ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Review Article

Cancer and New Expectations

Frank J Carr*

2314 Ecton Lane Louisville, Kentucky, United States

***Corresponding Author:** Frank J Carr 2314 Ecton Lane, Louisville, Kentucky, United States.

Received: February 21, 2024; **Published:** July 18, 2024

Abstract

Cancer exists in four different types: acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia and chronic myeloid leukemia and often begins within the lymphatic system [1]. It can affect various organelles, such as the mitochondria, microtubules, peroxisomes, lysosomes, microglia and influence microautophagy [2-5]. Cart cells can now be altered by CHISPR technology. So that modified t-cells can be adapted, to attack cancer cells [11]. In the case of triple-negative breast cancer, if seems blocking by tariquidar of p-glycoprotein, can help, and improve survival of those patients [20].

Keywords: *Mitochondria; Peroxisomes; Lysosomes; Microglia; STK38; Microautophagy; CART Cell Technology; Antiaminopeptides; Lysine-Specific Histone Demethylase1A*

It seems very clear, the uncontrolled growth of cells, as a result of over multiplication, can result in the formation of tumor cells. Cancers that does not travel to other parts of the body, are called benign, whereas other forms of cancer that may migrate, away from their original site, are referred to as malignant.

Cancer may exist as a number of types of tumors, the most common form is carcinomas, and often occur in the skin or tissues, which covers the outer covering of internal organs and glands. These types of cancers are more common and can occur with prostate cancer. Sarcomas are cancers of supportive tissues of the fat, muscles, nerves, tendons, joints, blood vessels, cartilage and or bone, whereas Leukemias are cancers of the blood, and result when cells begin to change in a manner, resulting in overproduction of cells. There are four different types of Leukemias, acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia and chronic myeloid leukemia and begin within the lymphatic system. Cancers can spread through the lymph nodes. An example would include Hodgkin lymphoma and non-Hodgkin lymphoma [1].

Organelles, during caner involvement

Mitochondria can have an affect on many organisms, when impaired by viruses. This can occur often with lung involvement. Mitochondria, although found in every cell, genes that are responsible for their formation, are located in the nucleus, associated with nuclear DNA and mitochondrial DNA. Other studies on mitochondria may exhibit being affected by SARS-|CoV-2 proteins, where these viral proteins, may bind to mitochondrial proteins of cells, and may as such, lead to mitochondrial dysfunction. Even though recovery after Covid19, there may be a tendency, for recovery to occur in the lungs, and its function restored, other major organs, may still be impaired. It therefore seems likely that the various levels of mitochondrial function could have a bearing on the severity of COVID-19 [2].

Other organelle involvement would include microtubules, peroxisomes, lysosomes, and the involvement of the microautophage. Microtubules are important, in that they form the microscopic road, providing the necessary framework, that supplies for the growth, and "backbone of the cells". They also are important, in that they regulate and control growth, and if the control of their regulation results in or disfunction occurs, thus could lead to cancer, and or neurological disease [3]. Peroxisomes in themselves are important in the removal of materials associated cellular waste materials. In removing "toxic substances" and fats and in doing so, help in they also are in important, in preventing serious diseases. However, a problem in which their ability to function could lead to hearing loss, sight loss, and diseases such as, Alzheimer's, diabetes or cancer [4]. Malfunction can occur during "biogenesis that result in mutations in Pex1 or Pex6, a rare genetic disorder, in which certain patients' cells, which are unable in forming peroxisomes. It therefore is clear that peroxisomes are very important also for the maintenance of cell function, and in health and disease prevention [4]. Lysosomes are also essential like other organelles, in that they are essential in the repair of "cellular" components of cells. Because they provide removal of damaged cellular components and pathogens Tin terms of longevity, recent research experiments have shown the depletion of the regulators of microautophagy increased the rate of senescent cells and shortened lifespan in *C. elegans* [5].

