Abstract

Irisin is a recently discovered hormone secreted by muscle and adipose tissue (1). Irisin is responsible for “browning” of fat and therefore is implicated in playing a role in fat and energy metabolism. Because energy metabolism is closely linked to reproduction, we hypothesized that irisin may have independent effects on gonadotropin production. In this study, we examined the effects of irisin on LH and FSH secretion in murine pituitary cells and on estradiol (E2) secretion in human granulosa cells.

Methods

The adult mouse pituitary cell lines (mPitA12, mPitA19) and human granulosa cells (MPC-5) were obtained from CellLines Biosystems Inc or Cedars Sinai Medical Center. Pituitary cells were incubated in Dulbecco’s Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100 U penicillin and 100 mg/ml streptomycin at 37°C with 5% CO₂, 90% humidity in M199 medium supplemented with 10% FBS, 10 ng/mL gentamicin, and 250 ng/mL amphotericin B. Cells were incubated for 19 hours with the same medium containing either GnRH (0, 10, 20, 30, 40, 50 nM), irisin (0, 10, 20, 30, 40, 50 nM), or insulin (0, 10, 50 ng/mL) plus irisin (0-150 ng/mL). E2 concentration in the culture medium was measured by ELISA (MyBioSource San Diego, CA).

Conclusions: In these preliminary in-vitro experiments, irisin appeared to have effects in both pituitary and ovarian cells, suggesting that irisin may play a role in regulating reproductive function. To confirm and to understand the mechanisms of these interactions will require further study.

Results

Figure 1. GnRH effect on LH production in mouse pituitary cells

Figure 2. LH production in response to insulin alone.

Figure 3. Insulin + irisin effect on LH production.

Figure 4. FSH production with insulin alone.

Figure 5. Effect of insulin on E2 production in human granulosa cells

Figure 6. Insulin effect on E2 production in human granulosa cells

Figure 7. Interaction of insulin and irisin; effect on E2 production

Results

Irisin alone or insulin alone stimulated E2 production in human granulosa cells. When irisin and GnRH were used together, the stimulatory effect of GnRH on LH production was abolished. Irisin alone had no effect on LH or FSH secretion when used alone or in combination with GnRH, insulin, or insulin and GnRH. Taken together, these preliminary experiments suggest that irisin may have effects on reproductive function. To confirm these data and to explore the mechanisms of these effects will require future studies.

Conclusion

In these preliminary in-vitro studies, irisin was not found to have independent effects on gonadotropin production. When GnRH and irisin were used in combination, however, stimulatory effect of GnRH on LH production was abolished. Irisin alone or insulin alone stimulated E2 production in human granulosa cells. When a combination of irisin and insulin was used, no stimulatory effect on E2 production was observed. Taken together, these preliminary experiments suggest that irisin may have effects on reproductive function. To confirm these data and to explore the mechanisms of these effects will require future studies.

Introduction

Irisin is a recently discovered hormone secreted by muscle and adipose tissue (1). Irisin is responsible for “browning” of fat and therefore is implicated in playing a role in fat and energy metabolism, insulin resistance and metabolic syndrome (MetS). Irisin is cleared from Fibronectin type III domain-containing protein 5 (FNDC-5) and is induced by PGC1α, a co-activator – a modulator of uncoupling protein-1 expression in obesity, energy metabolism, insulin resistance and MetS. Irisin is closely linked to reproduction, we hypothesized that irisin may have independent effects on gonadotropin production. In this study, we examined the effects of irisin on LH and FSH secretion in murine pituitary cells and on estradiol (E2) secretion in human granulosa cells.

Methods

The adult mouse pituitary cell lines (mPitA12, mPitA19) and human granulosa cells (MPC-5) were obtained from CellLines Biosystems Inc or Cedars Sinai Medical Center. Pituitary cells were incubated in Dulbecco’s Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100 U penicillin and 100 mg/ml streptomycin at 37°C with 5% CO₂, grown to 70-90% confluence, trypsinized and then incubated for 68 hours under the same conditions. The cells were further incubated for another 24 hours in 6-well plates with 2% fetal bovine serum (FBS), 100 U penicillin and 100 mg/ml streptomycin at 37°C with 5% CO₂. Cells were cultured for 10 hours with the same medium containing either GnRH (0, 10, 20, 30, 40, 50 nM), irisin alone (0, 10, 20, 30, 40, 50 nM), insulin alone (0, 10, 50 ng/mL) plus irisin (0-150 ng/mL). E2 concentration in the culture medium was measured by ELISA (MyBioSource San Diego, CA).

Conclusions: In these preliminary in-vitro experiments, irisin appeared to have effects in both pituitary and ovarian cells, suggesting that irisin may play a role in regulating reproductive function. To confirm and to understand the mechanisms of these interactions will require further study.

Results

Irisin alone or insulin alone stimulated E2 production in human granulosa cells. When irisin and GnRH were used together, the stimulatory effect of GnRH on LH production was abolished. Irisin alone had no effect on LH or FSH secretion when used alone or in combination with GnRH, insulin, or insulin and GnRH. Taken together, these preliminary experiments suggest that irisin may have effects on reproductive function. To confirm these data and to explore the mechanisms of these effects will require future studies.

Conclusion

In these preliminary in-vitro studies, irisin was not found to have independent effects on gonadotropin production. When GnRH and irisin were used in combination, however, stimulatory effect of GnRH on LH production was abolished. Irisin alone or insulin alone stimulated E2 production in human granulosa cells. When a combination of irisin and insulin was used, no stimulatory effect on E2 production was observed. Taken together, these preliminary experiments suggest that irisin may have effects on reproductive function. To confirm these data and to explore the mechanisms of these effects will require future studies.

References