SLS NEWSLETTER

ISBN: 978-81-940854-0-9

YEAR: 2019 VOL: 1 ISSUE 2 (Jan – June19)

SCHOOL OF LIFE SCIENCES

B.S. ABDUR RAHMAN CRESCENT INSTITUTE OF SCIENCE AND TECHNOLOGY

CHENNAI – 600048. TAMIL NADU. INDIA

Editors-in-Chief
Dr. S. Hemalatha & Dr. D. MubarakAli

Associate Editors
Dr. R. Karthi keyan
Dr. P. Ashok Kumar
Dr. Khurshid Alam Khan
Dr. Soumen Bera
Dr. Nessar Ahamed
Dr. Shazia Jamal
Dr. M. Sangeetha
Dr. M. Wasima
Dr. S. Sudarkodi
Dr. Subhamoy Banerjee
Dr. Gulsaz Shamim
Dr. U. Vimal Kumar
Dr. Mohd Waseem

Honorary Editors
Dr. Jung-Wan Kim, Korea
Dr. Sang-Yul Lee, Korea
Dr. R. Praveenkumar, Denmark
Dr. A. Parveez Ahamed, USA
Dr. Jie Chen, China
Dr. Hafiz Iqbal, Mexico
Dr. K. Saravanakumar, Korea
Dr. D. Rajesh, Malaysia
Dr. A. Pugazhendhi, Viet Nam
Dr. PT. Venkatesh, Germany
Dr. N. Thajuddin, India
Dr. JIS. Khatter, India
Dr. N. Senthilkumar, India

Managing Editors
Nasir Hussein, A.E.
Sriram. B
Hajira Fathima

Technical Editors
Ranjani, S
Sathya, R

Published by
School of Life Sciences
B. S. A Crescent Institute of Science and Technology
Chennai – 600048
Tamil Nadu, India
ISBN: **978-81-940854-0-9**
Year: 2019
Vol: 1
Issue: 2 (Jan – June, 2019)
Total number of pages: 25

Communication should be sent to:

Co-ordinator - SLS Newsletter
School of Life Sciences
B. S. Abdur Rahman Crescent Institute of Science and Technology
Chennai – 600048, Tamil Nadu, India

newsletter.sls@crescent.education
slsc.newsletter@gmail.com

Mobile : +91-9943535774
Phone : +91-044-2240380

Contents

Research and Opportunities in SLS

S. Hemalatha
School of Life Sciences
B.S.Abdur Rahman Crescent Institute of Science and Technology
Chennai – 600048, Tamil Nadu, India

❖ Pronounced Features of School of Life Sciences

- Established in the year 2013.
- Well qualified and dedicated members of faculty with Ph.D. and Post-Doctoral experience from abroad.
- Highly motivated and meritorious students.
- State of art Lab facilities.
- 12 laboratories facilitated in the 7 storey SLS Block.
- Semester patterned and choice based learning with flexible credit system.
- 360^{o} feedback including all the stakeholders.
- Management strategy involves Class Advisor & Faculty Advisor.
- Wired and Wi-Fi internet connection all throughout the block.
- Collaboration with premier institutes and industries globally.
- Exclusive Department Library & Seminar Hall.
- International conferences are organized every year in association with universities abroad and sponsored by DST-SERB and ICMR, TNSCST.
- Several Workshops, Seminars, Guest Lectures, Industrial Visits have been organized.
- Motto of the School : ***Creating employers and not employees***
- Journal club conferences held by Undergraduates and research scholars.
- Research grants secured from DST, ICMR, DBT, BIRAC, and TNSCST.
- Faculty members serving as Editor and reviewers in Elsevier and other scientific publishers.

❖ Workshops Organized

❖ Two days workshop on "Plant Tissue culture" held on Jan 24 & 25, 2019
❖ Two days FDP workshop on “Plant Tissue Culture Technology” held on Jan 26 & 27, 2019
❖ Two days workshop on "Molecular Biology Techniques” held on Feb 11 & 12, 2019
❖ Two days workshop on “Clinical Flow Cytometry (Multi colour) held on April 11-12, 2019
❖ Three days workshop on “Computational biology” held on June 17-19, 2019

❖ International Internships

Students were sent to Missouri University, USA (2), University of Montana, USA (1) and John Hopkins University, USA (1) for 3 months internship during June- August 2019 and undergraduate research internship program was established.

❖ Outreach and Social responsibility

Science Day for School students held on Feb 26, 2019

❖ Awards and Honours

Dr. D. MubarakAli, Assistant Professor awarded a "*Dr. P. Daisy Memorial Award for the Excellence in Life Science"* Conferred by Holy Cross College, Tiruchirappalli, India held on January 07-08, 2019

❖ Sponsored Project:

MubarakAli, D., Santhoshkumar, M and Aravindh, A sanctioned a project on *ES017: Phycoremediation of CO_2 level in suburban area via CO_2 sequestration by native microalgae : An Ecofriendly approach* from TNSCST under the scheme of TNSCST-SPS 2018-2019

❖ Invited talks delivered in seminars

- MubarakAli, D delivered talk on "*Solution plasma process based nanobiocomposites*" held on 21.02.2019 at **Avinashilingam Institute for Home Science and Higher Education for Woman, Coimbatore,** Tamil Nadu, India

- MubarakAli, D delivered talk on "*Microalgal Biotechnology: Applications and Opportunities*" held on 25.01.2019 at **B.S.A Crescent Institute of Science and Technology, Chennai**, Tamil Nadu, India

