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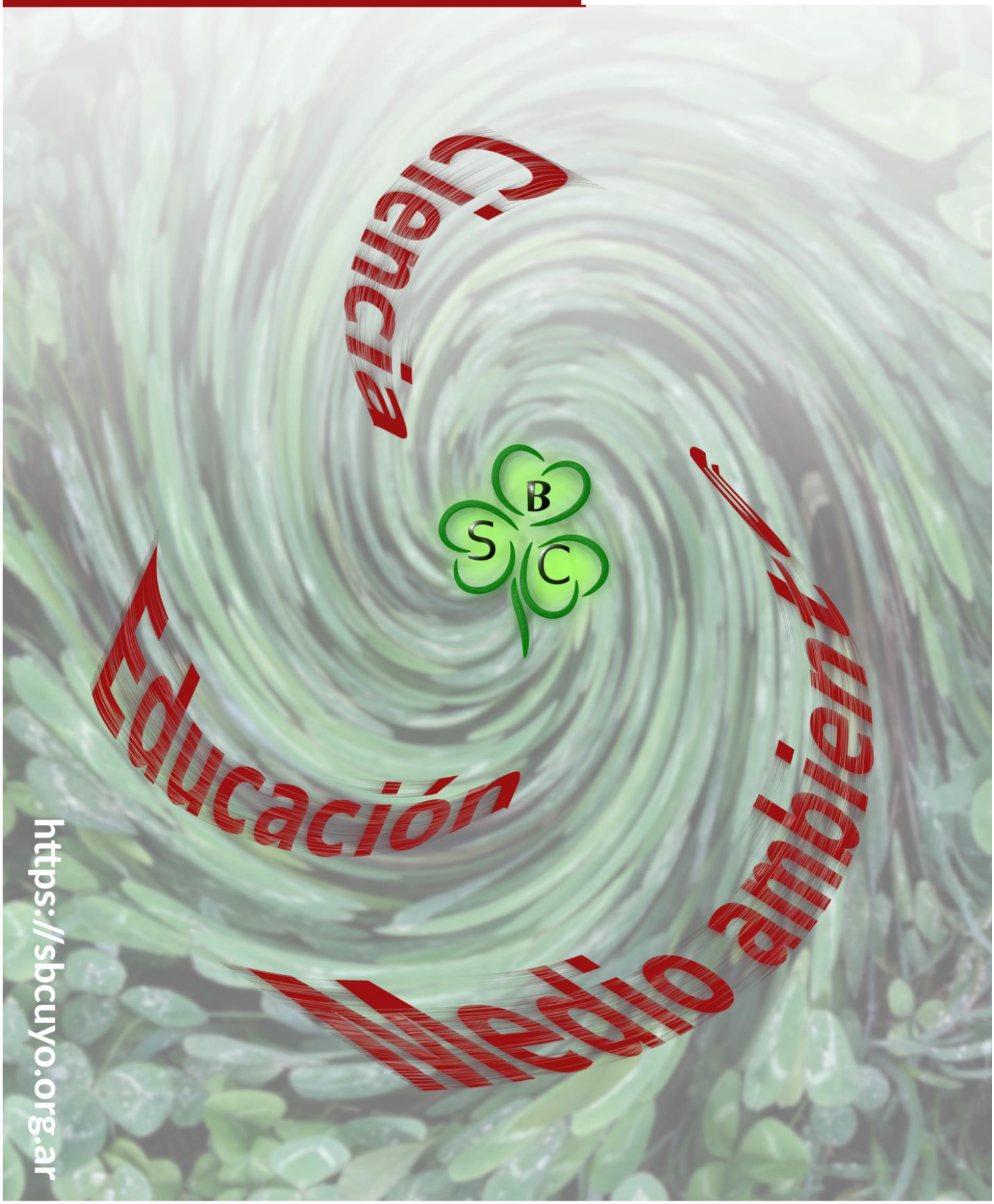

CONFERENCIAS Y SIMPOSIOS

Conferencia Inaugural

BIOETHICAL CHALLENGES AGAINST TECHNOLOGICAL ADVANCES IN REPRODUCTIVE BIOLOGY.

