**A Novel Anti-ACTH Antibody (ALD1613) Neutralizes ACTH Activity and Reduced Glucocorticoids In Rats and Nonhuman Primates**


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**Introduction**

ACTH is a 40 amino acid hormone produced by the pituitary gland as a result of corticotropin-releasing hormone (CRH) stimulation. CRH stimulates the production of ACTH in the anterior pituitary gland, which in turn stimulates the zona fasciculata of the adrenal gland to produce glucocorticoids. ACTH secretion is regulated by feedback mechanisms involving circulating glucocorticoids and central nervous system factors.

**Aldosterone**

Aldosterone is a steroid hormone secreted by the zona glomerulosa of the adrenal gland. It plays a critical role in the regulation of blood pressure, cardiovascular function, and electrolyte balance. In the context of this study, aldosterone levels were measured in the plasma of rats to assess the effectiveness of ALD1613 in reducing ACTH-driven aldosterone production.

**Methods**

Generation and identification of anti-ACTH antibodies, New Zealand White rabbits were immunized with unmodified human ACTH. The polyclonal antibodies and isotype controls were identified by antigen-recognition ELISA using unperturbed and iodinated ACTH.

**Aldosterone-1613 conjugate production**

The conjugate anti-ACTH antibodies were produced by conjugating ACTH to MC-24 and MC-25. The conjugates were incubated with fresh plasma at a 1:1 ratio and then analyzed for ACTH levels using an ELISA assay.

**Aldosterone-1613 characterization**

The ability of ALD1613 to antagonize ACTH activity was measured using an in vitro binding assay. ALD1613 bound to ACTH with a Kd of 0.8 pM, indicating high affinity and specificity.

**Aldosterone-1613 neutralization in vivo**

A pharmacodynamic study was conducted in Cynomolgus monkeys to assess the effect of ALD1613 on plasma corticosterone levels. Monkeys were administered ALD1613 or vehicle at various dosages, and plasma corticosterone levels were measured at different time points post-administration.

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