- MubarakAli, D delivered talk on "The Best Ways to Prepare *Nanomaterials*" held on 07-8.01.2019 at **Holy Cross College (**Autonomous**), Chennai**, Tamil Nadu, India

- MubarakAli, D acted as a chair person for the plenary session in the "*National Conference on Recent Trends in Microbiome Research: Exploring the Microbial Diversity*" on held on March 20-21, 2019 at **Pondicherry University,** Puducherry (UT), India

- MubarakAli, D acted as a chair person on February 21-22, 2019 at **Avinashilingam Institute for Home Science and Higher Education for Woman,** Coimbatore**,** Tamil Nadu, India

-

❖ Publication details (2019)

Research Article: 15

Review article: 3

Book chapter: 2

❖ OPINION

Importance of professional ethics in the productivity of the organization

Nikhat Hamza

B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai - 600048, Tamil Nadu, India

The economy is in deceleration and jobs are scarce. People try hard and use all the personal influences to get a job. There is a survival trait among all of us, however, this survival trait if acquired by an incompetent person is likely to lead to the toxicity in an organization. The survival trait perse is not negative if the person uses it to upgrade and meet the expectations of the organization will not only add in the productivity of organization but will also help in individual development. If the survival trait is combined with insecurity perception creates a lot of conflicts and unethical behaviour among the employees. Hence to sustain themselves these employees use a battery of techniques.

One such technique is writing letters against peers, superiors, and organizations irrespective of departments and duties. This kind of behaviour is destruction in the working environment and loss of productivity. One question is why it is so pronounced in India? It is one of the traits developed from the colonial past. The colonial bosses who have no proper feedback mechanism relied on this form of feedback.

It is natural to have grievances as the resources are limited and individual demands are increasing, moreover, the nonacceptance of people from diverse cultural backgrounds and behaviors also leads to insecurity. This leads to a lack of trust and formation of mutually destructive groups.

When people work together grievances are expected but to settle the grievance every organization has its respective managers or HR process. Employees can talk or formally complain instead of writing and hurting the dignity of others. The grievances should either pertain to the performance, work environment or compensation. When

the grievance is pointing to a person or vilification of the person from another department/ area it is not a grievance but settling of personal petty issues, afraid of not being heard. Less workload or inability to work for their role could also be one of the reasons for such behaviour.

This also indicates that the employee is concerned about her/his insecurity rather than organizational goal. If these letters are given cognition by organization, there will be an incentive to write more letters and divert the superior from addressing the goals.

How to organization should address these issues?

This can be addressed by having a strong feedback mechanism.

1. There should be a trust in the organization such that genuine professional respect and collegiality should prevail.
2. Managers should be trained to address the departmental issues as and when they arise
3. The anonymous letters should be replied with a message that this will not be entertained, at the same time it will be treated as unethical behaviour of the employees.
4. Professional ethics shall be inculcated in the employees.
5. Proper design of workload suitable to the persons competent level should be given

Sometimes these letters may not be by their own volition and may be instigated by another person to settle their egos. Superiors should ignore such mutually destructive behaviours and infuse teamwork and belongingness for the betterment of organization as well as employees.

Author correspondence: Dr. Nikhat Hamza, Director, HR & FTA, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai - 600048, Tamil Nadu, India.
Phone: 91-044-22759200; E.Mail: directorhr@crescent.education

❖ **RESEARCH ARTICLE**

A Proteomic Insight into the mechanisms of Curcumin with Electrical Pulses in Triple Negative Breast Cancer Cells

Lakshya Mittal[1], Ignacio G. Camarillo[2,3], Raji Sundararajan[1*]

[1]School of Engineering Technology, Purdue University, West Lafayette, IN 47907, United States of America

[2]Department of Biological Sciences, Purdue University, West Lafayette, IN 47907, United States of America

[3]Purdue Center for Cancer Research, Purdue University, West Lafayette, IN 47907, United States of America

Abstract

Triple negative breast cancer (TNBC) is an aggressive and metastatic subtype of cancer, with poor survival and high recurrences. TNBCs lack the expression of three main receptors, making them difficult to target, which highlights a critical need of new therapies. Considering this, we used electrical pulses (EP) with curcumin (Cur) against MDA-MB-231 TNBC cells. We utilized the high-throughput mass spectroscopy-based proteomics technique to gain the mechanistic insights into the effects induced by Cur+EP in the TNBC cells. Our results highlight that the Cur+EP regulates the multiple proteins to induce cell death in MDA-MB-231 cells.

Keywords: Curcumin, proteomics, electrical pulses, triple negative breast cancer, MDA-MB-231

1. Introduction

Curcumin is the yellow pigment of turmeric, a natural herbal spice is used for over 5000 years, both in Indian cooking and in Ayurveda. Curcumin holds various attractive properties, including anti-oxidant, anti-bacterial, anti-cancerous, anti-septic and is useful to treat many diseases, including various cancers[1,2]. It is also shown to be effective against TNBC cells[3,4].To further potentiate curcumin's efficacy against TNBC,

EP are applied[5–7]. EP application creates the transient pores in the cell membrane, which increases the delivery of external molecules into the cells, in a phenomenon called Electroporation[8]. Electroporation when used to deliver the chemotherapy is called Electrochemotherapy (ECT), which is rapidly gaining momentum for advanced tumors in clinics across Europe[9,10]. Electrochemotherapyis a physical procedure, which is applicable to all histologies of cancer, with exceptional success[9–11]. ECT is primarily used with bleomycin and cisplatin in clinics, which are infamous for their costand severe side-effects[9]. Considering this, it is critical to explore the use of natural compounds, such as curcumin with ECT.

