The Use of Atglistatin to Control Blood Glucose and Insulin Resistance During the Acute Stress Response

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Diabetic Patients and Hyperglycemia

- Hyperglycemia is an excess of glucose in the bloodstream
- Common occurrence following trauma or surgery
- Associated with worse neurologic outcome, increased risk of nosocomial infections, prolonged ICU and hospital length and increased mortality

- Clinical Problem:
  - Diabetic patients who undergo surgery have higher post-operative morbidity and mortality rates
  - Current treatment involves intensive insulin therapy and close monitoring of blood glucose levels due to the risk of hypoglycemia

Counterregulatory Hormones
- Catecholamines, Glucagon, Cortisol, Growth Hormone

Proinflammatory Cytokines
- TNFα, IL1, IL6

Acute Stress-induced Hyperglycemia
- Surgery
- MI/Stroke
- Trauma/Hemorrhage
- Sepsis

Adipose Lipolysis
- Peripheral insulin resistance
- Increased hepatic glucose output
Atglistatin

Solution: Researchers at the University of Virginia have discovered that administration of atglistatin can attenuate glucose excursions and insulin resistance arising post-operatively

- Targets adipose tissue lipolysis immediately before surgery
- Atglistatin could fulfill the need for a non-insulin dependent, pharmacological therapy to prevent post-operative hyperglycemia and insulin resistance
Attenuation of hyperglycemia by Atglistatin

Mice introduced to hemorrhage are treated with Atglistatin and compared to control hemorrhage. Blood glucose levels are measured throughout the hemorrhage surgery.
Attenuation of insulin resistance by Atglistatin

Activation status of insulin signaling pathways, in hemorrhage treated animals, demonstrating insulin resistance is attenuated with Atglistatin treatment in both adipose tissue (WAT) and skeletal muscle.
Intellectual Property

- UVA Tech ID: HARRIST-SIHG
  - Title: Compositions and method for regulating adipose tissue lipolysis, insulin-resistance, and hyperglycemia
    - US Application 15/760,990 Filed March 16, 2018