Characterizing Exposure to Airborne Mouse Allergen in Animal Care Staff at a Biomedical Research Facility

By
William Marc Adkins, B. Gordon, R. Lynch,
R. Clinkenbeard and M. Phillips

Introduction

- There are approximately 90,000 workers in the United States working with laboratory animals[1]
- 21 percent will become sensitized to Laboratory Animal Allergen (LAA) [1]
- Almost two thousand will develop occupational asthma [1]

Classes Of Animals Housed in This Facility

- Immunocompromised
- Transgenic: Animals expressing a foreign protein
- Gnotobiotic: Animals with a defined microbial flora
- SPF: Specific Pathogen Free

Animals

- With the advent of Transgenic technology it is possible to have a mouse model that duplicates the human response to pathogens
- Some research animal lines exist nowhere else other than the specific facility that engineered them
- Scientific careers are often riding on the success of these animals

Animals

- It can cost around $1000 per mouse to have a transgenic mouse created
- The national success rate for this procedure is only 25%
- In order for a line to become established transgenic animals need a high level of environmental protection

Protection Strategies

1. Facility
2. Room
3. Individual Cages

These can be approximated to Hierarchy of Control

Facility

- Normally, this level refers to the HVAC system
- 100% fresh air is used in intake
- Pressure differentials between animal areas and support areas
- Animals that arrive from non approved sources are sent to a quarantine facility

Animal Rooms

- Room Ventilation rate is 20 Air Changes per Hour
- Each room has its own air intake and exhaust ducting
- Rooms are designed to minimize mixing of air between rooms
- Must be able to contain animal movement

Individually Ventilated Cages

- Can be run either positively or negatively pressured in respect to room pressure
- When run in positively pressured mode prevents macroenvironmental contaminants from entering cage.
- This mode is ideal for protecting animals

Individually Ventilated Cages

- When run in negatively pressured mode, prevents contaminants from escaping cage.
- This however exposes animals to cage contaminants
- This mode is ideal for protecting animal care staff

Alternative Design Gentle Air Ventilated Rack System

- This is the design that this facility has selected to house the mice colonies in.
- It is a strictly positive pressure system
- Each rack holds up to 144 mouse cages per rack
- Each cage provides 75 in^2 floor space
- Each cage receives 60 Air Changes per Hour
- It allows the animals to be changed out at a two week schedule


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Positively Pressurized Racks Leak


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Human Health

- A health risk to animal care technicians is exposure to laboratory animal allergen

LAA Symptoms

- Rhinitis [2]
- Conjuctivititis [2]
- Contact Dermatitis [2]
- Asthma [2]