Further it is imperative to understand the mechanisms of the enhanced effects induced by curcumin when delivered with EP. Considering the complex signaling network present in cells, where thousands of proteins work in coherence to perform cellular functions, use of system-based proteomics approach allows us with an exciting opportunity to visualize simultaneous changes in thousands of proteins to comprehensively understand the mechanisms. Towards this, in this research, we utilized a high-throughput mass-spectroscopy based proteomics technique to understand the effects induced by Cur+EP in human TNBC MDA-MB-231 cells, which are highly aggressive and metastatic in nature.

2. Materials and Methods

2.1. Cell culture

The MDA-MB-231, human TNBC cells (ATCC®, USA) were cultured as monolayer in DMEM with 10% FBS, 1% Penicillin-Streptomycin at 37°C, 70–80% humidity, and 5% CO_2.

2.2. Treatment

The cells were trypsinized and were resuspended in fresh DMEM at 1×10^6cells/mL. The required volume from curcumin stock (Sigma, USA) was added to the cell suspension for 50μM curcumin treatment. For EP application, 600μL cells were transferred to 4mm gap TX electroporation cuvettes and eight square-wave, unipolar

pulses of 1 Hz frequency at 1200V/cm with 100μs were applied using BTX ECM830. The treated cells were reseeded with 2mL of fresh media in 6-well plates (0.6×10^6 cells/well) and were incubated for 12 h.

2.3. Proteomics

Following 12h of incubation, cells were scraped and were washed 3 times with 1xPBS. The samples were prepared, run and the data was analyzed, as described previously[12].In brief, the proteins were extracted from cells, peptides were purified and the samples were analyzed on the reverse-phase HPLC-ESI-MS/MS using the UltiMate 3000 RSLC Nano System coupled with the Q-Exactive HF Quadrupole Orbitrap MS (Thermo Fisher Scientific, USA) and a Nano-electrospray Flex ion source (Thermo Fisher Scientific), and the data was processed in MaxQuant[13]. Proteins with Label Free Quantification intensity (LFQ) ≠ 0 and spectral count (MS/MS) ≥ 2 in at least one of the two treatments were analyzed.The difference in log2 LFQ values [Δlog2 (LFQ intensity)] between proteins from Cur and Cur+EP was used to calculate fold change. Proteins with fold-change > 0.5 were considered to be differentially regulated. The regulated proteins were analyzed for interaction with localization and function inSTRING11.0[14].

3. Results and Discussion

Fig. 1 shows the interaction among the 219 upregulated proteins in Cur+EP treatment from Cur. The majority of upregulated proteins were localized in organelles, such as mitochondrion, and endoplasmic reticulum, and were involved in the transport and regulation of apoptosis. Among these, several heat shock proteins,such as HSPE1 (1.6×), HSPD1 (1.6×), HSP90B1 (1.04×), and HSPA5 (0.64×), which could be over-expressed in the cells in response tothe oxidative stress[15] caused by EP application[12,16]. Protein AIFM1 (0.86×)was also upregulated, which is released from mitochondrion intermembrane space into the cytosol and to the nucleus, where it functions as a proapoptotic factor in a caspase-independent pathway[17].These results highlight the key role of mitochondrion in mediatingthe apoptosis uponCur+EP treatment.

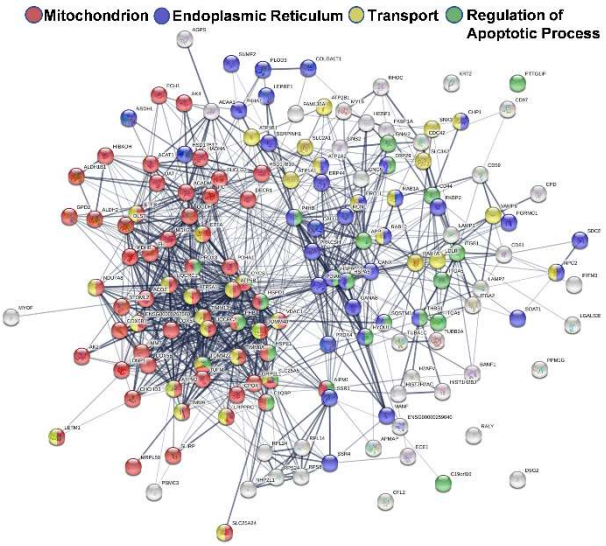

Fig. 1: Network of interaction among219 upregulated proteins using medium confidence (0.400) as minimum required interaction score. The node colors represent the localization and/or cellular processes for these proteins.

Fig. 2 shows the interaction among 234 downregulated proteins in Cur+EP treatment from Cur. These proteins were part of nucleus and the cytoskeleton, and were primarily localized in the cytosol. As we reported previously, among the downregulated proteins, 11 proteins were enriched in the glycolysis and 5 in the pentose phosphate pathway[12]. These proteins include key glycolytic proteins, such as PGM1 (5.01×), LDHA (1.6×), PGAM1 (1.28×), LDHB (0.62×), ALDOA(0.58×), which are localized in cytosol and play central role in the TNBC metabolism[18,19]. Protein HK1 (1.45×) was also downregulated, which along with LDHA, PGK1, and ENO2are part ofHypoxia-inducible factor 1(HIF-1) signaling pathway. The HIFs are linked with increase in invasion, metastasis, and resistance to chemo and radiation therapy, and HIF silencing resulted in altered lipid, glucose consumption and lactate production in MDA-MB-231 cells[20]. These results highlight the potential of Cur+EP treatment in targeting HIF-1 signaling pathway, which could be linked withthe glycolytic downregulation by Cur+EPin MDA-MB-231 cells.

