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Research Article

CAN THE CELL MOLECULES HAVE AN IMPACT ON RECURRENT EARLY PREGNANCY LOSS?

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A B S T R A C T

Regrettably, a pregnancy loss occurs because of various reasons. It causes an extraordinary outpouring grief, confusion, and fear. Recurrent pregnancy loss (RPL) causing anxiety, sorrow, pain, and upsetting. Miscarriage is the spontaneous loss of a pregnancy before 20th week. About 15 -20 % of known pregnancies end in miscarriage. Most miscarriages occur because the fetus is not developing normally. Problems with the baby's genes or chromosomes typically result from errors that occur by chance as the embryo divides and grows. In blighted ovum, when a fertilized egg develops a placenta and membrane, but no embryo. Intrauterine fetal demise occurs due to genetic abnormalities of the embryo. Gestational trophoblastic disease or molar pregnancy, the placenta develops into the fast-growing mass of cysts in the uterus, which may or may not contain an embryo

INTRODUCTION

Over the last few decades, there has been a paradigm shift in finding a cure of various human diseases with an emphasis in basic biomedical research from the study of disease in patients and their organs to its definition at the level of molecules and cells (1). With the new cutting-edge technologies in molecular biology are playing an increasingly important role in the diagnosis and management of various life-threatening human diseases and disorders (2). The present state of molecular biology in-depth understanding of structure and function of proteins, nucleic acids, and other macromolecules play a vital role in cellular physiology and pathophysiology as well. Further molecular biology offers state of the art in the understanding interaction between complex biological systems (3). The understanding the basic cellular processes including DNA replication, repair, and recombination, chromatin structure and remodeling, transcription, RNA processing, translation and regulation of transcription and translation is possible with detailed knowledge of molecular biology (4).

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Apart from core cellular events, several other biological functions including functions of noncoding RNAs, protein folding, processing and degradation, sorting and trafficking of proteins and RNA, signal transduction and intracellular signaling are completely dependent of in-depth knowledge of molecular biology (5). Additionally, the behavior of the cell in normal condition and during pathological condition involves several signal exchange by membrane processes, cell surface proteins, and cell-cell interactions.

Human biology is highly complex and dynamic requires detailed knowledge of biochemistry and molecular genetics to explore the molecular basis of disease (6). In the present scenario, the clinical medicine largely outlooks an integration of molecular biology, genetics, and biochemistry in finding a cure for high-risk human diseases and disorders (7). In the era of genomic medicine molecular biology stand in center bridging diagnostics and therapeutics for fruitful outcome. In the modern medicine, molecular biology becomes central pillar among biochemical, genetic, genomic, proteomic, transcriptomic, metagenomics, metabolomics, and pharmacogenetics (or pharmacogenomics) studies (8). At the beginning of the present century, more emphasis is given to metagenomics and metabolomics. Now researchers across the

globe have focused on metagenomics studies and molecular profiling in healthy and diseased condition to conclude (9). Indeed scope of molecular biology is uncountable and expanding with time. The epigenetics and transcriptomic studies are more crucial in present time to explore disease biology at the molecular level (10). The research finding in neurobiology and associated molecular events in neuronal tissues are underway, and one major area needs to be explored to understand the physiology of most complex organ in human body.

Significant Gap in Research

The modern medical and core molecular biology gained new dimensions in nucleic acid amplification and detection that resulted in a drastic change from conventional laboratory methods that rely on phenotypic expression of antigens or biochemical products, to molecular methods for the rapid identification of some infectious agents (11). New cutting-edge molecular methods have now progressed beyond identification to detect abnormal gene expression, genetic diseases, and antimicrobial resistance genes and provide public health information such as strain characterization by genotyping. These findings have enabled us in finding complete treatment and management of life-threatening diseases and disorders prevailing since many decades including diseases caused by microorganisms, viral infection, metabolic disorders, cancer and inflammatory disorders as well (12). Further, current scope finds a new avenue in resistance detection and viral load testing for the monitoring of responses to antiviral therapies. The high-risk diseases including cancer and inflammatory disorders including autoimmune disorders require a precise and early diagnosis to decide a precise therapeutic protocol completely relies on the application of medical molecular biology. The human Microbiome ecology reported the major cause of various diseases and disorders and advanced molecular biology provide a platform for profiling using metagenomics and metabolomics studies (13). Here, medical molecular biology scaled up in the diagnosis and finding management of pregnancy abnormalities and neonatal complications as well.

With these advancements, still, several diseases are prevailing and associated with human casualties and physical deformities in large scale. For examples, HIV infection and disease associated AIDs remain incurable despite long research findings in more than 30 years (14). Similarly, neurological disorders including Alzheimer's, Parkinson disease and multiple sclerosis, etc. remain a major challenge for conventional medicine and need even more sophisticated molecular findings. The drug resistance tumor and growing antimicrobial resistance associated in case of urinary tract infection, Mycobacterium tuberculosis, influenza and other kinds of flu need immediate attention (15). Now, researchers are looking molecular biology of microRNA, snRNA, and other small nuclear molecules. As a result, these secondary molecules are being profiled and are being investigated for their role in the onset of various diseases and management. Here, novel gene editing technologies including CRISPR/Cas has shown tremendous scope in disease management for cancer, infection and inflammatory disorders (16). During last few decades' significant developments have been made, but still lot of improvements are essential to fight life-threatening disorders.

