

Diabetes Induction in Mice
IACUC Standard Procedure
Effective Date: September 2021

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 injected intravenously via tail vein or retro-orbital sinus per the respective [tail vein](#) or [retro-orbital](#) standard procedures or i.p. with alloxan (70-90 mg/kg) or i.p. with streptozotocin (STZ) (200- 400 mg/kg).
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 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 [UCSF Rodent Anesthesia Guidelines](#). If making an incision, follow the [Osmotic Pump Subcutaneous Implantation](#) procedure to place the insulin pellet in lieu of the osmotic pump. Mice weighing less than 25 grams only require one insulin pellet; larger mice whose blood glucose is not controlled within a normal range (70-150 mg/dL) will receive two insulin pellets.
3. Alternative insulin treatments should be described in the protocol.

The protocol must identify:

- How you will monitor 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.*