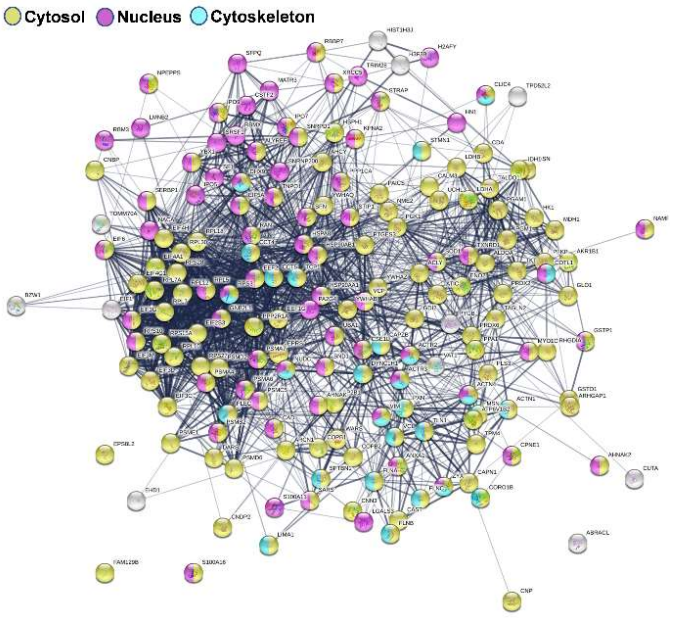

Fig. 2: Network of interaction among234 downregulated proteins using medium confidence (0.400) as minimum required interaction score.The node colors represent the localization for these proteins.

4. Conclusions

This study provides critical evidences into the mechanisms of Cur+EP against MDA-MB-231 cells. The Cur+EP treatment can mediate cell death in MDA-MB-231 cells by activating mitochondrion mediated apoptosis, while downregulating pathways responsible for cell survival and altered metabolism in these cells.

5. References

1. Goel, A., Kunnumakkara, A. B. & Aggarwal, B. B. Curcumin as ``Curecumin'': from kitchen to clinic. *Biochem Pharmacol***75**, (2008).
2. Aggarwal, B. B., Sundaram, C., Malani, N. & Ichikawa, H. CURCUMIN: THE INDIAN SOLID GOLD BT - The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease. in (eds. Aggarwal, B. B., Surh, Y.-J. & Shishodia, S.) 1–75 (Springer US, 2007). doi:10.1007/978-0-387-46401-5_1
3. Sun, X.-D., Liu, X.-E. & Huang, D.-S. Curcumin induces apoptosis of triple-negative breast cancer cells by inhibition of EGFR expression. *Mol. Med. Rep.***6**, 1267–1270 (2012).
4. Chiu, T.-L. & Su, C.-C. Curcumin inhibits proliferation and migration by increasing the Bax to Bcl-2 ratio and decreasing NF-kappaBp65 expression in breast cancer MDA-MB-231 cells. *Int. J. Mol. Med.***23**, 469–475 (2009).
5. Mittal, L., Raman, V., Camarillo, I. G. & Sundararajan, R. Ultra-microsecond pulsed curcumin for

effective treatment of triple negative breast cancers. *Biochem. Biophys. Res. Commun.***491**, 1015–1020 (2017).

6. Mittal, L., Raman, V., Camarillo, I. G., Garner, A. L. & Sundararajan, R. Viability and Cell Cycle Studies of Metastatic Triple Negative Breast Cancer Cells Using Low Voltage Electrical Pulses and Herbal Curcumin. *Biomed. Phys. Eng. Express***5**, 025040 (2018).
7. Mittal, L., Aryal, U. K., Camarillo, I. G., Raman, V. & Sundararajan, R. Effective electrochemotherapy with curcumin in MDA-MB-231-human, triple negative breast cancer cells: A global proteomics study. *Bioelectrochemistry***131**, 107350 (2020).
8. Haltiwanger, S. Why electroporation is a useful technique for cancer treatments. in *Electroporation-Based Therapies for Cancer* (ed. Sundararajan, R.) 103–125 (Woodhead Publishing, 2014). doi:10.1533/9781908818294.103
9. Marty, M. *et al.* Electrochemotherapy – An easy, highly effective and safe treatment of cutaneous and subcutaneous metastases: Results of ESOPE (European Standard Operating Procedures of Electrochemotherapy) study. *Eur. J. Cancer Suppl.***4**, 3–13 (2006).
10. Gehl, J. *et al.* Updated standard operating procedures for electrochemotherapy of cutaneous tumours and skin metastases. *Acta Oncol. (Madr).***57**, 874–882 (2018).
11. Campana, L. G. *et al.* Treatment efficacy with electrochemotherapy: A multi-institutional prospective observational study on 376 patients with superficial tumors. *Eur. J. Surg. Oncol.***42**, 1914–1923 (2016).
12. Mittal, L., Aryal, U. K., Camarillo, I. G., Raman, V. & Sundararajan, R. Effective electrochemotherapy with curcumin in MDA-MB-231-human, triple negative breast cancer cells: A global proteomics study. *Bioelectrochemistry***131**, 107350 (2020).
13. Cox, J. & Mann, M. MaxQuant enables high peptide identification rates, individualized p.p.b.-range mass accuracies and proteome-wide protein quantification. *Nat. Biotechnol.***26**, 1367–1372 (2008).
14. Szklarczyk, D. *et al.* The STRING database in 2017: quality-controlled protein–protein association networks, made broadly accessible. *Nucleic Acids Res.***45**, D362–D368 (2017).
15. Ikwegbue, P. C., Masamba, P., Oyinloye, B. E. & Kappo, A. P. Roles of heat shock proteins in apoptosis, oxidative stress, human inflammatory diseases, and cancer. *Pharmaceuticals***11**, (2018).
16. Mittal, L., Aryal, U. K., Camarillo, I. G., Ferreira, R. M. & Sundararajan, R. Quantitative proteomic analysis of enhanced cellular effects of electrochemotherapy with Cisplatin in triple-negative breast cancer cells. *Sci. Rep.***9**, 13916 (2019).
17. AIFM1 gene - Genetics Home Reference - NIH. Available at: https://ghr.nlm.nih.gov/gene/AIFM1#resources. (Accessed: 30th October 2019)
18. Lanning, N. J. *et al.* Metabolic profiling of triple-negative breast cancer cells reveals metabolic vulnerabilities. *Cancer Metab.***5**, 6 (2017).
19. McCleland, M. L. *et al.* An integrated genomic screen identifies LDHB as an essential gene for triple-negative breast cancer. *Cancer Res.***72**, 5812–5823 (2012).
20. Bharti, S. K. *et al.* Metabolic consequences of HIF silencing in a triple negative human breast cancer xenograft. *Oncotarget***9**, 15326–15339 (2018).

