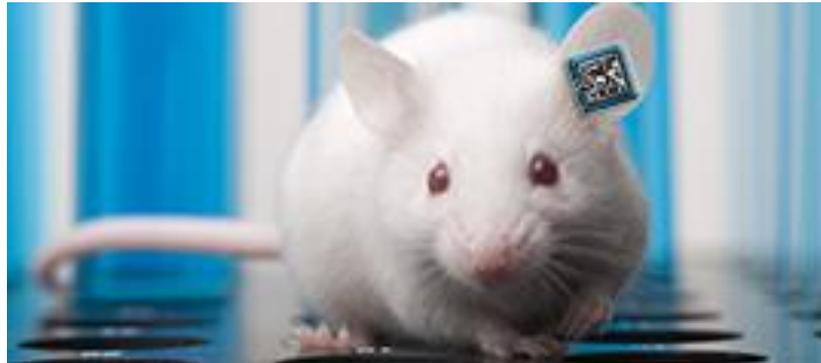


<http://muromachi.com/en/archives/english/2157>





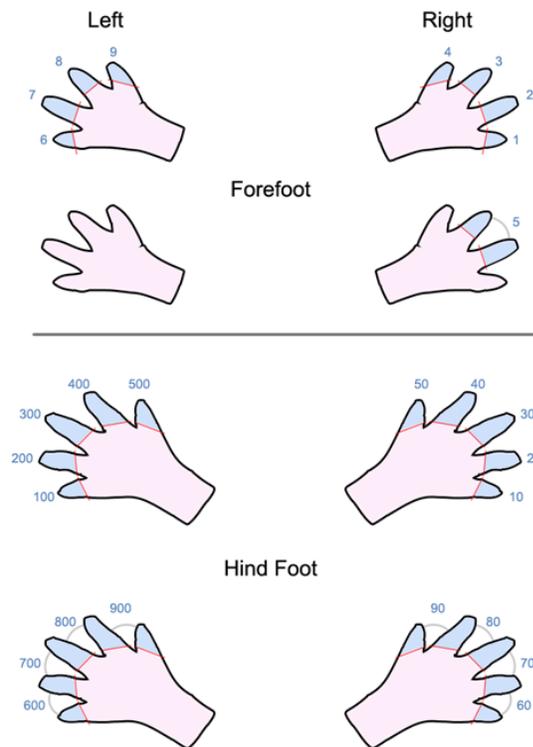
<http://www.locusttechnology.com/Microchips.html>



<https://rapidlab.com/>

***The Guide for the Care and Use of Laboratory Animals (the Guide, NRC 2011)*** states:

“As a method of identification in small rodents, toe-clipping should be used only when no other individual method (ear tag, ear punch, microchip or tattoo) is feasible.” (pg. 75)



### 3. 投藥技術

- 腹腔注射 (Intraperitoneal, IP)
- 肌肉注射 (Intramuscular, IM)
- 皮下注射 (Subcutaneous, SC)
- 靜脈注射 (Intravenous, IV)
- 餵食管餵食 (Oral gavage)

## 腹腔注射

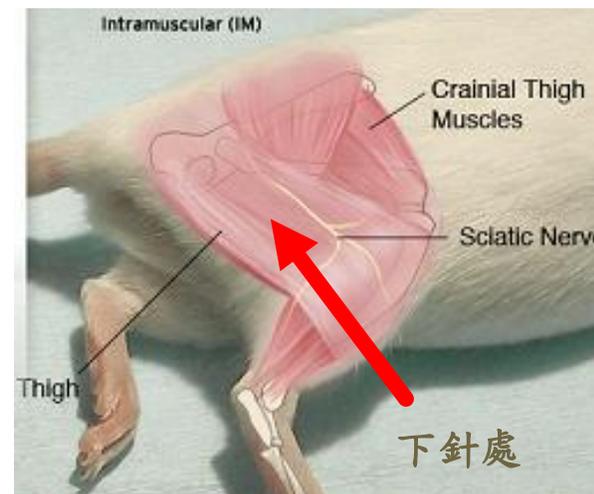
1. 使頭部朝下，由下腹中線偏左或偏右約1-2 mm 處下針，約插入3-5 mm 即可開始將藥劑送入腹腔。
2. 下針會感覺針頭穿過皮下及腹壁，避免將藥劑注入皮下，當針頭碰觸到消化道時，消化道會有自主的反射，少有將針插入消化道的情形。
3. 藥劑注入時須試吸針筒以確定注射位置。如有血液或其他液體，表示不適當的位

- 注射位置：右下腹部，腹腔內
- 毛皮以酒精棉擦拭消毒
- 下針後回抽，確認下針位置無誤



## 肌肉注射

1. 行肌肉注射時，最好有一助手在旁協助，由一人保定，另一人投藥。
2. 可將藥劑注入有任何骨骼肌部位，一般多將藥劑注入大腿(股骨)後側之肌肉。
3. 以酒精棉擦拭欲注射部位，注射針插入臀部肌肉。
4. 試吸針筒以確定注射位置(如有血液倒流入針筒，表示不適當，須重新插入)
5. 慢慢地將液狀藥劑注入。避免注入太快，以防組織創傷。



## 皮下注射

1. 可選擇頸部或軀幹部皮下做為注射位置。
2. 保定後以酒精棉擦拭欲注射部位
3. 於拇指與食指擰起皮膚交疊處，插入注射針。
4. 拇指與食指感覺針頭之位置，注入藥劑時，也可以這二手指感覺是否藥劑確實注入皮下。
5. 注射油性藥劑時，停止動作數秒，才將注射針抽出，可減少油性藥劑漏出之機會。