When lysosomes become damaged, cells must be capable of monitoring, and addressing the damage, and signaling a response, in order to be able to respond to lysosomal damage [5]. Lysosomal damage can be addressed by a protein called Serine-threonine kinase 38 (STK38), and is essential, and important in initiating a response for lysosomal damage. STK38 next works with the protein complex called protein sorting complex called the "endosomal sorting complex", which is required for the transport (ESCRT) machinery, "linked" to lysosomal repair. STK38 also needs the additional protein called the vacuolar protein sorting 4' (VPS4), to damaged lysosomes, and is important in the disassembling the ESCRT machinery, at the end of the repair process. Additionally lysosomal membrane repair, occurring by the ESCRT machinery is "mediated by microautophagy". Lysosomal repair is coordinated by the autophagy-related protein 8 (ATG8s) molecules (A key autophagy proteins and gamma-aminobutyric acid receptor-associated proteins (GABARAPs), which are required for the process. ATG8s are also "modified with lipid extensions" and the main process involved in autophagy, non-canonical lipidation ATG8s, are thus "lapidated" into single membrane endolysosomes. According to these researchers a depletion of regulators of microautophagy are "crucial for the "initial recruitment of the ESCRT machinery for repair of damaged lysosomes" [5].

Immune involvement

As has been demonstrated by previous investigators, an immune response most often begins with the beginning reaction with the inflammatory response, which is a complex process, by a key switch to transmit signals, and "activated by gene expression", leading to the transfer of phosphate molecules to "modulate" their function. Thereby this series of cascades of enzyme driven reactions is responsible for activating gene transcription and leading to inflammation. A process that begins, and which leads by, the release of cytokines, "pro-inflammatory signaling molecules", which may lead to a cytokine storm. Thus, inflammation is a very well-regulated process, and complicated, and only is beginning to be more investigated, in terms of the targeted nucleotide-binding sites, and the kinases, where phosphate transfer occurs [6].

Other immune cells important in an immune response are the dendritic cells, which are the first responders. These cells can migrate throughout the bodies tissues, and for some reason orient themselves one after one, along the outer vessel walls, with the better availability of cytokines, the activity is also enhanced [7]. T cells, which are important in the fight against pathogens and cancer, have a unique way of controlling genetic expression. In that they have a receptor, which can relay information from the cell membrane to the nucleus. They do this by a receptor called retinoic acid receptor alpha, and uniquely on a site in the cell membrane, where can control "gene expression programs in the nucleus". It appears according to the author, t cells must first begin to fight disease by first beginning triggered, by a form of the retinoid acid receptor alpha (RAPα). Once t-cells are activated or triggered, molecules such as kinases are able to add phosphates to proteins with adaptors, direct available proteins to assemble, into an activation complex, called a TCR signalosome, just inside the cell membrane. The TCR signalosome is very important, in that it relays information, from inside and outside the cell [8].

Other immune involvement

Other immune cells, such as microglia cells, which play are a significant role inflammation, could offer a key, to "uncontrolled inflammation, which can occur in diseases, such as Parkinson's and Alzheimer's disease. The implication is that overzealous inflammation could be linked to overactivity of the microglia cells, within the brain itself. This researcher believes that by tampering down the excessive over activity of microglia, through a better understanding of nanomedicine, could lead to treatments, which could remedy and or protect from neuron involvement [9]. T cells can target according to Massachusetts Institute of Technology, can only detect the presence of one tumor antigen at a time, and if that tumor antigen is not present, then that cancer could be missed, and not attacked. Their research has contributed the idea that a special vaccine, might be possible to booster the response of engineered T cells, called the chimeric antigen receptor (CAR) T cells, in an effort to create new T cells, that can target "other tumor antigens". In itself, a vaccine in a process they describe, as antigen spreading. Where these CAR-T cells are engineered to display receptor, treatments are designed to recognize a "specific tumor antigen and found on cancer cells". Thus, improving the chances, for example, in glioblastoma cells by targeting tumor antigens, by the use of engineered CAR-T cells [10]. Another interesting aspect of CAR T cell therapy, which involves the "genetic modification of both CAR T cells" and blood stem cells, is by which a small piece of CD45 structure, and or epitope where CAR T cells bind the CD45 molecule. In this way the "altered version of CD45" is still works but differs enough from normal CD 45 that anti-CD45 CAR T cells do not recognize and attack, in a way where ant-CD45 CAR T cells are no more capable of recognizing the newly engineered CAR T cell [11]. In essence, when engineered cells are infused, the CAR T cells kill the cancer cells that bear normal CD45. This new and exciting approach, "not only keeps anti-CD45 CAR T cells" from attacking each other, or stem cells in addition, "enables swift destruction of blood cell cancers" [11].