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Bioethics is a space for study and reflection in the construction of positions based on unstoppable scientific and technological advances. Thanks to the advances of science, solutions have been discovered for numerous problems of humanity with clear positive consequences, but also, there have been situations with undoubted bioethical objections. Given these challenges and dilemmas, bioethics analyzes the cost and benefit of each advance. The question arises, "Is everything that is technically possible ethically acceptable?" The bioethics debate about the human right to decide about your body, sexuality, reproductive rights, how to face the disease, aging and the right to die with dignity. It provides tools and builds a regulatory framework on which laws can be generated to achieve general welfare within the framework of freedom. Reproductive biology exhibe numerous bioethical challenges such as assisted fertilization, gamete manipulation and genetic editing. The genetic edition of human embryos using the CRISP Cas9 technique has caused a scientific revolution. CRISPR CAS 9 means short, palindromic, grouped and regularly interspaced repetitions. The genetic edition of human embryos raises the possibility of avoiding diseases of genetic transmission, improves xenotransplants, improve the quality of milk and meat but also, the possibility of changing the genome and choosing traitsspecail features is very risky. Many scientists fear eugenics (good origin) or the application of the biological laws of inheritance to the perfection of the human species. So, ¿are all possible applications of CRISP Cas 9 known today? What are the limits? There is still much to define, for example, the ecological risk of altering natural evolution and use in biological terrorism. An impasse is required to reflect on the consequences and where we want to go as a species.

Conferencia:

SEXUALLY-TRANSMITTED INFECTIONS: WHAT´S NEW ABOUT THE CONTROL OF *CHLAMYDIA TRACHOMATIS*

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Chlamydia trachomatis (Ctr) is the most common bacterial cause of sexually transmitted infections (STIs). The World Health Organization (WHO) estimates that 131 million are infected each year, mainly young people of reproductive age. In women, Ctr causes cervicitis, endometritis, salpingitis, which frequently persist along time leading to serious complications such as pelvic inflammatory disease, spontaneous abortions and tubal infertility. Newborns, when infected in the birth canal, can develop conjunctivitis and pneumonia; whereas men can suffer urethritis, prostatitis, and epididymitis. Ctr is the main cause of preventable blindness or trachoma worldwide. There was an epidemiological alert in Argentina in August 2018 for the appearance of venereal lymphogranuloma. The asymptomatic nature of most of the infections makes diagnosis and treatment difficult. Besides, the lack of a preventive vaccine and the antibiotic resistance increase reveal the need for new tools for the prevention and control of chlamydial infections. Ctr invades cervical epithelial cells through numerous receptors, many of them glycosylated, and survives and multiplies intracellularly in a vesicle called inclusion. We have shown the release of a glycan-binding protein, galectin 1 (Gal1), in cervical tissues under inflammation. This lectin engages glycosylated bacterial proteins, like MOMP (Major Outer Membrane Protein) and OmcB, to glycosylated cervical epithelial cell receptors such as PDGFR and various integrins. Acting as a bridge between bacterial and eukaryotic glycans, Gal1 promotes invasion, increasing not only the number of infected cells but also the number of inclusions per cell and the number of bacteria per inclusion. Lactose, glycanases or neutralizing antibodies against glycosylated receptors decrease the magnitude of chlamydial infections. In agreement, mice KO for complex N-glycan-forming enzymes and Gal1 are less susceptible to infection. These findings suggest that hijacking bacterial glycan-Gal1-glycosylated receptors bridge could be a new tool to prevent cell invasion and overall Ctr infection. Once inside the cell, Ctr avoids its degradation in the phagocytic pathway by hijacking Rab proteins, the main controllers of intracellular transport. By bacterial-driven mechanisms, certain Rabs are recruited to the chlamydial inclusion while others are excluded. We have described that Ctr intercepts Rab14-mediated transport not only to evade fusion with lysosomes but also to acquire sphingolipids synthesized at the Golgi apparatus. Molecular mechanisms underlying how these bacteria manipulate intracellular transport are a matter of intense study. We demonstrate that Ctr provokes Akt phosphorylation along its entire developmental life cycle and recruits phosphorylated Akt (pAkt) to the inclusion membrane. As a consequence, Akt Substrate of 160 kDa (AS160), also known as TBC1D4, a GTPase Activating Protein (GAP) for Rab14, is phosphorylated and therefore inactivated. Phosphorylated AS160 (pAS160) loses its ability to promote GTP hydrolysis, favoring Rab14 binding to GTP. Akt inhibition by an allosteric isoform-specific Akt inhibitor (iAkt) prevents AS160 phosphorylation and reduces Rab14 recruitment to chlamydial inclusions. iAkt further impairs sphingolipids acquisition by Ctr-inclusion and provokes lipid retention at the Golgi apparatus. Consequently, treatment with iAkt decreases chlamydial inclusion size, bacterial multiplication, and infectivity in a dose-dependent manner. Similar results were found

in AS160-depleted cells. By electron microscopy, we observed that iAkt generates abnormal bacterial forms as those reported after sphingolipids deprivation or Rab14 silencing. Taken together, our findings indicate that targeting the Akt/AS160/Rab14 axis could constitute a novel strategy to limit chlamydial infections, mainly for those caused by antibiotic-resistant bacteria.