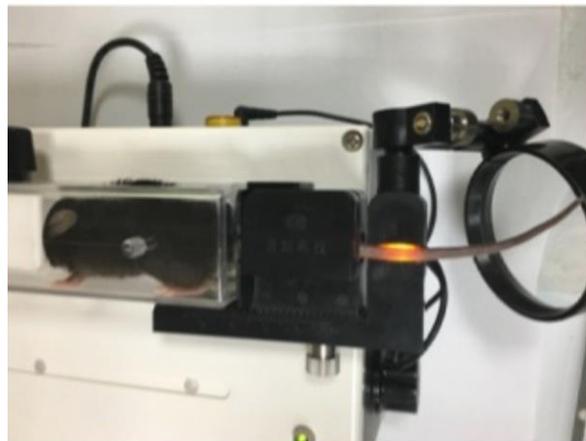
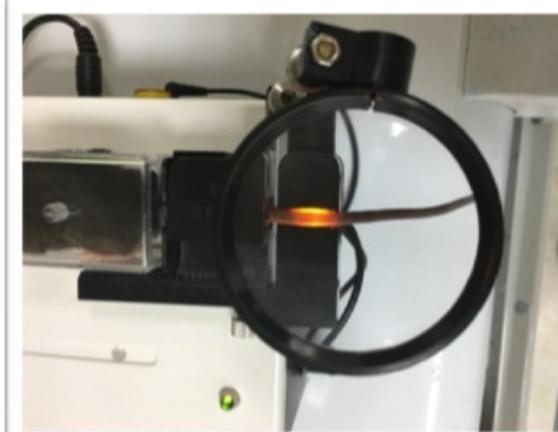
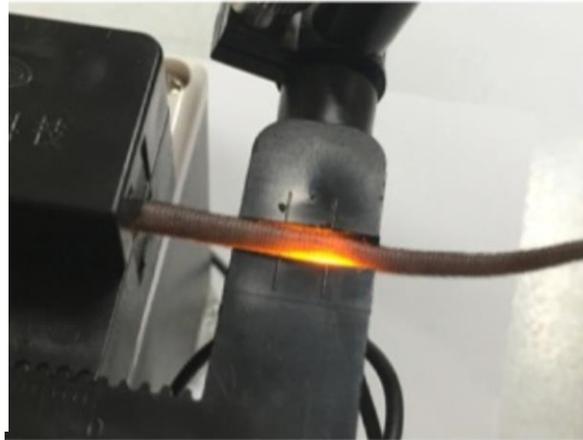
- 注射位置：背部皮膚皮下組織中
- 毛皮以酒精棉擦拭消毒
- 下針後回抽，確認下針位置無誤



## 靜脈注射

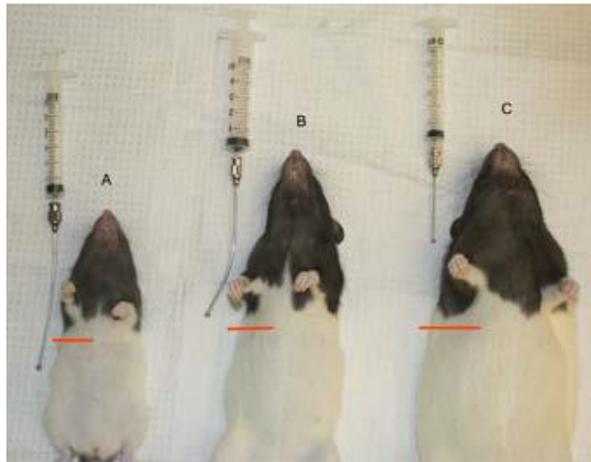
1. 小鼠之尾部共有4條血管，由於皮薄透明，血管皆明顯易見，小鼠尾之腹側有一條動脈；而兩側及背側為靜脈。這些血管接近尾根處較為粗大，故可行注射。
2. 在行尾根靜脈注射時，需應用保定架，一手捏緊鼠尾並拉直，由近尾根約10-15 mm處，以與尾皮呈20-30°角向心下針，下針時應注意針尖之斜面應朝上，針尖入靜脈時會有一霎那「通暢」





## 管餵

1. 保定(PS.大鼠兩人操作較佳)
2. 使身體盡量拉長且頭頸要直，估計針頭插入之深度，一般齧齒動物的胃約在胸骨劍狀軟骨處。
3. 經口將胃管球形頭置入口腔插入，經喉背滑入食道達胃內部，插入時感到不順暢可能是插入氣管，需重新再操作
4. 若將液體灌入氣管將造成動物死亡
5. 遇動物激烈掙扎時，需將動物放回飼養盒中待動物恢復再行操作。



## 4. 採血方法

1. 採血量與恢復時間
2. 尾靜脈採血
3. 臉頰採血
4. 隱靜脈採血
5. 心臟採血
6. Capillary Microsampling (CMS)

## 老鼠身上可以採到多少血？

1. 動物體內的血液量，依據動物的大小體重而異
2. 就不同動物別而言，體中的血液量約是55 - 70 ml/kg BW或體重的**5.5 - 7 %**
3. 以20-40 g 小鼠而言，全身血液約有1.1 to 2.8 ml

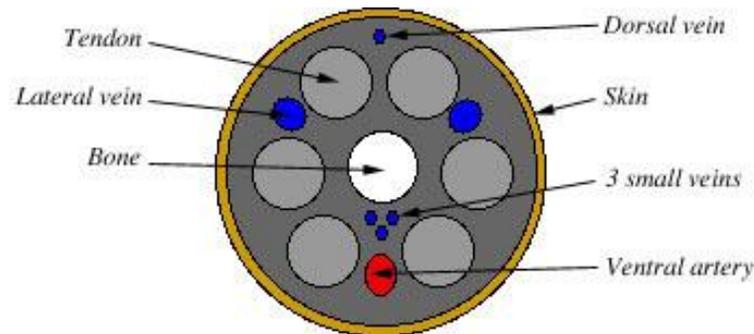
## 採血(連續)後恢復時間

1. If **15%** TBV (總血量) / wait **4 weeks**
2. If 10% TBV / wait 2 weeks
3. If 7.5% TBV / wait 1 week

# 尾靜脈採血

1. 以保定器保定小鼠。
2. 以熱水(40°C)或40-100W 燈照射全身加溫或局部加溫。
3. 抽血處需先用酒精棉擦拭消毒。
4. 用拇指在上食指在下抓住2/3 尾部。
5. 食指上提姆指下壓彎曲成一個轉折點。
6. 於轉折點下方下針。
7. 抽完血用酒精棉按壓止血。

小鼠



# 臉頰採血

1. 大小鼠面頰部特有的小血管束在下頷後面（如圖1），這個點是眼窩靜脈，下頷靜脈和其他靜脈走經大小鼠面部區域的一點，最終彙集形成頸靜脈的起始端。在下頷骨的後面，方向朝向耳朵。
2. 採血針紮進大小鼠面部，穿刺時可以感覺到下頷骨，但要儘量避免刺傷下頷骨，實驗人員需手持小鼠的後頸部為小鼠營造一種輕鬆的環境，抓小鼠肩胛骨之間的皮膚，而不是抓住兩隻耳朵(會造成皮膚或者面部血管扭曲)。
3. 穿刺部位採血，待採血完畢時用無菌紗布壓住出血口10-30s可止血。