A new and exciting technology is being tested for detecting foreign DNA. Involves the use of engineered bacterial DNA, by using CHISPR technology, and by detecting for "free-floating DNA sequences" at the genetic level, an comparing predetermine predetermined cancer sequences. In their research on *Acinetobacter baylyi*, which is capable of the uptake of DNA, and "using CRISPR to analyze it". Other results from the colleagues Susan Woods and Josephine Wright, were able to use *Acinetobacter baylyi*, as a sensor for identifying DNA from KRAS, a mutated gene, occurring in many cancers. The significance, is that cancers such as colorectal cancer, could be screened in such way as to prevent the progression of this disease [12]. The use of RNA sequencing is also a technology, that can be used to protein-coding and "RNA dark matter in blood and improve the identification of specific cancer types such as pancreatic, lung, esophageal, for early detection of disease [13].

Other additional immune features

Researchers at the University if Singapore discovered during research for Blastocystis S17, have an interesting aspect of this organism's metabolism, with the ability of this microorganism, to produce the substance called indole-3-acetyldehye (13AA). It has the ability to bind immune cells in the gut, and been shown to promote" inflammation. It's the author's assumption, that by inhibiting this chemical in a sense, promote gut health by use of gut helpful microorganisms, such as *Lactobacilli* [14]. Other important research is in the new enzyme ribozyme called SAMURI, in that it is a tool, that "labels" RNA visible with dyes, making it possible to modify other RNA molecules specifically at the specific adenine site. In this way, ribozyme can serve as a tool to study metabolic pathways, as they interact with molecules, in a much better way for research [15]. Another significant object relating to immune protection, could be the ability of the immune system, through innate immunity, to "combat the ability of viruses to infect", by the production of antimicrobial peptides. These synthetic antimicrobial peptides provide antimicrobial activity, by disrupting microbial membranes [16]. Another important aspect of research related to research on the zebra fish, could help in a better understanding, in the formation of the blood-blood barrier. It seems that a gene called spock1, a seems to be involved in changes in the gene expression, in endothelial cells and pericytes in the blood-brain barrier. It seems that Spock1 proteins "initiates the proper formation of the barrier during development and helps maintain then after" [17]. In addition, secreted membrane bound proteins, such as Neuritin and Brorin, are significant in memory signaling, and the "recruitment and stabilization of additional glutamate receptors, and important in the sustained signally through neurons". Although

this research was primarily centered on eye disorders, it could have implications, in providing more insight into nerve transmission, and related issues, such neurological disease [18]. In regards to t-cells to recognizing cancerous tumor cells, resides in a small piece of RNA (microRNA or miRNA called let-7), which is highly expressed in member cell's [19].

Cancers initiative, various forms, and neurological disease

One key protein that controls gene activity during "embryonic development and thru life", is the protein called lysine-specific histone demethylase 1A of LSD1, which can lead to the formation of too many proteins a driving force, lead towards cancer formation [20].

Cancer and like other forms of cancer, can have relapses at times, breast cancer can also experience early, and poor survival rate, particularly aggressive triple-negative breast cancer (TNBCP), with limited treatment options. Researchers however, at Medical University Viennas's Center for Cancer Research, have discovered that the blocking by tariquidar of P-glycoprotein, can help "prolong" the survival of test organisms during research [21].

