



## G-Klotho Frag 33

### About

G-Klotho Frag 33 is a recombinant form of the Klotho protein, studied for its role in healthy aging, brain and kidney function, and metabolic regulation. It works by enhancing FGF23 signaling and modulating oxidative stress, calcium balance, and cellular repair pathways.

\*These products are for research use only and are not intended for human consumption, medical use, therapeutic use, or diagnostic purposes. They are not to be used in foods, drugs, cosmetics, dietary supplements, or any products intended for humans or animals. Peptides are not sterile, have not been tested for safety or efficacy in humans, and must not be injected, ingested, inhaled, applied to the skin, or administered in any form. No product sold is intended to treat, cure, mitigate, or prevent any disease.

## What's Included

- One vial, concentration: 10mg/10mL

### Reconstitution kit

- (20) 29-30G subq needles
- (1 ) 5 mL syringe
- (1) 25G needle with syringe
- (1) 10 mL bacteriostatic water

### Clinical Research Potential Benefits:

- May support brain function, cognitive clarity, and neural repair
- May promote longevity, skin regeneration, and cellular health
- May enhance kidney, cardiovascular, and calcium-phosphate balance
- May reduce systemic inflammation and protect against neurodegeneration
- May boost energy, libido, and reproductive health

## Reconstitution & Administration\*

\*Instructions start on page 2

### Clinical Research Suggested Use:

- Draw up 25-50 units (250-500mcg) into the syringe
- Administer 2-3x weekly on nonconsecutive days
- Duration: 12 months
  - 3 months on, 30 day break, 3 months on, 30 day break, 6 months on
- Reconstitute: add 10mL of bacteriostatic water into the to the lyophilized powder vial
- Injection type: intramuscular or subcutaneous injection

## G-Klotho Frag 33 Reconstitution

### One

#### Prepare

**STEP 1:** Remove plastic covers, clean vial and bacteriostatic water top with alcohol pad for 15 seconds

**STEP 2:** Using the large syringe from your administration kit, pull out 10mL of Bacteriostatic water

- It may take a few repetitions to load your syringe with the 10mL with no air pockets

**STEP 3:** Once you've loaded your syringe, slowly inject the 10mL of Bacteriostatic water into your G-Klotho Frag 33 vial:

- On its side to not damage the bonds of the product
- Do not shake, gently swirl if needed
- Allow the solution to sit for at least 5 minutes

**\*Supplies:** 5 mL syringe (large), 25G needle, Bacteriostatic water, G-Klotho Frag 33 vial, Alcohol pad

### Two

#### Pull

**STEP 1:** With the smaller needle draw up 25-50 units of the G-Klotho Frag 33 into the small syringe from your kit

**\*Supplies:** 29G-30G subcutaneous syringe with needle (small), Alcohol pad

### Three

#### Inject

**STEP 1:** Clean the injection area with an alcohol pad

**STEP 2:** Inject subcutaneously (see pg 3)

- Repeat 2-3x weekly on nonconsecutive days
- Duration: 12 months
- 3 months on, 30 day break, 3 months on, 30 day break, 6 months on

## Injection Steps

### Subcutaneous Injection steps:

#### 1 Choose & Clean the Injection Site

- Use the abdomen (3 inches from the belly button), thigh, or upper arm. Rotate sites to prevent irritation. Clean the area with an alcohol swab and let it dry.

#### 2 Inject

- Pinch 1 to 2 inches of skin, insert the needle at a 90° angle, and slowly push the plunger down.

#### 3 Remove the Needle & Dispose

- Pull the needle out at the same angle, apply light pressure with gauze (don't rub), and dispose of the syringe in a sharps container.

#### 4 Monitor for Reactions

- Mild redness or soreness is normal. Seek medical help if you experience severe pain, swelling, or an allergic reaction.

### Intramuscular Injection steps:

#### 1 Choose & Clean the Injection Site

- Use the thigh (vastus lateralis), upper arm (deltoid), or glute (ventrogluteal or dorsogluteal muscle).
  - Rotate sites to prevent soreness. Clean the area with an alcohol swab and let it dry.

#### 2 Inject

- Stretch the skin taut, hold the syringe like a dart at a 90° angle, and insert the needle quickly and smoothly. Slowly push the plunger down to inject.

