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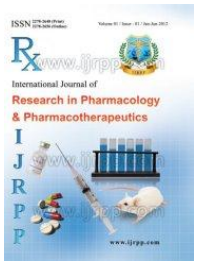

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A breakthrough in the research of infertility with discovery of izumo and juno surface protein: A review

Srijita Dutta

Dept. Of pharmacology, nshm college of pharmaceutical technology NSHM knowledge campus, Kolkata- group of institutions 124(60). B.l.saha road, Kolkata-700053

***Corresponding author: Srijita Dutta**

E-mail id: srijitadutta1991@gmail.com

ABSTRACT

For fertilization to happen, the foremost is sperm and an egg cell. In detailed study on fertilization, scientist had shown the mystery behind fertilization, that most important is the surface protein receptors, which is found on the surface of an egg cell, named Izumo and a similar complimentary receptor found on the surface of sperm cell, named Juno. Discovery of Izumo and Juno has created a breakthrough in the field of infertility research which will surely help infertile patients with a new ray of hope.

KEY WORDS: Fertilization, surface protein receptor, Izumo, Juno.

INTRODUCTION

Fertilization is the culminating event in sexual reproduction and requires the fusion of haploid sperm and egg to create a new, genetically distinct, diploid organism. Sperm attain the ability to fertilize the egg within the female reproductive tract by exposing previously obscured receptor proteins onto their surface following the macrodome reaction [1]. Once fertilized, both the oolemma and zone pellucid are biochemically altered making the egg unreceptive to additional sperm thereby reducing the chances of creating nonviable polyploidy embryos [2].

Several receptor proteins have been implicated in the gratitude and/or fusion process [3], but just two significantly affect fertility in vivo: Izumo a surface on sperm cells [4] and Cd9 receptor on eggs [5-7].

Sperm cell structure and function

In most species, there are just two types of gamete, egg sperm. The egg is among the largest cells in an organism, while the sperm (spermatozoon, plural spermatozoa) is often the smallest. The sperm, is optimized to propagate the paternal genes by exploiting this maternal investment, it is usually highly mobile and streamlined for speed and efficiency in the task of fertilization. Competition between sperm is fierce, and the vast majority fails in their mission: of the billions of sperm released during the reproductive life of a human male, only a few ever manage to fertilize an egg. Sperm Are Highly Adapted for Delivering Their DNA to an Egg. Typical sperm is simple and artistically more interesting; the size of sperm is about 60µm long and

contains several structures that are highly adapted for reaching and penetrating a secondary acolyte. Sperm has 2 major parts, head and tail. In the head of most animal sperm there is a specialized secretary vesicle called the acrosomal vesicle. This vesicle contains hydrolytic enzymes that may help the sperm to penetrate the egg's outer coat. When a sperm contacts an egg, the contents of the vesicle are released by exocytose in the so-called macrodome reaction; in some sperm, this reaction also exposes or releases specific proteins that help bind the sperm tightly to the egg coat. The motile tail of a sperm is a long flagellum. The flagellum of some sperm (including those of mammals) differs from other flagella in that the usual 9 + 2 pattern of the axon me is further surrounded by nine outer dense fibers [8].

Egg cell structure and development

Egg is the female sex cell, or gamete. In zoology, the Latin term for egg, ovum, is frequently used to refer to the single cell, while the word egg may be applied to the entire specialized structure or capsule that consists of the ovum, its various protective membranes, and any accompanying nutritive materials. The human female reproductive cell is also usually called an ovum. The egg, like the male gamete, bears only a single (haploid) set of chromosomes. Egg cell structure is very complicated and is quite interesting, in human, egg cell starts its journey by first becoming primordial follicles in ovary. A few primordial follicles start to grow, developing into primary follicles. Each primary follicle is surrounded by a layer of granulose cells. Outermost granulose cells rest on basement membrane. Primary acolyte found in primary follicle. As primary follicle grows, it forms a zone pellucid layer between primary acolyte and granulose cells. Struma cells surrounding the basement membrane begins to form a theca follicular layer. With continuing maturation, a primary follicle develops into a secondary follicle. Inner most layers of granulose cells become firmly attached to the zone pellucid and are now called corona radiate. Follicle eventually becomes larger and becomes mature graffian follicle and in this follicle the primary acolyte (2n) gets transformed into a secondary acolyte (n) and a first polar body. Once secondary acolyte is formed, it begins meiosis 2 but stops at metaphase. Mature follicle soon ruptures and release secondary acolyte, a process known as Ovulation. After ovulation, secondary acolytes is now called as an egg cell, which is freely moved into the fallopian tube and will be there until it get fertilized by sperm[9,10].