Cancer and neurological diseases

In a recent study regarding melanoma, it has been recognized that a protein that is active within immune cells, is also active inside melanoma cells, "helping promote tumor growth". Therefore, the immune system is influenced by internal factors and by external factors as well. The protein they discovered is called NR2F6, and is significant, in that it was found both within tumor cells, as well as active immune cells, and could lead to better treatments for resistant melanoma cancer therapy [22]. The neurological disease Parkinson, the disease cannot be detected and diagnosed based on biomarkers, in blood or body fluids, but may be detected based on the "ideas of structural biomarkers", that may be used to recognize structural changes in proteins detected, particularly by measuring the proteome (totality of all proteins in a sample), called LLiP-MS which is capable of very sensitive detecting structural changes in proteins [23]. Other important considerations besides, the "loss of dopaminergic neurons and the presence of Lewy bodies, and Lewy neurites, current treatments have centered on motor symptoms" and dopamine replacement therapy, as well as surgery. Age is a significant risk factor along with other health risks, such as toxins and pesticides. The most common cause of "monogenic Parkinson disease" (PD) is mutations in the "leucine-rich repeat kinase 2 (LRR K2) gene. LRRK2-associated disease onset, disease progression, and motor symptoms. Mutations in the GBA (glucosylceramidase beta) gene are a significant risk factor for the identification of PD today. Along with pathological factors, such as, alpha-synuclein aggregations, disruption of calcium homeostasis, and decreased calcium levels in PD astrocytes, inflammation creates a contributing factor. Furthermore, PD astrocytes have demonstrated astrocytes with "altered Mitochondrial function, and low mitochondrial" DNA copy number the researcher also notes, evidence that LRRK2 and GBA mutant astrocytes are likely to contribute to PD progression [24]. Other aspects of Parkinson's, seems to in how are incorporated within neurons, impairs mitochondrial function, but also the Golgi apparatus exhibits metabolic defects, while alpha-synuclein is responsible for "disrupting inter-organelle communication". In essence, the main "culprit, alpha-synuclein", disrupts cellular metabolism [25]. Research by Northwestern had discovered that a dysfunction at the neuron synapse can lead to deficits in dopamine and neurogeneration and the genes Parkin and PINK1, are important in the recycle old mitochondria. However, if mutations in either PINK1 or Parkin can lead to the development of Parkinson's disease, "because of ineffective mitophagy". The author suggests the development of drugs that could boost Parkin, could "potentially prevent degeneration of dopamine neurons" [26].

Neurological diseases

Huntington disease is a disease characterized as a neurodegenerative disorder due to the "repetitions of glutamine amine acids, in specific proteins", which causes the aggregation of proteins, in deposits that are damaging, and cause "cellular dysfunction, and death".

This researcher's work centered on chloroplasts, that are able actively able to withstand levels of toxin of protein deposits, by the presence of the plant SPP protein as was show by their improved motility of the test organisms *C. elegans* [27]. In the case of the neurological disease, amyotrophic lateral sclerosis or ALS, it was found by blocking the "expression of the protein, called as alph-5 integrin, by monoclonal antibodies, could protect motor function, and delay the "progression of the disease" [28]. According to Children's Hospital Colorado, there is a "Ground breaking treatment" for cystic fibrosis and called cystic fibrosis transmembrane conductance regulator modulator, the drug is called elexacaftor/tezacaftor/ivacaftor (ET) and DA is approved for patients 12 years old and older. It restores the malfunctioning protein [29]. According to Ruhr-University Boctum, the "deposition of clumped proteins" in the brain clearly is the "causal link between protein aggregates" and neurodegeneration and that proper protein balance in the cell, is associated with a key protein called TDP-43, where its dysfunction, is characteristic of amyotrophic lateral sclerosis, and frontotemporal dementia. This researcher attributes much of the problem, with declining protein functionality, cand be attributed to the misfolding of proteins, a "crucial role" in the disease process. In that researcher has recognized that misfolded prion proteins, can trigger clumping, and inactivation of TDP-43, where misfolding can result in the loss of "physiological function, and impair important physiological processes in the cell [30]. With the treatment of Alzheimer's, the combination of phosphorylated tau, and MTBR-tau243 (in cerebrospinal fluid], researchers were able to access cognitive function, as well as progression of disease [31]. Research by the University of California has found that microglia are of key of importance in the clearing of beta-amyloid plaques, transplantation of "healthy hematopoietic stem cell and progenitor cells, can "enhance microglia health and protect against multiple levels of Alzheimer's pathology" [32].