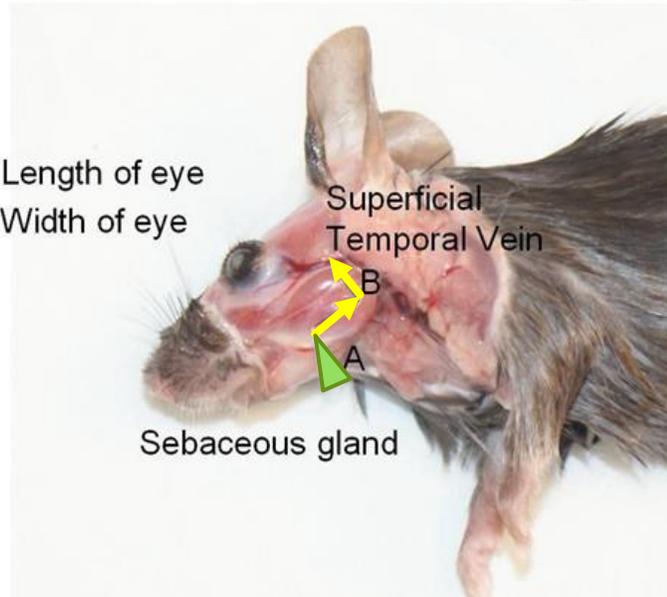


MEDIpoint, Inc.  
[http://www.medipoint.com/html/animal\\_lancets.html](http://www.medipoint.com/html/animal_lancets.html)

- 左右兩臉頰可以輪流採血
- 對小鼠的傷害很小
- 血液的品質佳
- 出血量約0.2 ml
- 需留意動物呼吸狀態
- 適用於小鼠

## An Important Landmark

- A = Length of eye
- B = Width of eye



## 小鼠

# 隱靜脈採血

1. 將大小鼠徒手保定或者將動物塞進適當直徑與長度的透明塑膠管或保定器
  2. 剔除大腿外側之皮毛，即可在踝關節的上下端見到隱靜脈
  3. 將剃毛部位以酒精消毒，以23~30 G的針頭刺開隱靜脈
  4. 採血完畢以酒精棉壓迫數秒即可止血
- 左右腳可以輪流採血
  - 傷害很小
  - 血液的品質佳
  - 出血量約0.15- 0.2 ml
  - 適用於小鼠與大鼠

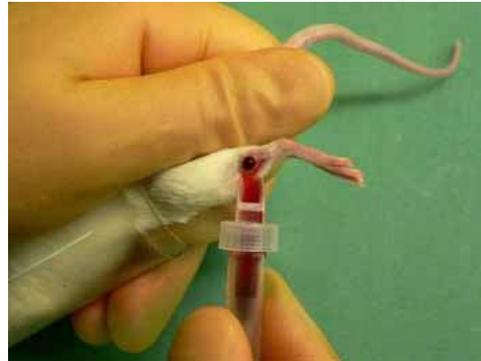
1



2



3



## 心臟採血(活體不建議使用)

1. 將動物進行麻醉或安樂死
2. 選用適當的針投與針筒  
例如：小鼠-1ml/26G  
大鼠-3ml/24G
3. 將動物攤平於桌面
4. 以約10-30度角下針
5. 出現回血後緩慢將血液抽出



# Capillary Microsampling (CMS)

## Microsampling:

The volume of blood sample is generally less or equal 50 $\mu$ l

<https://www.nc3rs.org.uk/microsampling>

A promotional banner with a light blue background. On the left, the text reads "One Mouse; One PK" in a large, dark font, followed by "The Magic of Capillary Microsampling" in a smaller, dark font, and "Case Study from MedImmune" in a white font. On the right, there is a photograph of a brown mouse. Above the mouse is a dark blue button with the text "Learn how" in white.

One Mouse; One PK  
The Magic of Capillary Microsampling  
Case Study from MedImmune

Learn how

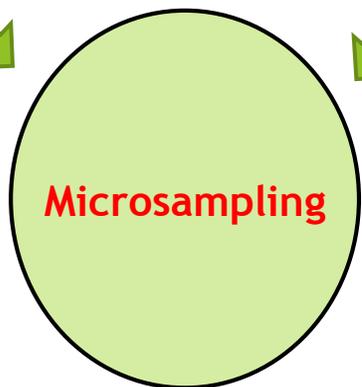
<http://page.gyrosproteintechnologies.com/one-mouse-microsampling-offer>

Resources

- Reduced facility costs
- Fewer animals needed
- Fewer material/compound required

Animal Welfare

- Less stress
- Less invasive
- Sampling quickly
- Fewer animals needed
- Alternative sampling routes
- Reduced warming
- Reduced blood loss
- Reduced holding/restraint



Scientific

- All animals sampled
- Better PK/PD and TK/TD profiles
- Multiple endpoints from one animal
- Alternative sampling routes
- Rehabilitation of animal for comparison studies

**20**  
mice

**4**  
mice

*Creating PK profiles by mouse serial sampling reduces animal usage and enables more data points.*

<http://page.gyrosproteintechnologies.com/one-mouse-microsampling-offer>

charles river

**MICROSAMPLING: LESS IS MORE**

 Efficacy and safety assessments require blood collection from study animals to gather data on the effects of a drug compound.

**WHAT IS IT?**

It is a method to collect a very small amount of blood, typically  $\leq 50 \mu\text{L}$  (ICH S3A Q&A document).