Fertilization process

The process of human fertilization is a complicated one, but the egg and sperm will unite in the long run. The egg will sit waiting for one sperm out of up to 150 million that begin the race, and it will merge with that sperm to create human life. Human fertilization begins with a woman's menstrual cycle. This cycle prepares a woman's body for fertilization. About half way through this cycle, the woman's body is ready to begin the process of human fertilization. It is at this point that an egg cell is released, or ovulated, into the Fallopian tube. Inside this Fallopian tube, fertilization will take place. The sperm have some big challenges ahead to complete this journey. For instance, the sperm have to complete this journey within 12-48 hours of the egg being ovulated, or else they will die. About 85% of the sperm are not properly structured for travel. This leaves only about 15% of the sperm to complete the journey to the egg. This process, from ejaculation to the remaining sperm reaching the egg, takes about 20 minutes. At this point, there are only a few dozen sperm left that actually make it to the egg. The remaining sperm begin to surround the egg, and they race to be the first and only sperm to actually fertilize the egg. The head of each sperm begins to release an enzyme to breakdown the egg membrane, the outer layer of the egg.

Once the first sperm penetrates through the membrane of the egg, the egg will begin to emit an electric signal. The electric signal will trigger little sacs that are located just below the egg membrane, cortical granules, to release their contents into the space surrounding the egg. This reaction will push the remaining sperm back. Within 48 hours, the remaining sperm will die [11].

Izumo, the sperm cell surface protein receptor

So far, medically, genetically and biologically, people know that fertilization occurs when an egg cell meets a sperm cell which recognize each other and then fuse to create an embryo. But how do these

cells recognize each other? How human body does decides which lucky sperm cell will meet the lucky egg cell and become a human being? This question arises so many times in mind of people. Certain researchers curiously started focusing on this particular portion of fertilization taking egg cell and sperm cell on count. Result which came was breakthrough and mind blowing. A team of Japanese researchers in 2005 discovered an immunoglobulin protein on the surface of sperm cells and described it as a 'fusion-related antigen'. This newly discovered surface protein was named as 'Juno' after a Japanese marriage shrine. Though, Japanese researchers were not able to identify the complementary surface protein in the egg cell. But discovery of Juno has created a history in the field of fertilization research. It was able to answer many queries related to infertility and opened the avenue for further research in this territory [12].

Juno, the egg cell surface protein

Finally the mystery behind fertility was solved with the discovery of protein receptor on the surface of egg cell by a team of British researchers headed by Dr. Gavin Wright, from the 'Welcome Trust Sanger Institute'. The team has reported their research in Nature journal in April 2014 and stated the identification of an external cell receptor that lines the surface of egg cells and facilitates recognition between the two reproductive cells – the sperm and egg. Researchers have named it 'Juno', after the Roman goddess of marriage and fertility [13].

Izumo, Juno and fertilization science

After discovery of Juno, British researchers produced a series of genetically altered mice that yielded egg cells lacking Juno protein. The change was resulted in all of the laboratory grown mice became infertile, this study clearly demonstrate the importance of Juno's function in mammalian fertilization process. In the same manner, previous research demonstrated that male mice those are unable to express Izumo protein also became infertile. In egg cell, the surface receptor was detectable during the initial fertilization phase; it rapidly disappeared from the egg cell's surface, thereafter, becoming almost entirely undetectable within just 40 minutes of fusion between the egg and sperm. One possibility is that because Juno is shed off as vesicles after fertilization, this creates a zone of 'decoy eggs' confined within the perivitelline space that could bind to and efficiently neutralize incoming macrodome-reacted sperm to increase the potency of the sperm block. Based upon these findings, researchers have suggested Juno's disappearance could serve a functional mechanism, preventing each individual egg cell from fusing with multiple sperm cells – an eventuality that would result in a non-viable embryo. These has solved a long-standing mystery in biology by identifying the molecules displayed on the sperm and egg which must bind each other at the moment female get conceived [14-18].

Breakthrough in fertilization research

Excellent work of Japanese and British researchers has given a breakthrough in fertilization research with a new hope for infertility patients. Knowledge of Juno protein's existence could, conceivably, be used in the development of new contraceptives and fertility treatments by means of extracellular receptor legend interaction that could be blocked for contraception or promoted to increase fertility. The finding has the potential to aid couples attempting in vitro fertilization (IVF), Wright explained, a costly and lengthy procedure. Researchers are now screening infertile women to understand whether defects in the Juno receptor are a cause of infertility. If so, a simple genetic screening test could help women having difficulty conceiving naturally find the appropriate treatment [19].

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