An additional interesting characteristics of *Candida albicans* is that it produces enzymes called aspartic proteases (Saps), that allows for this organism to breakdown the blood-brain barrier, and subsequently, be able to enter the brain. The same aspartic proteases also allow it to break down "the amyloid precursor protein" into AB-like peptides enzymes, to activate microglial brain cells, via called Toll like receptor 4 and thus allowing *Candida* to enter the brain. Accordingly, it is the endogenously produced peptides (amyloid precursor proteins) in our brain, that are broken down, that generate toxic antibody peptides [33]. Their research on Leukemia lymphoma, research by the University of Texas El Paso, has discovered a compound that for cancer of the immune system. A project called UTEP, which tested 1,300 different compounds on human cancer cells, thiopheneF-8, as a promising compound that successfully killed leukemia and lymphoma cells, could be a potential "life saving drug" [34]. With a severe form of brain cancer called glioblastoma, macrophages are recruited, treatments are primarily by radiation and chemotherapy, and most anti-cancer drugs are of only of little value, in that their ability to "penetrate brain tissues". However, their research did demonstrate that, with long-term patients, with RNA sequencing, that one gene, LGALS1, may be a promising target, in which future drugs, might target for "tumor regression" [35]. In regard to bladder cancer, a clinical trial seems to indicate that 43 percent respond with a complete response with "no detectible cancer with the combination treatment of chemotherapy and immunotherapy" [36].

Summary

Cancer exists in four diverse types; acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia and chronic myeloid leukemia and often begins within the lymphatic system [1]. Various organelles may be affected such as the mitochondria, which may be impacted during a Covid 19 infection [2]. Other organelles involved may be impacted are microtubules, peroxisome, lysosomes, and can be in the form of micro autophagy [3]. In the case of microtubules, they are important, since they form the framework of the cell, whereas peroxisomes remove excess cellular waste [4]. Lysosomes are significant particularly during cellular damage [4,5]. In the immune system accordingly, T-cells first need to activate or triggered in order to fight disease by a form of the retinoid receptor alpha. Once T-cell is activated or triggered thru molecules, such as kinases, which are able to add phosphates to proteins with adaptors, with adaptors, direct available protein assemble into a activated complex called a TCR signalosome, which relays information from inside and outside the cell [6]. Although inflammation is a normal initial immune response, in glioblastoma, turning down our activity of microglia cells, could lead to better understanding for rain in cancer [10].