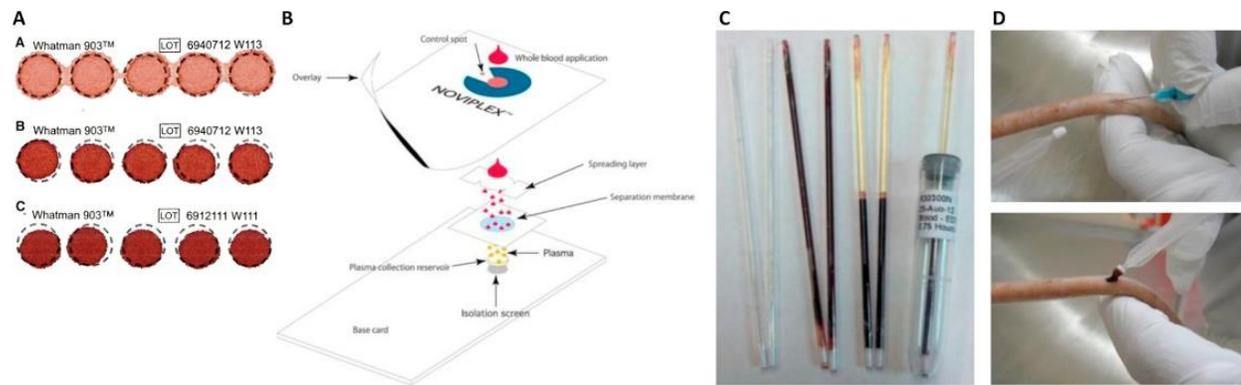


**ENDPOINTS**

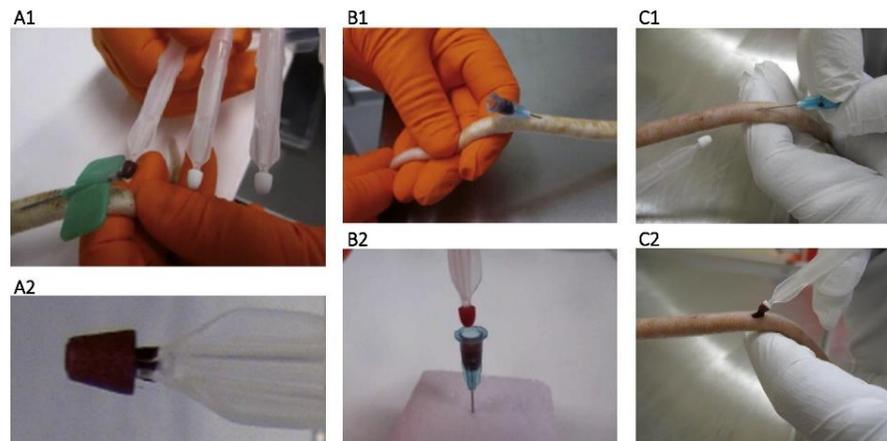
Microsampling has been validated for numerous endpoints:

BIOANALYSIS	PHARMACODYNAMICS	CLINICAL PATHOLOGY
ANTI-DRUG ANTIBODIES	BIOMARKERS	IMMUNOTOXICOLOGY

<https://www.criver.com/products-services/safety-assessment/toxicology-services/microsampling?region=3701>



Gwenaël Nys, et. al (2017) [TrAC Trends in Analytical Chemistry](#)  
[Volume 97](#), December 2017, Pages 326-332



Miranda G.M. Kok and Marianne Fillet [Journal of Pharmaceutical and Biomedical Analysis](#)  
[Volume 147](#), 5 January 2018, Pages 288-296

# Use of Microsampling in Oncology Projects: Reduction & Refinement

Zena Wilson representing, Oncology iMED, Bioscience, AstraZeneca, UK



## Introduction

In drug development projects, compounds with promising *in-vitro* properties are selected for *in-vivo* testing to look at basic properties such as tolerability and blood levels. Many compounds are eliminated from screening cascades at this step as they do not have the appropriate drug-like properties to produce positive results in later disease models.

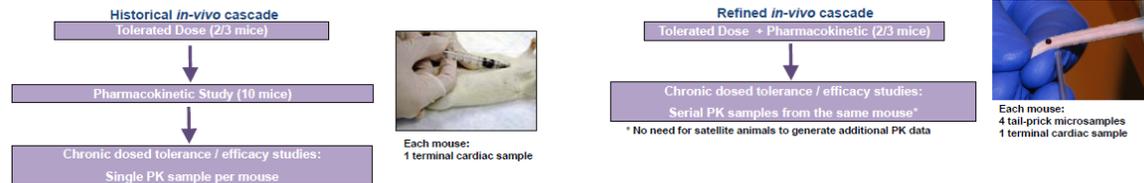
In the majority of cancer drug discovery projects this initial *in-vivo* work tends to comprise of a rapid test to make sure there is no overt toxicity that would cause animal welfare issues (known as a tolerated dose study or TD) followed by a pharmacokinetic study (or PK) to investigate drug absorption and elimination.

Using mice in routine PK studies can be challenging as the total blood volume of mice, often less than 1.5 ml, limits the size and number of samples that can be collected. Advances in bioanalytical techniques have opened up the potential to use smaller sample volumes (microsamples) to assess drug exposure, whilst minimising the physiological effect of taking large blood volumes.

Historically within AstraZeneca Oncology groups we have used two mice on the TD study and a further ten mice used to provide a 24 hour PK profile comprising of six time-points.

Several years ago we introduced a revised methodology for this initial *in-vivo* work package. By using smaller volume blood samples from the mouse tail vein we have been able to take timed samples from the animals used on the first TD study, as well as a terminal blood sample at the end of that study, to provide some of the information normally obtained from the subsequent PK work.

In addition we have introduced serial bleeding taking samples during the time course of chronic studies (tolerance and efficacy) to obtain more dynamic PK measurements.



## Method

Adequate training is necessary for blood collection using the microsampling technique.

This bleeding technique can be followed after warming the mice in a warming chamber to dilate the blood vessels prior to taking the sample (however more experienced individuals find this warming step is not necessary).

Alternate sides of the tail should be used and successive needle punctures moved towards the tail base.



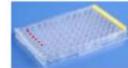
Samples are collected by a simple prick to the tip of the mouse's tail with a 25g needle. The blood is collected accurately with an EDTA coated 20ul micro capillary tube.



The blood sample is diluted into 80ul of PBS.



Samples are centrifuged to give a diluted plasma supernatant.



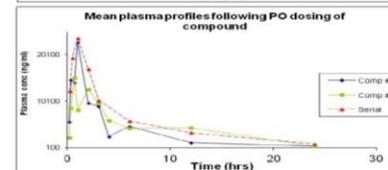
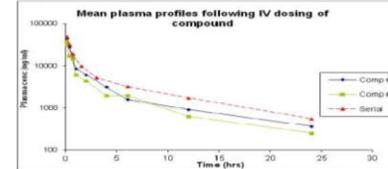
Supernatant is removed (70ul) and frozen in a 96 well plate. These samples are now ready for analysis.

Once the sample has been taken blood flow is stopped by applying finger pressure on a piece of soft sterile swab placed at the blood sampling site before the animal is returned to its cage.

## Validation Data

Before this method was routinely adopted by the Oncology group at AstraZeneca, Alderley Park there was a significant amount of data generated comparing composite PK studies (cardiac puncture or vena cava) and tail vein microsampling (serial) to ensure that the data was comparable between the two methods.

Examples of the data sets shown below demonstrate the accuracy and scientific validity of using this technique for PK analysis.



Data sets were generated across a number of projects dosing historical and novel test agents to increase confidence in the microsampling method.

#### Introduction & Aim

- Non-clinical toxicity studies in juvenile rats are required by FDA and EMA, prior to performing clinical trials in pediatric populations. Toxicokinetic (TK) assessment of the tested compound is essential for each toxicology study.
- The conventional volume (200 µL) blood sample for TK assessment cannot be collected from main test pups, instead, satellite animals are used. Due to the small size of the juvenile rats, a terminal procedure is used to collect a single blood sample. A full pharmacokinetic profile requires repeated blood sampling, which means the number of main test animals.
- Capillary Microsampling (CMS) is a technique for obtaining small amount of blood (~30 µL) time points. This technique makes it possible to collect multiple blood samples from one rat pup, thereby reducing animal use in TK assessments.
- We have proved that CMS is feasible to collect multiple blood samples from juvenile rats at 4, 10, and 17 days of age. One remaining question is whether CMS would compromise key toxicological endpoints.
- In this project, we investigated the effects of CMS on toxicological endpoints including body and organ weights, clinical laboratory parameters and clinical signs.