LAA Symptoms

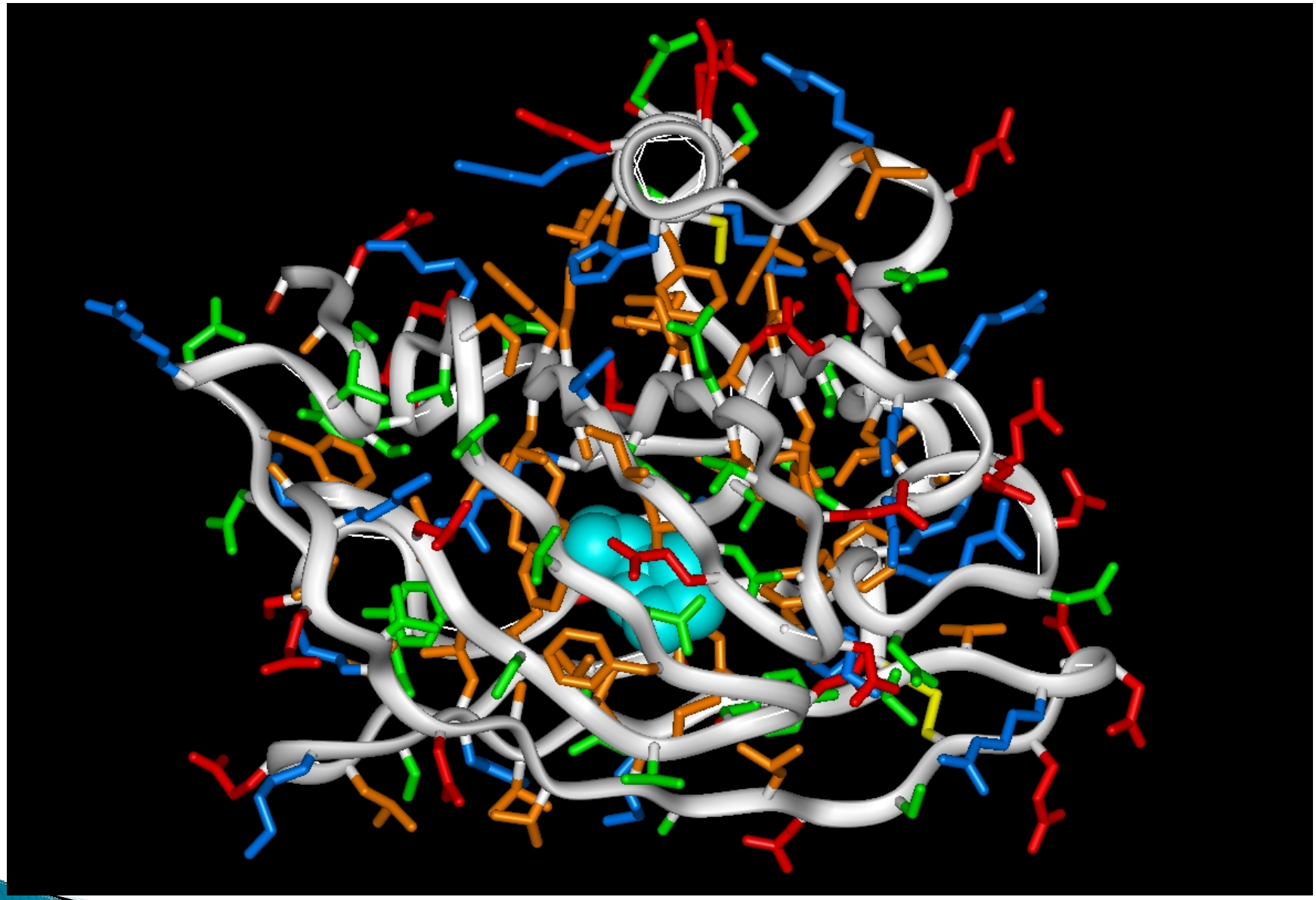
- Severity of symptoms can range from mild to life threatening [2]
- In rare cases anaphylactic shock can be initiated by animal bites [2]
- 10 percent of animal care technicians are at risk of developing asthma [2]

Mouse Allergens

- Mus m1 or Mouse Urinary Protein [3]
- Mus m2 [3]
- Albumin [3]

Mouse Allergen Characteristics

- Both Mus m1 and m2 are members of the lipocalin superfamily of extracellular transport proteins [3]
- Both are hydrophilic molecules between 16 and 19 Kilodalton [3]
- Both are found in mouse dander [3]
- Both have a common cell surface receptor site [3]
- Both function as phernome binding and transport proteins [3]



Allergy Development

- Allergy development is based on a individual being exposed to an allergy causing contaminant called an allergen
- After a period of time of exposure the individual will suddenly become sensitized
- After the individual becomes sensitized additional exposure will cause allergies in the individual

Allergy Development

- Development of allergies is based on many factors
- The most important is individual genetic susceptibility
- The next most important factors are the amount of exposure and the length of exposure

LAA Migration

- Another problem is that LAA migrates from the Animal Care Facility to areas where no animals are present [1]
- This exposes staff who do not have occupational contact with the animals [1]

In Practical Terms

- This institution houses approximately 13,000 mice, in 5 different animal facilities
- To accomplish this the institutional animal research department employs nine full time animal care technicians

Animal Care Technicians

- Each animal care technician spends about six hours changing their assigned cages
- In addition they spend about two hours performing cage checks in the morning
- They also tend to eat lunch in the departmental breakroom attached to the animal facility
- Each animal technician spends nine hours inside a potentially contaminated area

Study Hypothesis

- The animal care technicians are exposed to dust during the assigned cage changing
- This dust is generated by the animals activity inside the cage and carries LAA
- The dust is not confined to the inside of the individual cages

Study Design

- Informed Consent was obtained from four animal technicians
- Three of the study volunteers were assigned solely to the “Main” Animal Facility
- One technician was assigned to the “Dirty” animal facility. This technician and facility were used to determine worst case exposure.