Major Advances and Discoveries

The molecular diagnosis is a first and most crucial step in disease management. An early and precise diagnosis defines therapeutic measure and efficacy as well. Molecular biology has allowed us to revolutionize diagnostics, allowing us to perform previously impossible analysis of many diseases and reducing diagnosis' costs, thus increasing the sustainability of the national healthcare system (17). Diagnostic molecular biology is widely used in some areas including hematology, immunology, and microbiology with possibly the least developed area being clinical biochemistry. Apart from diseases such as cystic fibrosis and genetic hemochromatosis, most genetic diseases tested for in clinical biochemistry laboratories are rare in the general population (18). However, molecular methods are increasingly incorporated into all areas of pathology, not to replace current tests but as an aid in evaluating the future risk of disease. As a result, we have robust and effective diagnostic devices (diagnostic kits) for all major infections and against for metabolic diseases (19). Further, molecular biology diagnostic potential is not only limited to infection and metabolic disease but also applicable to several physiological parameters including a pregnancy test, serum biochemistry, enzyme and hormonal level. Its advancement of medical molecular biology enables us to develop a diagnosis of early detection of cancers, inborn error and various autoimmune disorders including rheumatoid arthritis (RA) (20).

Beside all these development still, lots of developments in diagnostics are required. Still, we do not have a precise diagnosis of many kinds of cancer including cervical cancer, breast cancer, colon cancer and leukemia. It's not because of we do not have a scientific understanding of this disease but mainly due to complex disease etiology and multiple inputs (21). These are area need to address immediately to develop not only a diagnostic device but also early diagnosis. Finding an antigen for molecular diagnosis is crucial task and researchers worldwide are working to identify a precise antigen in a different class of cancer. There is less known about human microbiota and associated diseases (22). In-fact, metagenomics studies started at the beginning of the current century and need more time to develop the molecular basis of diseases caused by alternation of Gut Microbiome. The available scientific literature demonstrates gut Microbiome is associated with most of the human diseases including inflammation, obesity, diabetes, and metabolic disorders as well. Here, medical molecular biology will be crucial in profiling gut Microbiome and change in metabolomics which can be used as a biomarker for early and precise diagnosis of disease (23). The future scope of medical molecular biology largely lies in the metagenomics, inflammatory disorders, and cancer diagnosis and in finding their management.Blood is an important connective tissue in a human, and other higher primates offer a supply of nutrients including molecular oxygen. The blood transfusion medicine is an emerging medical branch offer blood transfusion as part of the clinical pathology. Transfusion medicine (or transfusiology) is the branch of medicine that is concerned with transfusion of blood and blood components (24). It encompasses issues of blood donation, immunohematology and other laboratory testing, transfusion practices, therapeutic apheresis, stem cell collections, cellular therapy, and coagulation. Laboratory management and understanding of state and federal regulations

related to blood products are also a large part of the field (25). Alloantibodies to blood group antigens are produced because there are differences between the blood group antigens on the recipient and donor (or mother and fetus) red blood cells. Hence it is highly recommended to allow blood transfusion in similar blood group based on the molecular signature. Over the past two decades, there has been an astounding pace of growth in the field of molecular biology techniques and even more recently in the understanding of the basis of many blood group antigens and phenotypes (26). Now, we are now able to consider identification of blood group antigens in genetic terms and identification of blood group antibodies using molecular approaches.

Molecular genotyping of blood group among donor and recipient is mandatory in transfusion medicine. The field of transfusion medicine can now consider individualized transfusion treatment, i.e., matching donors with patients at multiple blood group loci in addition to the ABO and RhD systems. The medical molecular biology has provided state of the art in profiling antigen present on the cell surface of RBC and antibodies in plasma (27). The failure in molecular profiling and identification in molecular signatures result in alloimmunization risk. The credit goes to advance molecular biology tools and techniques in the identification of single nucleotide polymorphism (SNP) which are genetic variation highly complex and unpredictable. In these circumstances, despite matched molecular signature blood coagulation are quite common. Here, more precise and new cutting-edge molecular biology innovations are essential to avoid blood coagulation and enhance the efficacy of transfusion medicine (28). The maternal blood genotyping is quite useful in minimizing the risk of blood coagulation in while gestation period in case Rh+ male and Rh- female. Erythroblastosis fetalis is hemolytic anemia in the fetus (or neonate, as erythroblastosis neonatorum) caused by transplacental transmission of maternal antibodies to fetal RBCs (29). Erythroblastosis fetalis mostly occurs during second pregnancy while in first pregnancy antibodies are produced in case of Rh+ male and Rh- female. The transplantation biology is associated with the exploration of molecular signature and matching in between donor and recipient. Transplantation is the science of transferring a graft from one part of the body to another or from one individual to another (30). The graft may consist of an organ, tissue, or cells. If donor and recipients are the same individuals, the graft is autologous. Immunological tolerance and defining rejection as an immune mechanism provided a background which was considered by immunologists to be hopeless from clinical application. The human serum and immune system are highly complex do not allow any foreign object and start immediate rejection mechanism if mismatched tissue and organs were transplanted (31). There are increasing demands of various organs, and tissue and lack of compatible donor emerged as a major challenge for transplantation biology. Here, the molecular signatures (various antigens and antibodies including complement system) are essential to match before going for transplantation. The role of medical molecular biology becomes crucial in profiling these molecular signatures among donor and recipients. A perfect match for molecular signature allows acceptance of transplants (32). However, in several instances despite match in molecular signature immune rejection may occur which can be minimized by use of immune suppressant drugs.