Author correspondence: Dr. Raji Sundararajan, School of Engineering Technology, Purdue University, West Lafayette, IN 47907, United States of America

❖ MINI REVIEW

Cancer Immunotherapy: Targeting Inflammatory Tumor Microenvironment

Nada Rafat, Shazia Jamal and Neesar Ahmed*

School of Life Sciences, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai - 600048, Tamil Nadu, India

Abstract

Cancer is becoming a familiar term in today's world. Even though treatment is available, it is still one of highest causes of death worldwide. Its incidence is increasing at alarming rates each year. This shows that the treatment available isn't as effective or affordable to all. One of the main reasons behind ineffective treatment is new resistance methods that these rogue cells develop and the side effects. Tumor microenvironment (TME) plays a major role in development of these resistance mechanisms as it consists of various factors that can contribute to these changes. Information and novel discoveries regarding the TME do not only help increase our understanding of cancer but also opens up new pathways and targets for diagnosis and therapy[1]. TME is essential for tumor growth, progression and metastasis as it acts as a supplier of vital nutrients[1]. It is mostly a medley of cancer and non-cancer cells. A whole network is created due to interactions between these heterogeneous populations of cells creating an environment suitable for the tumor to thrive. This kind of surrounding is habitually found in cases of solid tumor. It could be in benign or metastatic stage[2]. Here, the tumor acts as an organ in itself, with stroma as its supportive tissue[3]. Apart from the malignant cells, one of the non-malignant cells present within the TME is the cancer associated fibroblasts originating from endothelial, myoepithelial and smooth cells. They are involved in Epithelial-Mesenchymal-Transition (important for metastasis)[4], desmoplasmic reaction, paracrine signalling, secretion of various enzymes that aid in immunosuppressive environment to fight anti-tumor immunity among many other functions[5]. The other components present are Extracellular Matrix (ECM), pericytes, immune cells, adipocytes and vascular endothelial cells. ECM gives physical support and is remodelled by the tumor to help its progression. Its breakdown is a deciding factor for the extent of metastasis that is controlled by the amount of cytokines and chemokines secreted by the tumor[4]. Endothelial cells are responsible for angiogenesis to provide oxygen and nutrients to the growing tumor while pericytes support this vasculature. Adipocytes help in tumor growth by allowing cancer use its fatty acids and metastasis by releasing adipokines[4]. Immune cells and their role in the TME will be discussed elaborately in this minireview.

Keywords:

1. Introduction

1.1. Inflammatory Tumor Microenvironment

Inflammation in the tumor microenvironment is now being considered as the seventh hallmark of cancer[6]. It plays a major role in not only the progression of cancer but the initiation as well[7]. It alters the expression of several genes that lead to genomic instability causing the tumor cells to be in a state of continuous mutation[8]. Genetic instability furthermore leads to activation of numerous oncogenes and suppression of tumor suppressor genes. The accumulation of these genetic variations cause tumor cells to proliferate and progress faster while making the microenvironment heterogeneous in nature. This portrays the significance of inflammation in cancer[9]. It involves the work of several cytokines, chemokines, infiltrating leukocytes and transcription factors. These include interferons, interleukins, Matrix Metallo-proteins , growth factors etc. They help tumor grow by assisting in angiogenesis, matrix remodelling or breakdown, immunosuppression and metastasis[10]. Inflammation seen is chronic in nature and the immune cells involved are from both innate and active immunity. The underlying causes of this can be infection, genetic alterations or damage of tissues[11]. STAT 3 and NF-κB are stated to be the key regulators of inflammation in tumor growth[11]. Both of these transcription factors are present in cancer and immune cells and its downstream processes are seen to be activated in numerous cancers which involve expression of genes like Bcl-2, c-Myc, Cyclin D, HIF1-α etc[10]. The expression changes in the genes mentioned earlier aids in progression of cancer by evading apoptosis, unlimited cell proliferation and hypoxia. They also hinder with the maturation of dendritic cells. Inflammation also downregulates the DNA repair mechanisms. Tumor Associated Macrophages are one of the immune cells that are primarily involved in amplifying inflammation in the tumor microenvironment[10].