#### Materials, Methods & Results

Wistar Han juvenile rats at postnatal day (PND) 4, 10 and 17 underwent CMS via submandibular vein (SubV), tail vein (TV) or jugular vein (JV) for a maximum of 3 times in a 24-hour interval. Animals were terminated one day (acute group) or 7 days (chronic group) after CMS. Blood was collected at termination for clinical laboratory parameters by decapitation or from the aorta when deeply anaesthetized using isoflurane.

Acute and chronic effects of CMS on haematology and bio-chemistry parameters, body and organ weights (livers and livers, only chronic) were tested. Data were compared between CMS groups and their concurrent un-sampled controls. Clinical signs were monitored in life. The study design and summarized results are shown in the table below.

	PND4 (5/real/group)	PND10 (5/real/group)	PND10 (5/real/group)	PND17 (5/real/group)	Jugular vein (JV)
Photo					
Method	Submandibular Vein (SubV)	Submandibular Vein (SubV)	Submandibular Vein (SubV)	Tail Vein (TV)	Jugular vein (JV)
Frequency	3 x 33µL 2 x 33µL 1 x 33µL	3 x 33µL*	3 x 33µL*	3 x 33µL	3 x 33µL
Time Points (Time Post Dosing)	0.5, 2, 4 0.5, 2 0.5	0.5, 2, 4	0.5, 2, 4	0.5, 2, 4	0.5, 2, 4
Termination	PND 5 (Acute) PND 11 (Chronic)	PND 11 (Acute) PND 17 (Chronic)	PND 18 (Acute) PND 24 (Chronic)	PND 18 (Acute) PND 24 (Chronic)	PND 18 (Acute) PND 24 (Chronic)
Clinical signs	All pups in brake on cheek after one-time sampling; haematomas disappeared the day after	No findings	3/20 pups clinic signs and abnormal posture during blood sampling; animals terminated immediately after sampling	No findings	No findings
Body Weight	No difference	No difference	No difference	No difference	No difference
Organ Weight (Spleen and Liver)	No difference	No difference	No difference	No difference	No difference
Haematology	Acute group males and females: NI Chronic group males: 3 x SubV group white blood cells ↓ Chronic group females: 3 x SubV group haemoglobin ↓	Acute group males and females: Red blood cells, haemoglobin, haematocrit ↑ Chronic group males and females: Mean corpuscular haemoglobin concentration (MCHC) ↓	Acute group males: Red blood cells ↓ Acute group females: Red blood cells, haemoglobin, haematocrit, MCHC, neutrophils ↓ Chronic group males and females: No difference	Acute group males: Red blood cells ↓ Acute group females: MCHC ↓ Chronic group males: Monocytes ↓ Chronic group females: No difference	Acute group males: Red blood cells ↓ Acute group females: MCHC ↓ Chronic group males and females: No difference
Bio-Chemistry	Acute group males and females: NI Chronic group males and females: No difference	Acute group males: Triglycerides ↑ Acute group females: No difference Chronic group males: Glucose ↑ Chronic group females: No difference	Acute group males: No difference Acute group females: Triglycerides ↓ Chronic group males and females: Alanine aminotransferase (ALT) ↑ Chronic group females: No difference	Acute group males: No difference Acute group females: Triglycerides ↓ Chronic group males and females: No difference	Acute group males: No difference Acute group females: Triglycerides ↓ Chronic group males and females: No difference

\* Repeated sampling is possible by alternating the side of cheek.  
\* Animals were not actually dead and "time after death" refers to time after 8 am, which would be a typical time of dosing in a once daily dosing study.  
NI: not applicable due to insufficient blood volume for these assessments on PND 5.  
No difference: no difference compared to the control group.  
↑: increase ↓: decrease

#### Summary & Conclusion

- Removing maximum 3x32 µL blood over a 24 h period did not adversely affect standard toxicological endpoints such as clinical observations, body weights, organ weights or biochemistry parameters in both male and female pups which were microsampled at PND 4, 10 and 17.
- Acute effects of CMS on haematology parameters were found. Changes such as decreased red blood cells, haemoglobin and haematocrit, and increased reticulocytes were observed. Among those, decreased red blood cell count, which appeared in all the acute groups, can serve as a sensitive biomarker for the CMS induced acute blood loss.
- Most of the changed haematology parameters came back to control levels after 7 days, indicating a good recovery of the animals. Decreased haemoglobin remained in the PND4 chronic group when the pups were microsampled for 3 times, suggesting a maximum of 2 CMS samples in 24 hours for PND4 pups. As acute effects on haematology parameters were observed, it is not suggested to use the main animals for TK blood sampling.
- CMS is feasible in juvenile rats for TK assessment. Utilizing this method could reduce the use of satellite animals 3-6 fold.

## One Mouse, One PK.....The Magic of Capillary Microsampling and the Gyrolab™ Assay Platform

Sufyan Maqbool, Jo Goodman, David Fairman, Dominic Corkill, BSU & Bioanalytical Sciences, Clinical Pharmacology & DMPK (CPD) Ove Jonsson, Michael Spreadborough, Christopher Smith



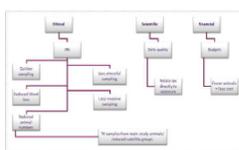
#### Introduction

Capillary Micro sampling (CMS) is a flexible technique for collection and handling of small exact volume of liquid matrices (plasma and/or serum).

The CMS technique can be scaled down to enable repeated pharmacokinetic (PK) sampling of plasma and serum from mice, to determine drug exposure of the 150 KDa antibody.

A PK assay on Gyrolab™ immunoassay platform can be used to measure the concentration of drug in different matrices. Thus enabling construction of concentration-time profiles

#### 3R (Reduce, Refine, & Replace)

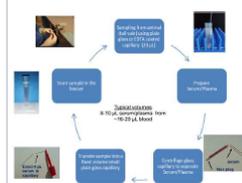


#### Why Use Capillary Micro Sampling (CMS)

... is a flexible technique for collection and handling of small exact volumes of liquid matrices, such as blood, plasma or serum.