#### 3 Remove the Needle & Dispose

- Pull the needle straight out, apply light pressure with gauze (don't rub), and dispose of the syringe in a sharps container.

#### 4 Monitor for Reactions

- Mild soreness or redness is normal. Seek medical help if you experience severe pain, swelling, or an allergic reaction.

## G-Klotho Frag 33 Mechanism of Action

- **Klotho-FGF Axis and Co-Receptor Function:**
  - G-Klotho Frag 33 is a transmembrane and soluble protein that functions as an essential co-receptor for the fibroblast growth factor (FGF) family, particularly FGF23, FGF19, and FGF21. By binding to FGF receptors (FGFRs),  $\alpha$ -Klotho and  $\beta$ -Klotho enhance ligand affinity and receptor stability, forming a FGFR-Klotho-FGF signaling complex that orchestrates mineral balance, energy metabolism, and cellular longevity.
- **$\alpha$ -Klotho and FGF23 - Phosphate and Calcium Regulation**
  - **Renal Phosphate Homeostasis:**
    - $\alpha$ -Klotho partners with FGF23, a hormone secreted by bone osteocytes, to regulate phosphate and calcium metabolism. This complex suppresses renal phosphate reabsorption by downregulating sodium-phosphate cotransporters ( $\text{Na}^+/\text{Pi}$ ) in the proximal tubule.
  - **Vitamin D and Mineral Balance:**
    - FGF23- $\alpha$ -Klotho signaling also inhibits 1,25-dihydroxyvitamin D synthesis, decreasing intestinal calcium and phosphate absorption. The combined effect maintains mineral equilibrium and prevents hyperphosphatemia-related tissue calcification.
- **$\beta$ -Klotho with FGF19 and FGF21 - Metabolic Regulation**
  - **FGF19 Pathway:**
    - $\beta$ -Klotho forms a receptor complex with FGF19, regulating hepatic metabolism by reducing bile acid synthesis, increasing glycogen storage, and enhancing insulin sensitivity. These actions improve glucose homeostasis and lipid balance.
  - **FGF21 Pathway:**
    - Through  $\beta$ -Klotho, FGF21 signaling promotes glucose uptake, lipolysis, fatty acid oxidation, and thermogenesis in adipose tissue and liver. This contributes to improved metabolic flexibility and energy expenditure.

## G-Klotho Frag 33 Mechanism of Action

- **Intracellular Signal Transduction**
  - **FGFR Activation:**
    - Ligand binding induces FGFR dimerization and autophosphorylation, triggering downstream signaling cascades:
      - MAPK/ERK pathway - regulates gene expression for cellular growth and metabolic function.
      - PI3K/Akt pathway - promotes mitochondrial energy metabolism and cell survival.
      - STAT signaling - modulates inflammation and cell proliferation.
    - These pathways collectively mediate the regenerative and protective effects attributed to Klotho-FGF signaling.
- **Exosomal and Regenerative Roles**
  - **Enhanced FGF Delivery:**
    - Klotho-containing exosomes stabilize FGFs, protecting them from degradation and improving targeted receptor delivery to FGFR-expressing tissues.
  - **Signal Amplification and Repair:**
    - Exosomal Klotho increases FGFR expression and sensitivity, amplifying downstream signaling to promote angiogenesis, tissue regeneration, and cellular repair.
- **Systemic Biological Effects**
  - **Phosphate and Calcium Homeostasis:**
    - Maintains balanced mineral metabolism through FGF23- $\alpha$ -Klotho signaling.
- **Metabolic Regulation:**
  - Improves insulin sensitivity, reduces gluconeogenesis, and enhances lipid oxidation via  $\beta$ -Klotho-FGF19/21 pathways.
- **Mitochondrial and Cellular Longevity:**
  - Reduces oxidative stress and supports mitochondrial integrity through PI3K/Akt and SIRT-linked mechanisms.
- **Anti-Inflammatory and Anti-Aging Actions:**
  - Downregulates pro-inflammatory cytokines, enhances autophagy, and slows cellular senescence.
- **Combined Biological Impact:**
  - G-Klotho Frag 33 functions as a master regulator of mineral metabolism, metabolic efficiency, and cellular longevity. Its coordinated interactions with FGF23, FGF19, and FGF21 integrate endocrine, metabolic, and regenerative signaling, promoting energy homeostasis, tissue repair, and anti-aging resilience across multiple organ systems.