Diabetes Induction in Mice
IACUC Standard Procedure
Effective Date: August 2024

UCSF Office of Research
Institutional Animal Care and Use Program

Description of procedure:

Induction of Chemically Induced Diabetes:

1. Weigh mice and measure baseline blood glucose level of animals (age 6 weeks or older) following the IACUC Standard Procedure for Glucose Monitoring of Blood.
2. Recipient mice are with alloxan (70-90 mg/kg) injected intravenously via tail vein, retro-orbital sinus or intraperitoneally (IP), or with streptozotocin (STZ) (200- 400 mg/kg) injected IP.
3. Beginning the day after the alloxan or STZ injection, blood sugar levels of each mouse are checked daily or every other day for 5-7 days by following the Glucose Monitoring of Blood IACUC Standard Procedure.

Maintenance of Chemically induced Diabetes:

1. Two to five days after the development of diabetes (as indicated by blood glucose levels) mice receive an insulin-secreting pellet if further long-term study is necessary.
2. Insulin pellets, releasing approximately 0.1 U /24 hr for >30 days, are implanted subcutaneously using a manufacturer's trocar or by surgical incision following the IACUC Rodent Surgery Guidelines. If making an incision to implant insulin pellet, follow the same instructions as for the Osmotic Pump Implantation IACUC Standard Procedure, but instead of implanting an osmotic pump you will implant insulin pellet. Follow dosing guidelines provided by the manufacturer of the insulin pellet. Depending on the manufacturer, mice weighing less than 25 grams may only require one insulin pellet; larger mice whose blood glucose is not controlled within a normal range (70-150 mg/dL) may receive two insulin pellets.
3. Alternative insulin treatments should be described in the protocol.

The protocol must identify:

- Plan for monitoring for pain and distress (e.g. monitor body weight, glucose monitoring)
- Criteria for euthanasia

NOTE: More frequent cage changes, alternate bedding, or method of housing may be required due to polyuria.

Agents: STZ, alloxan, insulin pellet, anesthetics (for implantation of the insulin pellet). All agents administered to animals should be listed in the "Agents" section of RIO IACUC protocol.

Adverse Effects: Adverse effects should be listed in the "Adverse Effects" section of the RIO IACUC protocol. Supportive care and treatment should be included in the protocol.

Examples of potential adverse effects include: Uncontrolled diabetes leading to weight loss, hypoglycemia, or dehydration

References:

1. Deeds MC, Anderson JM, Armstrong AS, Gastineau DA, Hiddinga HJ, Jahangir A, Eberhardt NL, Kudva YC. 2011. Single dose streptozotocin-induced diabetes: considerations for study design in islet transplantation models. *Lab Anim*. 45(3):131-40
2. Graham ML, Janecek JL, Kittredge JA, Hering BJ, Schuurman HJ. 2011. The streptozotocin-induced diabetic nude mouse model: differences between animals from different sources. *Comp Med*. 61(4):356-60.
3. Hayashi K, Kojima R, Ito M. 2006. Strain differences in the diabetogenic activity of streptozotocin in mice. *Biol Pharm Bull.* 29(6):1110-9.
4. Li RL, Sherbet DP, Elsbernd BL, Goldstein JL, Brown MS, Zhao TJ. 2012. Profound hypoglycemia in starved, ghrelin-deficient mice is caused by decreased gluconeogenesis and reversed by lactate or fatty acids. J Biol Chem.