#### CMS a Step by Step Approach



#### Study Design

Animal Group & Route	Sampling time points (hours)						NI Terminal blood only	NI Terminal blood only
	1	3	24	48	72	96		
Group 1 CMS (5, 17, 24)								
Group 2 CMS (4, 7, 24)								

- Only 24 & 96 hour time points compared for both CMS & Non-CMS
- Number of Mice: 4 in each group
- Dose: 10 mg/kg
- Route of administration: Intravenous
- Mice: Male C57BL/6
- Molecule: Control Antibody (IgG)
- Matrix Serum

**Non-CMS**  
To obtain a complete profile to match CMS sampling 20 mice will be required

**CMS**  
Complete profile with 9 time points using 4 animals (<10% total blood volume in 28 days)  
Reduce and refine animal use  
- Maximize scientific value  
- Increase productivity  
- Reduce costs

**CMS is low-tech and easy to implement**

#### The Gyrolab™ Immunoassay Platform

- Nano litre scale technology with streptavidin-coated column structures for instant capture binding
- Flow through sandwich ELISA format: Biotinylated Capture-Analyte-Alexa 647 labelled detection
- Reduced reagent use
- Robustness (less operator dependent)
- Increased throughput
- PK assay on Gyrolab™ utilises reagents to detect human immunoglobulin G (IgG) in any animal matrix

#### Equivalence between CMS & Non-CMS



#### Conclusion

- Animal numbers can be drastically "REDUCED"
- Sampling from main study animals will "REFINE" PK/TK data
- CMS can be used to collect small blood volumes
- The Universal PK assay on Gyrolab™ eliminates the need for antibody pair screening
- Gyrolab™ allows a lot of flexibility in the CMS setting where limited sample is available
- Possibility of multiplexing by using Gyrolab™ all from one sample

**Thanks Your Participation**

## **Resources:**

行政院農業委員會動物保護資訊網

<http://animal.coa.gov.tw/html/>

### **NC3Rs:**

<https://www.nc3rs.org.uk/3rs-resources>

### **Journal of Visualized Experiment (JoVE):**

**Manual Restraint and Common Compound Administration Routes  
in Mice and Rats**

<https://www.jove.com/video/2771/manual-restraint-common-compound-administration-routes-mice>

### **MEDIpoint, Inc. :**

[http://www.medipoint.com/html/animal\\_lancets.html](http://www.medipoint.com/html/animal_lancets.html)

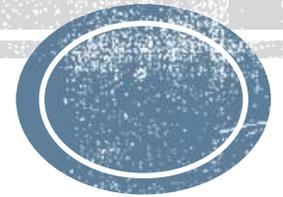
### **The Jackson Laboratory**

<https://www.jax.org/jax-mice-and-services/customer-support/technical-support/breeding-and-husbandry-support/mouse-identification>



# 實驗動物福祉於動物 房內之落實與應用：

20180823 公用動物設施 獸醫師 陳昱卉



# 實驗動物?福祉?

## 實驗動物：

- 何謂「動物實驗」? 凡是使用動物進行任何科學研發之程序，皆可稱之為動物實驗。而使用之動物，無論是脊椎或無脊椎動物，皆稱之實驗動物。在一般具動物保護相關法律之國家，所規範的實驗動物僅指脊椎動物。

## 動物福祉 Animal welfare

Animal welfare is the **well-being** of animals.



# 動物福祉 *Animal welfare*

- 可能有不同的觀點或是立場，沒有絕對的對或錯。
- 會有正反兩派的說法
- 不違反大前提之下，都可以討論出共同的方向



# 5F

亦可稱之為五種自由(Five Freedoms)，略舉如下：

1. 免於缺乏營養、飢餓與乾渴之福利。
2. 免於疾病與傷害之福利。
3. 免於生理上及心理上不適之福利。
4. 免於恐懼與緊迫之福利。
5. 自然表現行為之福利。

當以上任何一項福利受損，便會對動物的生理和心理造成負面之影響。



# 3R

## Reduce 減量

使用較少量的動物已獲取相對所需資訊

利用一定量的動物以獲取最大限度的資訊

(在不增加疼痛或緊迫下)



# 3R

## Refinement 精緻化

修改飼養或實驗的程序，以強化動物福祉，並減少或消除疼痛或緊迫狀態

## Replacement 替代

採取不須使用動物的方法

例如:用模型/電腦/細胞..等



# 動物福祉的重要性



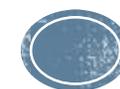
# 趨勢/社會議題

透過大數據與機器學習，機器在預測毒性已能比動物實驗準確

作者 Nana Ho | 發布日期 2018 年 07 月 17 日 21:00 | 分類 Big Data, 生物科技, 醫療科技 [Follow](#) [G+](#) [讚 256](#) [分享](#)

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## 家樂福目標全面賣非籠飼雞蛋 顧及動物福利



# 趨勢/社會議題

Ps [文章](#) [影音](#) [科資源](#) [聯絡](#) [分類](#) [問答](#) [泛科幻獎](#)

## 科學月刊

科學月刊

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### 模式生物生活環境豐富化，是大勢所趨、還是研究者的新挑戰呢？

2018/06/30 | 動物世界 文明足跡 生命奧祕 透視科學 | 標籤：動物福利 實驗方法 模式生物 豐富化

- 文/李依庭 | 東海大學生命科學系生物醫學組碩士。在領略過實驗百態後，嘗試承擔起文字的重量，但目光總不自覺被生醫產業吸引，現任《科學月刊》編輯。

在穿過滅菌設備、緊急沖淋器與無塵系統等相關設備後，從穿廊望去，一字排開的是 3 間並排房間。

左邊緊閉的門上透明玻璃窗，映入眼簾的是一個個堆疊放置在特殊架上的系統缸，架下的泵浦則隆隆作響的負責水缸內的各種恆定；持續往前走，在還沒走至下一道門前，就能聽到陣陣撞擊金屬的聲響，金屬架上安放著一個個的塑膠籠，上頭覆蓋著不鏽鋼網蓋；走廊盡頭的房間，是在聽到逐漸靠近的腳步聲後，從房門的另一側傳來的騷動聲響也漸趨急促，倚著玻璃窗，可以看到一個個巨大的飼養籠。

這裡是動物房，是斑馬魚、小鼠與兔子等各種模式生物的家，也是承載著每位研究者夢想與希望的所在。

↑ ↓ ↻ ↗



# 趨勢/社會議題

## NEW ZEALAND TO START ENCOURAGING ADOPTION OF FORMER LAB ANIMALS



Nadia Murray-Ragg

Social Media Coordinator and Freelance Journalist | Wellington, New Zealand | Contactable via [nadia@livekindly.co](mailto:nadia@livekindly.co)

Posted by [Nadia Murray-Ragg](#) | Jul 6, 2018



SHARE   

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Former lab testing animals may be given a second chance in New Zealand.