Area Monitoring

- An area sampling pump operating at a flowrate of 1 L/min trapping particles on a 37mm 1µm Teflon filter
- Using a full period continuous single sample
- 9 hour sampling time per room

Area Monitoring

- A background positive control room was used to create a worst case scenario.
- In this room conventional housing was simulated by using a ventilated rack with the blower disabled and the cage vent tops removed.

Personal Monitoring

- Personal airborne sampling pumps operating at 1 L/min again with a 37mm Teflon filter
- Using a full period continuous single sample
- 9 hour sampling period

“Dirty” Facility

- One study volunteer was assigned to the “Dirty” animal facility
- This facility and technician were going to be the worst case exposure scenario.
- IACAUC approval was obtained to simulate an open cage room with live animals

“Main” Animal Facility

- The sampling period was for ten working days
- This allowed for sampling of each room the technicians were normally assigned to during the two week change out cycle

Area Samples

- Each room the “Main” study volunteers were assigned to were also sampled for nine hours
- The “Dirty” area samples took place in the worst case exposure room.
- This room was changed out three times in two weeks

Area Samples

- The area sample purpose was two fold
- The first reason was to understand the environmental contamination present in each room
- The second purpose was to more fully understand the rate of contaminant removal from the facilities air handling system

Samples

- Each daily sample was quantified using a ELISA array
- ELISA stands for Enzyme Linked ImmunoSorbant Assay
- This particular type of assay is considered the "Gold Standard" for both protein detection and to calculate the amount of protein present

Samples

- A standard control curve was generated for each 96 well plate analyzed
- This control curve was used to calculate the amount of allergen present in each sample
- Those samples above the control curve were assigned a value of .5 times the maximum detected level
- Those numbers below LOD were assigned a value of .5 times of the lowest point before the linear portion of the curve

“Dirty” Facility Technician Numbers

- 10.49 ng/M^3
- 4.75 ng/M^3
- 16.00 ng/M^3
- The average exposure was 5.44 ng/M^3

“Dirty” Facility Technician Results

- 85% of the samples were below the detection limit
- The first sample inside the detection limit was due to changing out a separate room. During this change out a dust ball landed on the sample cassette
- The second sample inside the detection limit was due to the second changeout of the study room

“Dirty” Facility Technician Results

- The Third and highest sample was due to changing out a room without a transfer hood

“Dirty” Facility Room Results

- There was only one result above LOD in the worst case exposure room.
- Curiously this exposure occurred when there was no technician activity in the room
- It did occur one day after the first change out
- The allergen level on this day was 35.52 ng/M^3

“Main” Facility Technician Results

- Technician G Day 1 5.96 ng/M^3
- Technician G Day 2 10.27 ng/M^3
- Technician G Day 6 9.56 ng/M^3
- Technician U Day 6 12.45 ng/M^3
- Technician G Day 9 22.92 ng/M^3
- Average Technician exposure was 7.37 ng/M^3

“Main” Facility Room Results

- The only room results that were within the sample range was
- Room 4 Day 1 65.55 ng/Day
- Based on the usage of this room there is no way to tell if this was due to animal technician or research staff activity

Result Discussion

- Based on the large number of collected samples that were below detection limit of the assay
- 85%
- It would appear that the airhandling equipment of this particular instituion is effectively preventing the allergens present in the rooms from reaching the animal care staff

Results Discussion

- It would also appear that the institutional management animal handling protocols reduce the LAA exposure to the animal care staff technician
- However technician actions during change out may affect the individuals exposure

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Questions?