1.2. Immune Cells in the TME

Tumors have antigenic expression[12] yet they come up with various mechanisms that not only escape immune surveillance but make the immune cells work in their favour. The immune system consisting of dendritic cells, monocytes and lymphocytes[3], primarily involved in targeting cancer but due to certain factors present in the TME, they help in progression of tumor instead of regression. Macrophages are antigen presenting cells but the tumor secretes various factors or attractants that changes their phenotype and makes them Tumor Associated

Macrophages (TAMs).These TAMs help in angiogenesis, invasion, cell migration and metastasis[4]. They are also well known for accumulating in the hypoxic region and are the reason behind poor prognosis[11]. Similarly, the other Antigen Presenting cells (APCs), dendritic cells function is impaired in the tumor microenvironment due to chronic inflammation and suppression by T-lymphocytes leading to weak or no antigen presentation at all[4]. This further augments the failure of T and B lymphocytes to detect and kill cancer cells. One of the other cells involved are the Myeloid Derived Suppressor Cells (MDSCs), whose main function is antitumor immune response and metastasis[13]. MDSCs which represent the immature form of myeloid cells suppress immune system in antigen specific and non-antigen specific manner which chiefly involves T-cell suppression. In normal conditions, MDSCs are involved in tissue remodelling and act as barrier against infections[14]. Regulatory T-cells, a subset of T lymphocytes are normally regulators of other immune cells and suppress overactive immune system. However, in cancer, population of Treg markedly increases furthermore aiding in the progression of tumor by immunosuppression that directly affects Cytotoxic T cells (Tc), Natural Killer Cells (NK), Dendritic Cells and B Cells either by inhibition or suppression[15]. Tumor Infiltrating Lymphocytes constitute the majority of immune cells able to infiltrate tumor but due to numerous mechanisms employed by the tumor like inadequate display of tumor antigens or various cytokines that modulate T cell functions, T cells are exhausted before exerting any anti-tumor response[16]. Similar scenarios can be found in the cases of NK cells and B cells thereby showing the extent of effect that cancer has on immune cells.

1.3. Cytokines and their role in TME

Cytokines play a significant role in shaping of the tumor microenvironment. They are small protein molecules that are secreted by cells that enable communication and regulation between cells. To begin with, Tumor Necrosis Factor-α (TNF-α) is an inflammatory cytokine that mediates inflammation by producing reactive oxygen and nitrogen species that damages the DNA. This leads to tumorigenesis as it mediates cell proliferation and anti-apoptotic signals[17]. Interleukin-6, another pro-inflammatory cytokine has similar effects as of TNF- α but it promotes tumorigenesis by activating JNK/STAT signalling pathway. High concentrations of IL-6 are found in most cancer pateints.[17]Another pro-inflammatory cytokine is Interleukin 1. It is better known for amplification of metastasis process and are produced by macrophages in the tumor microenvironment[18]. Next, the anti-inflammatory cytokine, Transforming Growth Factor-β (TGF-β) is ubiquitous in nature and an effective regulator of cell growth[19]. During the

initial stages of cancer development, TGF-β acts as a tumor suppressor by inhibiting growth of normal hematopoietic, epithelial and stromal cells[19].However, as cancer progression takes place, the role of TGF-β can also change as tumor promoting helping in cancer initiation, progression and metastasis[20]. Interleukin- 10 is another anti-inflammatory cytokine that suppresses tumor growth by inhibiting macrophages and other pro-inflammatory cytokines like IL-6. Any deficiency in IL-10 is shown to increase inflammation[21]. Interleukin- 2 is an inflammatory cytokine that activates immune cells like NK cells and T-cells (tumor suppression) in initial stages of cancer which then prompts the release of cytokines like TGF-α and IFN-γ, perforin etc. It also activates signaling pathways like JNK/STAT, PI3K and MAPK in later stages of tumor (tumor promotion). IL-2 is one of the only cytokine that has been approved for Cytokine Gene Therapy, a type of immunotherapy[22]. Lastly Interferon-γ which is similar to IL-2 as both are pleiotropic cytokines[22,23]. It is produced by NK cells and Tc cells. It functions as an immune editor eliminating tumor in initial phases by modulating immune cells, stromal cell in TME or tumor cell itself. Although it is an effective agent for anti-tumor immunity, it has tumor promoter qualities that include establishment of immunosuppressive tumor environment by inducing homeostatic response or by recruiting immunosuppressive cells like MDSCs and Tregs[23].It is explicable that most cytokines exhibit dual role that include both tumor promoter and suppression, varying according to the tumor and host.

