

Science Education Collection

Introducing Experimental Agents into the Mouse

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Abstract

Many investigations performed in mice (*Mus musculus*) require the administration of an experimental agent to the animal. For example, it may be of interest to test the efficacy of a specific therapy, to induce a pathologic condition, or to administer anesthesia or palliative care. In order to ensure safe and efficient delivery, it is important to consider a variety of factors prior to the administration of the treatment.

This video, which reviews agent administration in the mouse, begins by highlighting properties to consider, such as viscosity, dose, and palatability, when planning the administration of an experimental agent. The subsequent discussion focuses on injection methods, including delineation of the structural components of the syringe and needle, how to interpret needle gauge, and safe mouse restraint methods for common injection sites. Detailed instructions are provided for performing subcutaneous (SC/SubQ), intraperitoneal (IP), and tail vein (IV) injections in mice. Furthermore, applications of these techniques as well as alternative administration routes are discussed.

Transcript

Many experiments depend upon the administration of agents to mice. Frequently, these agents are introduced to test their effect on a biological process. Agents can also play an important role in preparing animals for experimentation. In this video, we will discuss important considerations for administering experimental agents, tools for agent delivery, some specific routes of administration, and applications of these essential techniques.

So what factors must be considered when planning the administration of an experimental agent?

The first is the appropriate dose. Usually calculated in relation to the animal's weight, providing the correct dose of an agent is critical.

The route of administration is also important to consider. Properties such as the agent's palatability, viscosity, the amount to be administered, the target tissue, and the desired rate of dissemination will determine which of the many available administration routes you should choose. In this video we will focus on injection, which is one of the most efficient methods of agent delivery.

Before discussing how to perform an injection, let's get familiar with the principal tools for the technique.

We'll begin with the syringe. Liquids are held within the barrel, which is marked to allow accurate volume measurements. The plunger fits within the barrel and is used to drive movement of its contents. Finally, the syringe tip is the site of attachment of the needle hub. At the opposite end of the needle shaft you'll find a beveled tip. Be careful, it's very sharp!

Needle hubs are color coded to reflect their size, or "gauge", with higher gauge numbers indicating smaller needles. Gauges are chosen based on the desired route of delivery: the smaller or more sensitive the area, the smaller the needle required.

After selecting the appropriate needle and syringe for your experiment, draw the agent into the barrel by pulling back on the plunger. Air bubbles injected along with the agent can disrupt tissues and harm the experimental animal. Therefore, invert the syringe and gently flick the barrel, so that any bubbles will move towards the tip and escape. If possible, expel some excess agent to make sure the bubbles are completely removed.

Now that your syringe is locked and loaded, you're almost ready to perform an injection!

Before you start, it's important to equip yourself with the appropriate personal protective equipment, including gloves. Proper animal handling is also essential, and varies slightly depending on the injection site used.

For subcutaneous injections, which are often targeted below the dermis of the animal's neck, mice are restrained by "scruffing." First, hold the animal by the tail and allow it grip the cage lid. Then, firmly grasp the scruff, raising a tent of skin across the animal's shoulders.

The needle should be inserted at the base of the tented skin, and the agent dispensed with a firm, consistent pressure to the plunger. The injected liquid will be slowly absorbed into the bloodstream.

Intraperitoneal injections into the body cavity are absorbed at a rate similar to ingestion. To access the abdomen, turn the scruffed animal over, and tuck the tail securely under your pinky.

Then, mentally divide the animal's abdomen into 4 quadrants and insert the needle into the lower left or right quadrant. Apply firm, consistent pressure to the plunger to deliver up to several hundred microliters of agent. Alternatively, intravenous injections allow a more efficient, systemic delivery of experimental agent.

IV injections are most commonly performed in the tail veins. First, mice are warmed under a heat lamp for a few minutes, which causes the veins to swell and makes needle insertion easier. To keep the mouse steady during the injection, place it into a plastic restrainer, slipping the tail through a special hole in the back.

Identifying the correct vessel is imperative for successful intravenous injections. Be sure to find one of the two caudal veins on either side of the tail; not the artery on the underside of the tail.

Holding the needle bevel side up, insert it into the vein. If the needle is correctly placed, injection will cause the vein to change from dark blue to pale white in color as the agent moves through the vessel.

After each injection, discard the needle into a biohazardous sharps container without recapping. Never reuse the needle, as tips can become blunted and cause injury to the mouse.

Now that you're familiar with common injection methods, let's look at some practical applications of experimental agent delivery.

In many experiments, mice are infected with a specific pathogen to study disease progression as well host-pathogen interactions. For example, subcutaneous injections of antibiotic resistant bacteria cause lesions whose size is a readout for the pathogen's virulence. Alternatively, injections into the footpad can be used for live imaging of immune cell recruitment to the site of infection.

Mouse models are also useful for the study of cancer progression and therapeutics. To generate these models, injections can be used to rapidly and efficiently induce malignant growths in mice, both through the delivery of carcinogenic compounds and the implantation of cancer cells into host tissues.

However, injection is not always required for agent delivery. Intranasal inoculation, for instance, can be used to administer an agent of interest to the lungs to mimic and study respiratory disease progression. Another route, gavage, allows the direct administration of agent to the stomach to ensure a precise and accurate dosing not achievable through food- or water-based treatment.

You've just watched JoVE's overview of introducing experimental agents into the mouse. In this video we reviewed factors to consider when choosing an experimental agent, tools and strategies for mouse injections, and some applications of these critical techniques. Thanks for watching!