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Гонадотропин-рилизинг-гормон: биологическая роль, вакцины против GnRH, оптимизация бактериального синтеза

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Ключевые слова: гонадотропин-рилизинг-гормон (GnRH), иммунологическая стерилизация, вакцины против GnRH, проблемы бактериального синтеза.

Аннотация

Гонадотропин-рилизнг-гормон (GnRH) – это нейропептид, регулирующий половые функции у млекопитающих. Гормон вырабатывается клетками нейронов гипоталамуса, попадая в гипофиз, вызывает секрецию лютеинизирующего гормона и фолликулостимулирующего гормона, влияя на фертильность, половое созревание и менструальный цикл. В норме антитела не вырабатываются на GnRH из-за его низкой молекулярной массы, однако при конъюгации с химическим носителем, использовании B,T-клеточных эпитопов или других методов, в сыворотки крови появляются антитела против GnRH. Сегодня данный метод используется для иммунологической стерилизации животных, это позволяет контролировать уровень бездомных животных, численность потомства, снижать бурное поведение при половом развитии. Так существует коммерческий препарат improvac, используемый для иммунологической стерилизации хряков в качестве альтернативы хирургической кастрации. За счет образования антител против GnRH improvac позволяет снижать уровень андростенона и скатола, которые придают мясу хряков запах фекалий и/или мочи. Вакцины на основе GnRH могут также применяться у человека при лечении гормонозависимых опухолей: рак предстательной железы, повышенная секреция половых гормонов, миома матки, синдром поликистозных яичников, эндометриоз, рак груди, а также при преждевременном половом созревании. Heberprovac является кандидатной вакциной, прошедшей вторую фазу клинических исследований, для лечения рака предстательной железы у человека. В качестве альтернативы химического синтеза для получения вакцин на основе GnRH может быть использован микробиологический синтез. Использование *E. coli* в качестве продуцентов модифицированного GnRH позволяет удешевить стоимость вакцины, однако метод сопряжен с проблемами преодоления получения малорастворимых белковых форм препарата, низкой экспрессии, подбора штамма, плазмидных конструкций, условий культивирования микроорганизмов.

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Gonadotropin-releasing hormone: biological role, GnRH vaccines, optimization of bacterial synthesis

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Abstract

Gonadotropin-releasing hormone (GnRH) is a neuropeptide that regulates reproductive functions in mammals. The hormone is produced by neurons in the hypothalamus; once it reaches the pituitary gland, it triggers the secretion of luteinizing hormone and follicle-stimulating hormone, thereby influencing fertility, sexual maturation, and the menstrual cycle. Normally, antibodies are not produced against GnRH due to its low molecular weight; however, when conjugated with a chemical carrier, using B- and T-cell epitopes, or other methods, antibodies against GnRH appear in blood serum. Today, this method is used for the immunological sterilization of animals, which helps control the stray animal population, limit litter sizes, and reduce aggressive behavior during sexual development. For example, there is a commercial drug called Improvac, used for the immunological sterilization of boars as an alternative to surgical castration. By inducing the formation of antibodies against GnRH, Improvac reduces levels of androstenone and skatole, which give boar meat a fecal and/or urine-like odor. GnRH-based vaccines can also be used in humans to treat hormone-dependent tumors: prostate cancer, excessive secretion of sex hormones, uterine fibroids, polycystic ovary syndrome, endometriosis, breast cancer, as well as precocious puberty. Heberprovac is a vaccine candidate that has completed Phase II clinical trials for the treatment of prostate cancer in humans. Bacterial synthesis can be used as an alternative to chemical synthesis for the production of GnRH-based vaccines. Using *E. coli* as producers of modified GnRH reduces the cost of the vaccine; however, the method is associated with challenges such as producing poorly soluble protein forms of the drug, low expression levels, strain selection, plasmid constructs, and microbial cultivation conditions.