Bibliography

1. Cancer.Net. "What is Cancer?" ASCO Knowledge Conquers Cancer (2019).
2. Children's Hospital of Philadelphia. "COVID-19 cause mitochondrial dysfunction in heart and other organs, researchers find". ScienceDaily (2023).
3. Universite de Geneve. "Decphering the highway code of our cells". ScienceDaily (2020).
4. University of Munster. "A close-up of biological nanomachines: Researchers take a deep look at peroxisomal processes". ScienceDaily (2023).
5. Osake University. "Microautophage is essential for preventing aging". ScienceDaily (2023).
6. European Molecular Biology Laboratory. "Switching off the cytokine storm". ScienceDaily 14 (2023).
7. University of Wurzburg. "Immune cells in single file". ScienceDaily (2023).
8. La Jolla Institute for Immunology. "New research has major implications for controlling t cell activity: How a supposed 'nuclear receptor makes TCR signaling possible". ScienceDaily (2023).
9. American Institute of Physics. "Brains immune cells promising cellular target for therapeutics". ScienceDaily (2020).
10. Massachusetts Institute of Technology. "Vaccine delivers a boost to T cell therapy: The new strategy may enable engineered T cells to eradicate solid tumors such as glioblastoma". ScienceDaily (2023).
11. University of Pennsylvania School of Medicine. "Expanding the impact of CAR T cell therapy: An immunotherapy strategy against all blood cancers". ScienceDaily (2023).
12. University of California - San Diego. "Researchers engineer bacteria that can detect tumor DNA: Advanced biosensor leverages CRISPR to identify colon cancer". ScienceDaily (2023).
13. University of California - Santa Cruz. "New blood test for noncoding RA significantly improves cancer detection". ScienceDaily (2023).
14. National University of Singapore, Yong Loo Lin School of Medicine. "Gut Inflammation caused by substance secreted by microbe". ScienceDaily (2023).
15. University of Wurzburg. "New ribozyme can make RNA molecules accessible for click chemistry in living cells". ScienceDaily (2023).
16. New York University. "Novel molecules fight viruses by bursting their bubble-like membranes Targeting the membrane of a virus, rather than its proteins, could lead to a new generation of antivirals". ScienceDaily (2023).
17. Harvard Medical School. "Researchers uncover signal needed for blood-brain barrie". ScienceDaily (2023).
18. NIH/National Eye Institute. "Scientists discover external protein network can help stabilize neural connections". ScienceDaily (2023).
19. University of Massachusetts Amherst. "How a small strand of RNA is key to fighting cancer". ScienceDaily (2023).
20. Case Western Reserve University. "A new approach to stop cancer growth?". ScienceDaily (2023).
21. Medical University of Vienna. "Breakthrough in the fight against resistance in metastatic breast cancer". ScienceDaily (2023).

22. Sanford Burnham Prebys. "A two-for-one approach to boost melanoma immunotherapy: One protein could help scientists fight treatment resistant melanoma from all directions". ScienceDaily (2023).

23. ETH Zurich. "Protein shapes indicate Parkinson' disease". ScienceDaily (2022).

24. University of Eastern Finland. "Brain astrocytes show metabolic alterations in Parkinson's disease". ScienceDaily (2020).

25. Ecole Polytechnique Federale de Lausanne. "A deep look into the progression of Parkinson's Disease". ScienceDaily (2023).

26. Northwestern University. "Newly discovered trigger of Parkinsons's upends common beliefs". ScienceDaily (2023).

27. University of Cologne. "Plant chloroplasts promise potential therapy for Huntington's disease". ScienceDaily (2023).

28. Oregon Health & Science University. "Study raises possibility of immunotherapy treatment for ALS". ScienceDaily (2023).

29. Childrens"s Hospital Colorado. "Groundbreaking New Treatment for Cystic Fibrosis". Advances and Answers in Pediatric Health: Pediatric Health Advances. Recent Articles (2023): 1-5.

30. Ruhr-University Bochum. "This is how protein aggregates can trigger neurodegenerative diseases". ScienceDaily (2023).

31. Washington University School of Medicine. "Tau-based biomarker tracks Alzheimer's progression Novel marker found in cerebrospinal fluid also could speed development of Alzheimer's drugs". ScienceDaily (2023).

32. University of California - San Diego. "Stem cell therapy rescues symptoms of Alsheimer's disease". ScienceDaily (2023).

33. Bayer College of Medicine. "Fungal infection in the brain produces changes like those seen in Alzheimer's disease". ScienceDaily (2023).

34. University of Texas at El Paso. "Researchers discover compound that fights leukemia lymphoma". ScienceDaily (2023).

35. Max Delbruck Center for Molecular Medicine in the Helmholtz Association. "Avatars to help tailor glioblastoma therapies". ScienceDaily (2023).

36. The Mount Sinai Hospital/ Mount Sinai School of Medicine. "Advanced bladder cancer patients could keep their bladder under new treatment regime, clinical trial shows". ScienceDaily (2023).

Volume 20 Issue 9 September 2024