

Molecule increases pregnancy rate and number of offspring in cattle

August 17 2017

Researchers at Inpreha Biotecnologia, a company based in Jaboticabal, São Paulo State, Brazil, working in partnership with colleagues at the University of São Paulo's Ribeirão Preto School of Pharmaceutical Sciences (FCFRP-USP), have discovered a molecule that can increase bovine pregnancy rates and reduce early embryo loss. The resulting drug enhances reproductive efficiency in domestic animals such as cattle and horses.

"We've discovered a new application for the molecule. We've found no similar product under development in the animal reproduction market in Brazil or worldwide," said Marcelo Roncoletta, Inpreha's production and research director and principal investigator for the project.

Roncoletta and fellow researcher Erika da Silva Carvalho Morani both earned master's degrees and Ph.D.s in veterinary medicine and animal reproduction from São Paulo State University (UNESP) at Jaboticabal. Since they founded the company in 2008, both have sought to increase animal fertility and reproductive efficiency. One of their lines of investigation has aimed at reducing early embryo loss in bovine gestation based on hypotheses arising from studies of maternal recognition of pregnancy and maternal-fetal immune tolerance for pregnancy maintenance.

During their research, they read a scientific paper published in the late 2000s, according to which a recombinant protein in the β -galactoside-binding lectin family had immunomodulatory and anti-inflammatory

properties. This protein is active in many biological processes, including cell adhesion, and processes of proliferation and differentiation. Within the trophoblast, specialized cells of the placenta involved in the maternal-fetal interface, the protein confers immune privilege by modulating a number of regulatory mechanisms for establishing pregnancy and maintenance. Thus, the protein was recommended for use in assisted reproductive procedures such as [artificial insemination](#) and embryo transfer.

Following this discovery, they contacted a group of researchers at FCFRP-USP led by Professor Marcelo Dias Baruffi to find out whether the group had produced the recombinant protein and if they were interested in providing samples of it. In fact, the group has produced this recombinant protein and has studied its role in the mouse immune response to Chagas disease and, more recently, to dengue.

The partnership between FCFRP-USP and the company resulted in confirmation of the hypothesis that the molecule increases the bovine embryo implantation rate. As a result, the company has invested in large-scale production of the recombinant protein with the aim of meeting expected demand for the product in Brazil and abroad.

"The product is not designed to treat diseases or infertility, but to increase the reproductive efficiency of fertile animals submitted to artificial insemination and [embryo transfer](#) procedures," Roncoletta said. It has proved effective when administered on the day of insemination or seven days later, he added. It is administered by uterine deposition so that it is in contact with the endometrium, the mucous membrane that lines the inside of the uterus.

"Inoculation of the product is followed by a series of biological events that culminate in enhanced embryonic immune privilege," Roncoletta said. "This increases the likelihood of pregnancy establishment and

maintenance."

Initial tests

According to Roncoletta, the product was thoroughly tested in transfers of [embryos](#) produced in vivo and in vitro, where it was applied concurrently with embryo implantation, and in artificial insemination, where it was inoculated after semen deposition. The results of the tests showed that the product increased pregnancy rates in recipients of embryos produced in vivo by 14 percentage points (pp), in recipients of embryos produced in vitro by 7 pp, and in recipients of artificial insemination by 10 pp.

"To date, we've performed more than 10,000 inseminations in different breeds and herds, and the calves were born healthy, without neonatal or morphological alterations, confirming that the product is very safe as far as its pharmacology is concerned," Roncoletta said. It can be used in other species of mammals besides bovines and has been tested in artificial insemination of goats. The results were similar to those obtained in cows, according to Roncoletta. "The product has the potential to be used in any mammal," he said.

The researchers now plan to validate the product's effectiveness in horses, through a project also supported by FAPESP's PIPE program. The company currently has the capacity to produce 70,000 doses of the product per month. These are being used in tests. Once the product has been registered with MAPA and licensed for sale, Roncoletta expects production capacity to double.

"Based on product acceptance, we know we won't be able to maintain our present structure much longer," he said. "The idea is to expand in the future so as to meet demand."

Provided by FAPESP

Citation: Molecule increases pregnancy rate and number of offspring in cattle (2017, August 17)
retrieved 22 May 2024 from <https://phys.org/news/2017-08-molecule-pregnancy-offspring-cattle.html>

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