

Method for Making Hormone Heterodimer

Background

The glycoprotein hormones are a group of heterodimeric glycoproteins produced in the anterior pituitary gland and include luteinizing hormone (LH), follicle stimulating hormone (FSH) and thyroid stimulating hormone (TSH). These hormones are also found as excretion products in human urine. Significant quantities of human chorionic gonadotropin (hCG) hormone are found in the urine of pregnant women and LH and FSH are found in the urine of menopausal women. Deglycosylated hormone analogs and hormone analogs with prolonged half-lives or universal activities are useful in many clinical and commercial applications but are difficult to produce. For example, female infertility caused by high LH activity could be suppressed by the administration of hormone analogs that inhibit endogenous LH activity. However, the preparation of biologically active hormone is often impeded by changes to its native structure. **The present invention describes a method for the preparation of heterodimeric hormone analogs.**

Description of the Technology

Glycoprotein hormones comprise of a common alpha subunit and a hormone specific beta subunit. The substitution of the alpha subunit of one hormone with that of another does not alter the receptor binding properties of the recombined hormone while, the substitution of the beta subunit of one hormone with that of another alters the receptor binding specificity of the hormone. The crystal structure of hCG revealed that both alpha and beta subunits contain a cysteine-knot architecture. The present invention discloses a method for the preparation of a cysteine knot protein containing an alpha and a beta subunit resulting in biologically active heterodimeric protein analog. Specifically, the method involves attaching a dimerization domain to the amino termini of both alpha and beta subunit of a cyctein knot protein followed by dimerization of the subunits to form a heterodimeric protein analog. Alternatively, the heterodimeric protein analog can be made by attaching a dimerization domain to the amino termini of the alpha subunit and c-terminus of the beta subunit of a cyctein knot protein followed by dimerization of the subunits to form a heterodimeric protein analog. This method can be used to dimerize any cysteine knot proteins such as TGFbeta , PDGF, NGF, Veg1, bone morphogenic proteins, activin, and inhibin.

Advantages

- The method described in this invention can be used to dimerize any cysteine knot protein such as TGFbeta , PDGF, NGF, Veg1, bone morphogenic proteins, activin, and inhibin.
- The efficiency of combining the subunits of a heterodimeric protein is very high
- This strategy can be utilized in the preparation of any heterodimeric analog of glycoprotein hormones including hCG/hFSH and hCG/hTSH chimeras, and truncated glycoprotein hormone subunits
- The heterodimers produced by this method retain the properties of the native hormone.

Applications

- For the preparation of heterodimeric analogs of glycoprotein hormones
- For the preparation of heterodimers of any protein in the cysteine knot family

Patent Status

File RWJ 97-01/Moyle

- United States patent granted on November 6, 2002
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Licensing Opportunity

This technology is available for licensing non-exclusively or exclusively.

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