The role of medical molecular biology is to identify the main player involve in immune rejection and understand their mechanism at molecular level. In human, immune surveillance is governed by cell-mediated immunity and humoral immunity. There are additional players as well including compliment system. Any mismatched transplantation result in activation of CMI starts identification of non-self-entity and represent as antigen (APC) (33). The APC brings humoral immunity and complement system to remove the so-called foreign object. In the process of immune surveillance and defense mechanism, there are more than 100 molecules are associated. The role of medical molecular biology is to understand the precise role of each molecule and mechanism involved in their activation leading to graft rejection (34). Further, each player in defense mechanism (molecules) is derived from the different source and need a signal molecule for its activation. Various immunoglobulins are circulating in systemic circulation and lymph as well as part of adaptive/humoral immunity. Here, medical molecular biology becomes more significant in profiling these inflammatory and pro-inflammatory molecules (35). Further, development of immune suppressant drugs also needs an exact molecular mechanism and target points where the drug can act precisely. Hence, without understanding the molecular biology of the immune system and associated players including cells and molecules transplantation is impossible.

Where the Research go Next?

Prenatal diagnosis is a subfield of clinical genetics and gynecology that exemplifies the effective integration of theoretical and clinical medicine. Here, medical molecular biology plays a central role in the diagnosis of pregnancy abnormalities and neonatal diseases to find cure and management. The human pregnancy is quite long time and requires a complete care to avoid any post-pregnancy consequence to mother and newly born offspring as well (36). The molecular biology is playing a crucial role in entire gestation period start from confirmation of pregnancy as well. There are several chromosomal abnormalities (monosomy and trisomy), monogenetic diseases which are caused by single gene mutations and Polygenetic/multifactorial diseases, which are caused by mutations in several genetic areas as well as exogenous factors (36). These abnormities if not diagnosed in time and opted an immediate medical attention have long-lasting effects on newborn offspring. As a result, various syndromes including tuners and Klinefelter are the serious outcome of chromosomal abnormalities during pregnancy. Similarly, diagnosis of Rh factor is also essential before going for pregnancy which can be lethal to growing fetus (37). The material biochemistry profiling is routine test during pregnancy, for now, days using cutting-edge imaging and molecular biology. The advancement of medical molecular biology enabled us to diagnose several lethal infections including HIV during pregnancy.

The novel, cutting-edge medical molecular biology techniques have provided ease to avoid invasive prenatal diagnostic methods including chorionic villus sampling, amniocentesis placental biopsy, cordocentesis, and fetal biopsy associated with high risk of miscarriage. Apart from clinical diagnosis medical molecular biology is vital in studying growth and development of growing fetus during the entire gestation period (38). In recent years, the measurement of human chorionic gonadotropin (HCG) and pregnancy-associated

plasma protein A (PAPP-A) in maternal serum between the 11th and 14th weeks of pregnancy have become increasingly established in combination with nuchal translucency measurement and maternal age (combined first-trimester test). The medical molecular biology techniques also have a different aspect in determining the health status of the surrogate mother before going for surrogacy (39). The surrogacy is an option for a couple which is incapable of having a child due to gynecological complications. Here, medical profiling using cutting-edge medical molecular biology techniques are quite useful in finding a perfect surrogate. Despite all these advancements still, pregnancy abnormalities and neonatal diseases are looming around and need more advancement in medical molecular biology and associated technologies as well (40).

Current Debate

The medical molecular biology scope in modern human life is uncountable and associated with all the aspects including prevention, diagnostic and therapeutic. The impact of medical molecular biology on human life is so deep that we cannot imagine our daily life. The fruitful outcome of medical molecular biology offer precise diagnosis (biomarker and diagnostic kits), protects against invading pathogens (molecular therapeutics; drug and vaccines) and bring happiness, for example, pregnancy diagnosis kits. The indirect aspects of medical molecular biology offer a suitable donor for blood transfusion and organ/tissue transplantation as well. Recent developments in the field of medical molecular biology have provided a new and completely different way of understanding living organisms. Still, advancements in the field are underway to reveal hidden facts of human life precisely human brain and its functioning. Further, a new arena of human biology, i.e., human Microbiome ecology (HME) using metagenomics and metabolomics need more attention to understand how a change in human microbiota affect human physiology and trigger onset of several diseases. Overall medical molecular biology has a great scope of human life not only in developing the diagnostic device and therapeutic but also for the basic understanding of life at the molecular level.

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