REFERENCES

1. Mbeunkui, F. & Johann, D.J. Cancer ChemotherPharmacol (2009) 63: 571. https://doi.org/10.1007/s00280-008-0881-9Pubmed Google Scholar
2. Robert J. Gillies, Natarajan Raghunand ,Gregory S. KarczmarZaver M. Bhujwalla (2002) https://doi.org/10.1002/jmri.10181
3. Drea, Components of Tumor Microenvironment (2018)
4. Frances R.Balkwill, MelaniaCapasso and Thorsten Hagemann The tumor microenvironment at a glance (2012) J Cell Sci 2012 125: 5591-5596; doi: 10.1242/jcs.116392
5. Valerie S. LeBleu, Raghu Kalluri Disease Model & Mechanisms 2018 11: dmm029447 doi: 10.1242/dmm.029447 Published 19 April 2018
6. Mantovani A. Cancer: inflaming metastasis, Nature , 2009, vol. 457 (pg. 36-37) Google ScholarCrossrefPubMed
7. Landskron G, De la Fuente M, Thuwajit P, Thuwajit C, Hermoso MAChronic inflammation and cytokines in the tumor microenvironment (2014)
8. Francesco Colotta, Paola Allavena, Antonio Sica, Cecilia Garlanda, Alberto Mantovani, Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability, Carcinogenesis, Volume 30, Issue 7, July 2009, Pages 1073–1081, https://doi.org/10.1093/carcin/bgp127

9. Nowell PC. The clonal evolution of tumor cell populations , Science, 1976, vol. 194(pg. 23-8) Google ScholarCrossrefPubMed
10. Finger EC, Giaccia AJ. Hypoxia, inflammation, and the tumor microenvironment in metastatic disease. Cancer Metastasis Rev. 2010;29(2):285–293. doi:10.1007/s10555-010-9224-5
11. Yang L, Lin PC. Mechanisms that drive inflammatory tumor microenvironment, tumor heterogeneity, and metastatic progression. Semin Cancer Biol. 2017;47:185–195. doi:10.1016/j.semcancer.2017.08.001
12. Gajewski TF, Schreiber H, Fu YX. Innate and adaptive immune cells in the tumor microenvironment. Nat Immunol. 2013;14(10):1014–1022. doi:10.1038/ni.2703
13. PastakiKhoshbinA, Eskian M, Keshavarz-Fathi M, Rezaei NRoles of Myeloid-Derived Suppressor Cells in Cancer Metastasis: Immunosuppression and Beyond. doi: 10.1007/s00005-018-0531-9. Epub 2018 Nov 2.
14. Dmitry I. Gabrilovich DOI: 10.1158/2326-6066.CIR-16-0297 Published January 2017
15. Corthay A. How do regulatory T cells work?.*Scand J Immunol*. 2009;70(4):326–336. doi:10.1111/j.1365-3083.2009.02308.x
16. Mohammad DavoodzadehGholami, GholamAlikardar, YousefSaeedi, Sahel heydari, Johan Garssen, Reza Falak Exhaustion of T lymphocytes in the tumor microenvironment: Significance and effective mechanisms , Cellular Immunology, Volume 222, December 2017, Pages 1-14 https://doi.org/10.1016/j.cellimm.2017.10.002
17. Landskron G, De la Fuente M, Thuwajit P, Thuwajit C, Hermoso MA. Chronic inflammation and cytokines in the tumor microenvironment. J Immunol Res. 2014;2014:149185. doi:10.1155/2014/149185
18. Mantovani A, Barajon, Garlanda C IL-1 and IL-1 regulatory pathways in cancer progression and therapy,Immunol Rev. 2018 Jan;281(1):57-61. doi: 10.1111/imr.12614
19. Pasche B. Role of transforming grwoth factor beta in cancer, J Cell Physiol, 2001, Feb;186(2)153-68 DOI:10.1002/1097-4652(200002)186:2<153::AID-JCP1016>3.0.CO;2-J
20. Stover DG[1], Bierie B, Moses HL. A delicate balance: TGF-beta and the tumor microenvironment, J Cell Biochem. 2007 Jul 1;101(4):851-61 DOI:10.1002/jcb.21149
21. Oft M, IL-10: master switch from tumor-promoting inflammation to antitumor immunity, Cancer Immunol Res. 2014 Mar;2(3):194-9. doi: 10.1158/2326-6066.CIR-13-0214 DOI:10.1158/2326-6066.CIR-13-0214
22. Setrerrahmane S, Xu H. Tumor-related interleukins: old validated targets for new anti-cancer drug development. Mol Cancer. 2017;16(1):153. Published 2017 Sep 19. doi:10.1186/s12943-017-0721-9
23. Mojic M, Takeda K, Hayakawa Y. The Dark Side of IFN-γ: Its Role in Promoting Cancer Immunoevasion. Int J Mol Sci. 2017;19(1):89. Published 2017 Dec 28. doi:10.3390/ijms19010089

***Author correspondence: Dr. Neesar Ahmed,** Assistant Professor, School of Life Science, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai - 600048, Tamil Nadu, India. Phone: 91-044-22759215; E.Mail: neesar.sls@crescent.education

❖ MINI REVIEW

Peter 2.0 : World's first full Cybernetic Organism

Tejas K, Syed Zafar Sathiq S, Sudha and M, Gulsaz Shamim*

School of Life Science, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai – 600048, Tamil Nadu, India

Cybernetic organism or the more commonly used term a "Cyborg" is considered as an integration of human and machine. They don't simply represent the intrusion of a machine in human body (like a pacemaker) for repair or enhancement but also the coupling of human and machine brain. There have been many experiments for such merging which includes 1997 work on cockroaches at University of Tokyo where some of the motor neurons of the cockroach was attached to a microprocessor. Another experiment in 1998 witnessed linking a small robot to the antennae of a male silk moth, this enabled the male to respond towards female's pheromone.