The Ministry for Primary Industries (MPI), a public service department that manages farming, biosecurity, and animal welfare, announced its support for the rehoming of former lab animals in New Zealand. Animal rights organizations across the country praised its move. A petition, titled “Out of the Labs,” was delivered by the New Zealand Anti Vivisection Society (NZAVS) and Helping You Help Animals (HUHA) – both animal welfare-focused organizations pushing for compassion in the nation. MPI’s declaration of support follows the



# 趨勢/社會議題

素食話題 素食旅遊 活動報導 美食快訊 環保有機 動物保護 生活健康

首頁 > 動物保護

## 動物實驗化妝品將成過去式 加州參議院通過無殘酷化妝品法案

動物保護 2018/07/13 人氣：2386



首頁 > 新聞爆報 > 滾動新聞 >

## 禁化妝品動物實驗 緩衝期3年

日期：2015-04-17

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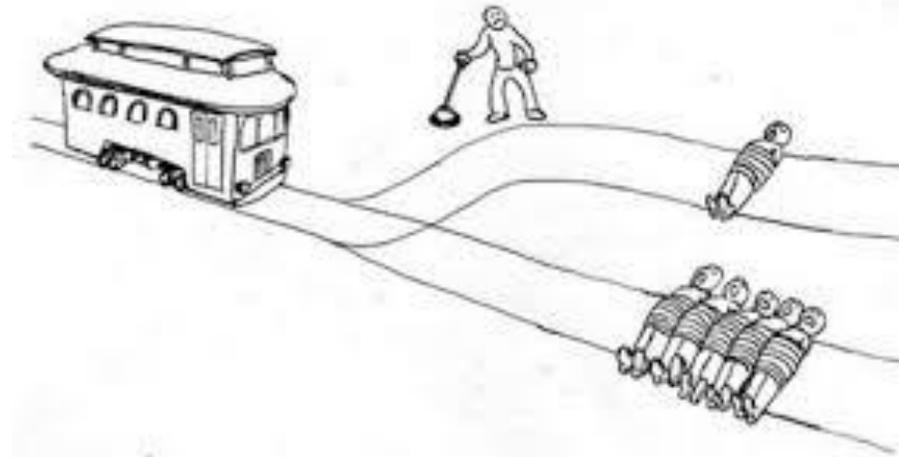
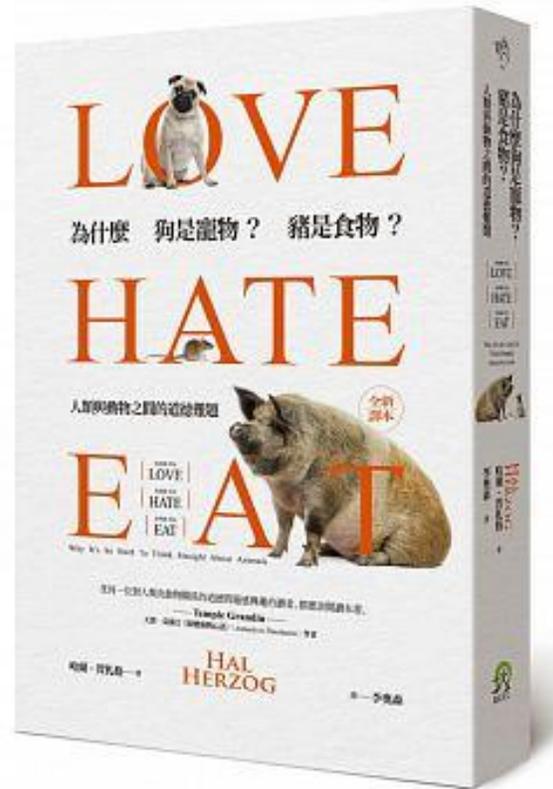
媒體小農  
捐款灌溉

記者 江幸芸/報導

台灣有機會跟上國際的腳步、禁止化妝品動物實驗嗎？台灣防止虐待動物協會（TSPCA）和立法委員王育敏今召開記者會，督促政府盡速修法，**禁止化妝品成品、半成品、原料、配料等進行動物實驗和販賣，並給廠商3年緩衝期**。台北市愛兔協會帶來紐西蘭大白兔站台，希望兔子、天竺鼠、倉鼠等動物別再為了人類「面子」犧牲。



# 道德的抉擇



3R

IACUC

5f

道德

社會輿論

金錢

操作技術

現行法規



**執行策略包含哪些面向**



# IACUC

- 我國於「動物保護法」第十六條即規定「進行動物科學應用之機構應組成動物實驗管理小組，以督導該機構進行實驗動物之科學應用。中央主管機關應設置實驗動物倫理委員會，以監督並管理動物之科學應用」。
- 農業委員會公布「動物實驗管理小組設置辦法」



# IACUC

- 動物實驗管理小組之任務包括：

審核所屬機構所進行之實驗動物科學應用計畫，各計畫執行人應填具動物實驗申請表，送管理小組進行審核。

- 提供所屬機構有關動物實驗設計之科學應用諮詢意見。
- 提供所屬機構有關實驗動物飼養設施改善之建議。
- 監督所屬機構實驗動物之取得、飼養、管理及應用等行為。
- 提供所屬機構年度執行實驗動物科學應用之監督報告，本項年度執行報告應於年度結束後三個月內報送行政院農業委員會備查



# IACUC

- (三) 利用動物進行科學實驗其需採用之實驗動物種類、品種、數量及實驗設計應先申請，並經所屬機構之動物實驗管理小組審議核可，始得進行。
- (四) 各機構所屬實驗動物管理小組，如發現所屬單位之動物科學應用違反本辦法相關規定時，得要求其限期改善，逾期仍未改善者，得終止其實驗動物之使用。



# PAM

## Post-approval monitoring (PAM)

### 計畫核定後的監督

- IACUC計畫審閱核定之後，對所有執行計畫所實施的各種監督方案
- 確保計畫在執行過程，如果有一點小偏離，透過監督措施，就先微調與修正，而不是等到累積成重大事件



