

论著

## 重组人集成干扰素 $\alpha$ 对金黄地鼠胚胎和胎鼠的毒性

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**摘要** 目的 研究重组人集成干扰素 $\alpha$  (rh-CINF) 在金黄地鼠着床后至产前给药对妊娠母鼠、胚胎发育和胎鼠的影响。方法 妊娠第0天金黄地鼠80只随机分成赋形剂对照组, rh-CINF 5, 30和100  $\mu\text{g} \cdot \text{kg}^{-1}$  4组。在妊娠第5~14天sc给药, 每日1次, 并在妊娠第15天解剖检查。活体检查指标包括妊娠期间的一般毒性反应、死亡情况和体重变化; 终末解剖检查指标包括母鼠主要脏器异常情况、黄体计数、子宫内植入数、吸收胎数、死胎数和活胎数; 活胎检查指标包括胎鼠体重、身长、尾长及外观、内脏和骨骼系统。结果 给药期间各组均未见一般毒性反应和死亡动物。rh-CINF 100  $\mu\text{g} \cdot \text{kg}^{-1}$ 组孕鼠在给药期间体重增长减缓(妊娠第5~15天增重: (13.1 $\pm$ 6.0) g vs (28.3 $\pm$ 4.5) g)、胚胎植入后丢失率增多(27.9% vs 5.2%)、活胎数减少(6.7 $\pm$ 1.4 vs 9.2 $\pm$ 1.1)、胎鼠平均身长较短((2.9 $\pm$ 0.12) cm vs (3.1 $\pm$ 0.10) cm)和平均体重下降((2.4 $\pm$ 0.21) g vs (2.8 $\pm$ 0.12) g); rh-CINF 30  $\mu\text{g} \cdot \text{kg}^{-1}$ 组孕鼠在给药期间体重增长有减缓趋势(妊娠第5~15天增重: (22.4 $\pm$ 6.3) g vs (28.3 $\pm$ 4.5) g)、胚胎植入后丢失率增多(12.5% vs 5.2%)和活胎数减少(8.1 $\pm$ 1.4 vs 9.2 $\pm$ 1.1); rh-CINF 5  $\mu\text{g} \cdot \text{kg}^{-1}$ 组孕鼠和胎鼠各项检测指标与赋形剂对照组比较无明显差异。在对胎鼠外观、内脏和骨骼系统的检查中, rh-CINF 3个剂量组中均未见有与药物相关的畸形或变异胎鼠。结论 rh-CINF 100和30  $\mu\text{g} \cdot \text{kg}^{-1}$ 时有一定的母体毒性和胚胎毒性, 但无致畸作用; rh-CINF 5  $\mu\text{g} \cdot \text{kg}^{-1}$ 对孕鼠、胚胎和胎鼠生长发育均无明显影响。

**关键词** [干扰素 \$\alpha\$](#)  [毒性作用](#) [胚胎和胎儿发育](#) [生殖毒性](#)

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## Embryo-fetal toxicity of recombinant human consensus interferon $\alpha$ in golden Syrian hamsters

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### Abstract

**OBJECTIVE** To investigate the potential embryo-fetal toxicity of recombinant human consensus interferon  $\alpha$  (rh-CINF), a recombinant non-naturally occurring human consensus interferon  $\alpha$ . **METHODS** Golden Syrian hamsters were sc given rh-CINF 0, 5, 30 or 100  $\mu\text{g} \cdot \text{kg}^{-1}$  from the fifth day through the fourteenth day of gestation, respectively. Clinical signs were observed and body weights were recorded before gestation and from the fifth day to the fifteenth day of gestation. On the fifteenth day of gestation, golden Syrian hamsters were sacrificed and necropsied for examination of corpora lutea, implantation, absorption, dead fetuses and live fetuses. The live fetuses underwent measurements in term of body weight, body length and tail length as well as a detailed external, visceral and skeletal evaluation. **RESULTS** No clinical signs were observed in all dose levels. rh-CINF 100  $\mu\text{g} \cdot \text{kg}^{-1}$  resulted in a lower maternal mean body weight gain (from the fifth day of gestation to the fifteenth day: (13.1 $\pm$ 6.0)g vs (28.3 $\pm$ 4.5)g), an increased post-implantation loss (27.9% vs 5.2%), a smaller litter size (6.7 $\pm$ 1.4 vs 9.2 $\pm$ 1.1) and a lower mean fetal weight ((2.4 $\pm$ 0.21)g vs (2.8 $\pm$ 0.12)g) and body length ((2.9 $\pm$ 0.12) cm vs (3.1 $\pm$ 0.10)cm). rh-CINF 30  $\mu\text{g} \cdot \text{kg}^{-1}$  resulted in an increased post-implantation loss (12.5% vs 5.2%) and a smaller litter size(8.1 $\pm$ 1.4 vs 9.2 $\pm$ 1.1). In rh-CINF 5  $\mu\text{g} \cdot \text{kg}^{-1}$  group, all maternal and fetal parameters were comparable to control values. There were no effects of treatment observed during the external, visceral and skeletal examinations of fetuses in rh-CINF 5, 30 and 100  $\mu\text{g} \cdot \text{kg}^{-1}$  groups. **CONCLUSION** rh-CINF 100  $\mu\text{g} \cdot \text{kg}^{-1}$  can produces maternal and fetal toxicity, and rh-CINF 30  $\mu\text{g} \cdot \text{kg}^{-1}$  can produces fetal toxicity, whereas no evidence for adverse maternal or fetal effects is noted in rh-CINF 5  $\mu\text{g} \cdot \text{kg}^{-1}$  group.

**Key words** [interferon  \$\alpha\$](#)  [toxic actions](#) [embryonic and fetal development](#) [reproductive toxicity](#)

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