Simposio 1: Nuevos horizontes en salud

A MOLECULAR APPROACH TO FEMALE AND ASSISTED REPRODUCTION

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In many modern societies, the proportion of women who delay childbearing beyond the age of 35 years has increased greatly in recent decades. They are falsely reassured by popular beliefs that advances in new reproductive technologies can compensate for the age-related decline in fertility, but science cannot beat the biological clock yet. Age is the single most important determinant of female fertility, either natural or treated, and it mainly impacts the quality of the oocyte. Even though the advances in science to know the factors that determine ovocyte quality are constantly growing, there is still much to discover. Our group is interested in characterizing the cortical reaction, a process in which cortical granules fuse with the plasma membrane to avoid polyspermy. Thus, the cortical reaction is the only defense mechanism that the oocyte has to prevent the penetration of two or more sperm cells and guarantee the development of the preimplantation embryo. Using techniques of molecular biology, indirect immunofluorescence, live imaging, transmission electron microscopy, and animal models we are contributing to the characterization of the cortical reaction and the biology of cortical granules. Based on our findings, we propose that cortical granules are fundamental organelles in determining ovocyte quality.

NANOTECHNOLOGY AND ITS IMPACT IN THE HEALTH SCOPE

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Nanotechnology is the study, development, and manipulation of systems at a nanometric scale. Furthermore, nanomedicine is the branch of medicine that takes advantage of nanotechnology knowledge in health care procedures. Nanomedicine is primarily concerned with the study of three fields of application of nanotechnology to the biomedical field: regenerative medicine, diagnosis, and treatment of different pathologies. A newly emerging field of application that arises from the combination of two of the traditional areas mentioned is teragnosis, where nanotechnological tools are enhanced and complemented to achieve a therapeutic and diagnostic effect simultaneously. In general, the behavior of the matter in the nanoscale offers multiple advantages over traditional therapies and diagnostic methods. There are various types of nanostructures, both organic and inorganic, where their composition, morphology, and different specific physicochemical properties directly or indirectly influence their pharmacokinetic and pharmacodynamic behavior, and finally, on their biomedical application. Another essential aspect for taking into account when developing nanostructured systems for use in health is the study of several characteristics related to its biocompatibility and its nanotoxicity. Currently, few biomedical nanotechnological alternatives have been approved for commercialization, and most of them are oriented to their application in cancer disease. Despite this, the versatility of nanotechnology allows its application in practically all health fields. In particular, our laboratory is working on the search for new nanotechnological alternatives for cardiovascular therapy, with promising results so far.

MYTHS AND TRUES ABOUT HEREDITARY BREAST CANCER

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Five to ten percent of breast cancer (BC) cases are inherited and they are associated with the inheritance of a gene that has a pathogenic variant and therefore does not fulfill its function. Hereditary (H) BC/Ovary (CO) Syndrome, caused by pathogenic variants in *BRCA1* and *BRCA2* genes, is the most common and the risk of BC in individuals carrying pathogenic variants in these genes can reach values of up to 80% throughout life.
Numerous myths about HBC generate confusion and uncertainty regarding the real risk of developing this disease. Cancer genetic counseling (CGC) identifies people who are at risk of developing BC. Based on the calculated risks, it is recommended to carry out molecular studies especially of the high penetrance genes *BRCA1* and *BRCA2* to determine the existence of germline variants. CGC allows to eliminate the myths about HBC, some of which are: 1) My BC is not H if I do not have relatives who have had this disease. 2) I should not perform genetic studies if my BC relatives belong to the paternal branch. 3) My risk for developing BC is low because I do not have *BRCA1* and *BRCA2* pathogenic variants. 4) As I already had BC, it makes no sense to carry out the genetic study even if I have clinical criteria of suspected HC. 5) Men of a family with a known pathogenic variant should not be tested.