# PAM

可包含的範圍：

- 手術區域(包含麻醉設備、無菌操作技術、管制藥品的管理及使用)
- 計畫有關的安全和健康議題
- 麻醉手術紀錄
- 實驗操作程序
- 影響到動物的有害事項

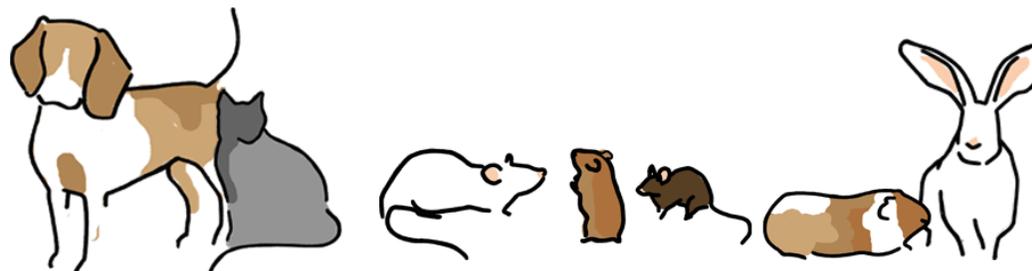


# 環境豐富化



# 目的

- 強化動物福祉
- 增加飼養環境的品質，動物有更多活動的選擇
- 增加行為的多樣性
- 減少異常或類似焦慮的行為產生
- 讓實驗可以更順利



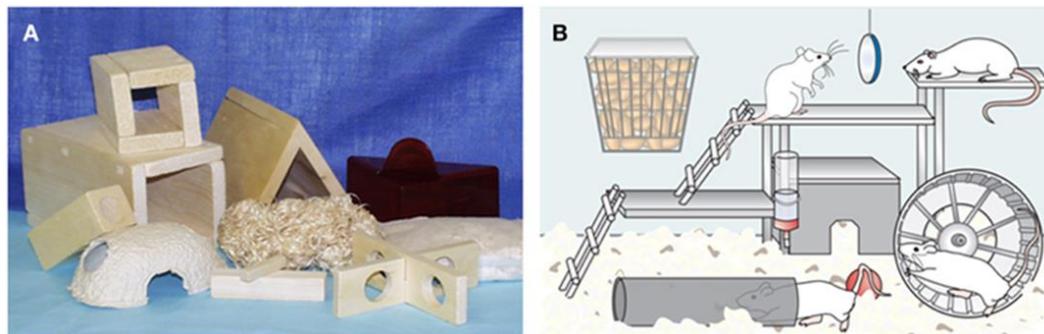
# 動物的需求

- 生理(吃/睡/庇護/排糞尿)
- 行為(社群/覓食/理毛/挖掘/築巢/啃咬等)



# 環境豐富化

- 社群的接觸性與非接觸性  
(不單獨飼養)
- 籠架的複雜度 / 築巢的材料 / 舊巢料



# 環境豐富化



A mouse at the University of Michigan in Ann Arbor is transferred from cage to cage in a tube, rather than being hoisted by its tail—a common, but stressful maneuver. AUSTIN THOMASON/MICHIGAN PHOTOGRAPHY

## Are happy lab animals better for science?

By David Grimm | Feb. 7, 2018, 12:00 PM

**ANN ARBOR, MICHIGAN**—If they weren't in the windowless basement of a cavernous biomedical research building, the "Aquatic Suites" might sound like a cushy vacation destination. But the zebrafish here at the University of Michigan (UM) still have it pretty good. In a large room full of aquaria, the striped, pinkie-size swimmers flit past fake green plants, white plastic tunnels, and multicolored marbles that may remind them of the bottoms of lakes and streams. These simple accoutrements are a luxury for creatures typically housed with little more than food and the water they swim in. And the enrichments may make the animals better at what they do: serving as important models for human disease.

For decades, lab animals such as rodents and fish have lived in barren enclosures: a small plastic box, few—if any—companions, and little else. The smaller the number of variables, the thinking went, the greater the accuracy of the experiment. But a growing number of studies suggests that

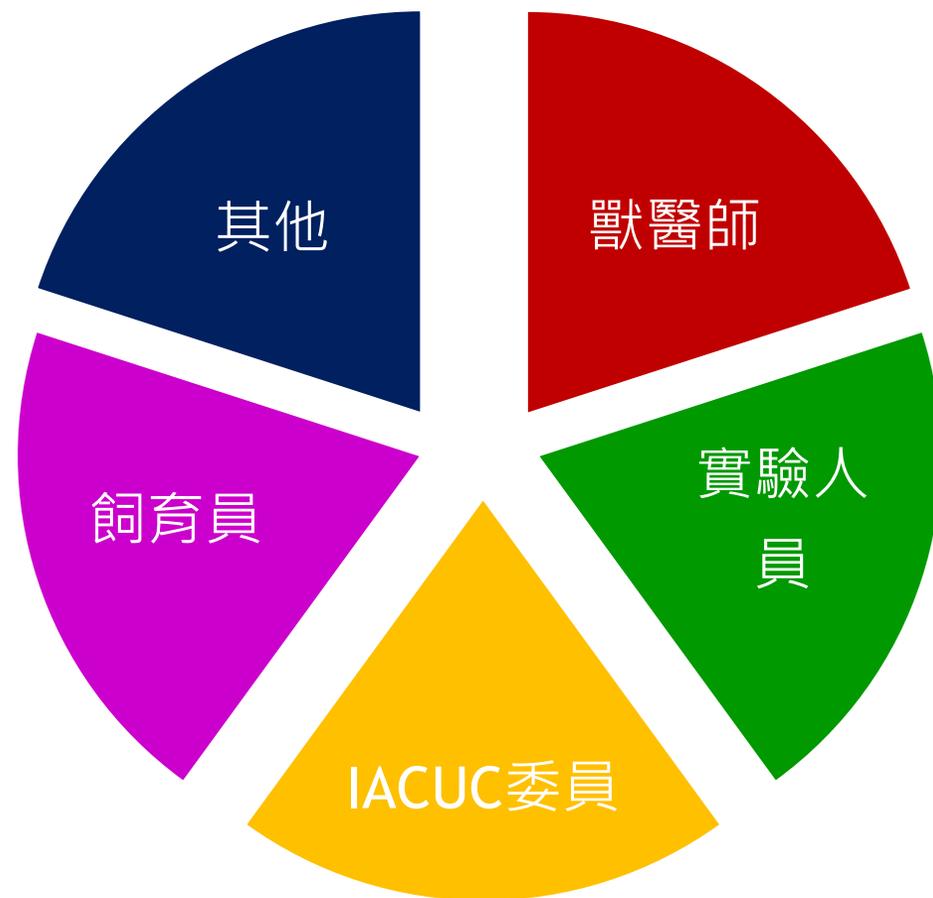


# 尊重與愛

- 必須對動物有所認識了解，更能設身處地思考



# 保持討論與溝通管道



# 落實於動物房之管理或規定



# 離乳天數規定

- 成鼠生長及活動空間
- 近親繁殖
- 費洛蒙
- 緊迫
- 環境衛生



# 飼養隻數限制

- 生長及活動空間
- 緊迫
- 環境衛生



# 異常狀況



# 人道終止標準

## Humane endpoints

- 不讓動物遭受無謂的痛苦
- 動物的健康狀況(緊迫等)，會影響內分泌.免疫...等等。
- 實驗數據可能受影響
- 體重減輕 / 虛弱 / 腫瘤 / 感染 / 癱瘓 / 食慾喪失...等狀況。



# 安樂死

- 無痛苦或焦慮狀態下迅速將動物導入無知覺或死亡狀態
- 根據物種 / 年齡 / 重量 / 狀態... 依據實際狀況考量



# 總結

- 社會道德
- 趨勢
- 法規面
- 同理心
- 持續學習精進
- 保持討論



# 延伸閱讀

- 動物保護資訊網
- 實驗動物照護及使用指南



# 問題與討論