In humans, an experiment in 1998 at University of Reading, involved surgical implantation of a silicon chip transponder in the upper left arm of Professor Kevin Warwick. Another experiment in 2002 resulted in putting the chip again, directly linked with the nervous fibres in the Prof. Warwick's arm. It was reported that movement and physical emotion exhibited signals on the nervous system.

Recent news in Daily mirror reported the transformation of a British roboticist Dr. Peter Bowman Scott-Morgan to the world's first full cyborg. The scientist, aged 61 is suffering from motor neuron disease - which affects nerves and causes weakness in muscles, eventually leading to paralysis. He has turned his pioneering work on his own body and is now undergoing transition to become fully robotic – from Peter 1.0 (a human) to Peter 2.0 (a cyborg). This transformation would involve irreversible change in Peter's whole body including the brain where his new form will be partly represented by hardware and partly by wetware (human brain cells and thought process), a perfect example of collaboration between human – Artificial intelligence and robotics.

The process of this transformation involves a series of complex surgeries including a laryngectomy to give up his physical voice so that the risk of saliva entering into his lungs is avoided. To preserve his expressions and facial reactions, Dr Scott-Morgan has developed an avatar of his own face before any muscle loss. Furthermore, a feeding tube, a catheter and a colostomy bag are inserted directly into his stomach, bladder and his colon, respectively.

In his last post as Peter 1.0 the pioneer scientist said " I'm not dying – I'm transforming". Not only the cyborg, its creation and survival but it will also be interesting to see how the world will respond to the creation of such superhuman cybernetic organism with enhanced senses.

Reference:

1. Kevin Warwick. 2003. Cyborg morals, cyborg values, cyborg ethics, Ethics and Information Technology, 5, 131-137.
2. Terminally-ill scientist is about to 'transform' into world's first full cyborg. October 11, 2019. https://www.mirror.co.uk/tech/terminally-ill-scientist-transform-worlds-20559021

***Author correspondence:** Dr. Gulsaz Shamim, Assistant Professor, School of Life Science, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai - 600048, Tamil Nadu, India. Phone: 91-044-22759215; E.Mail: gulsaz.sls@crescent.education

❖ RESEARCH HIGHLIGHTS

Long non coding RNA CASC21 exerts an oncogenic role in colorectal cancer regulating miRNA-7-5P / YAP axis

Architha Vijayalakshmi

Department of Biotechnology, School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India

E.Mail: architha.v@gmail.com

Research Highlights:

Colorectal cancer (CRC) is the cancer of the colon or the rectum located at the lower end of the digestive tract, it has been the most common cause of cancer related death in the world. So the identification of new targets is needed to develop a more effective strategy for CRC treatment. For this study human colorectal cancer cell lines- human colonic adeno carcinomic cell line (HT 29) and human colon cell line (SW 480) were used. The researcher has used the long non coding RNA (IncRNA) as they help in colorectal cancer treatment as potential therapeutic targets. It was found that the cancer susceptibility 21(CASC 21)shows an oncogenic role in colorectal cancer. The author states that this might be the novel targets for the treatment and also useful for cancer biology research. In the urge to find the novel targets the researcher using the SiRNA has silenced the expression of CASC 21 in the CRC cells. This knockdown has suppressed the growth ability and promoted the apoptosis which was found by various methods like CCK 8 assay, flow cytometry, also silencing the CASC 21 inhibits cancer cells migration and invasion which was assessed by wound healing and trans well assay. It was also found that CASC 21 functions as competing endogenous RNA (ceRNA) to regulate expression of YAP 1 by miRNA-7-5P sponging. Furthermore in this study it was found that CASC 21 regulates the CRC cells invasion where CASC 21 regulates miRNA-7-5P/YAP axis. The upregulation of YAP 1 could reverse the decrease in cell invasion which is caused by silencing of CASC 21 in both HT29 and SW480 cell lines. This study has been concluded that an

estimated 18% of IncRNA are related with the tumors and the CASC 21 acts as ceRNA which plays an oncogenic role. He also states this might be one good step in the treatment of colorectal cancer .

Reference:

Long non coding RNA CASC 21 exerts an oncogenic role in colorectal cancer through regulating miR-7-5P/YAP 1 axis, Journal of Biomedicine and Pharmacotherapy,Volume 121,January2020,109628.

https://www.sciencedirect.com/science/article/pii/S0753332219352503

***Author correspondence: Ms. Architha V.,** Department of Biotechnology, School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India. E.Mail: architha.v@gmail.com

❖ RESEARCH HIGHLIGHTS

Molecular Study of Vancomycin Resistance in Hospital Acquired Staphylococcus Infection

Mohamed Suhail Nawabjohn

Department of Biochemistry, School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India

E.Mail: suhaildgl@gmail.com

Staphylococcus aureus is a gram positive bacterium due to its virulence factors it may cause infections like skin abscesses, respiratory infection, and food poisoning etc., Penicillin is a choice of treatment for *S.aureus*. Methicillin shows resistance towards *Staphylococcus aureus* which is commonly known as MRSA. Vancomycin is an antibiotic that prevents the growth of bacteria. For certain MRSA infections, vancomycin is considerable. There is increase in vancomycin resistance in last few years. They studied vancomycin intermediate *S.aureus* (VISA) and vancomycin resistance *S.aureus* (VRSA) in relation to MRSA in nosocomial infection. Transposon Tn1546 are transferred by vancomycin genes A, B, C, D, E, G and L. Detection of vancomycin resistant gene van A, van B and van C was done by multiplex PCR. Coagulase negative (152) (41.6%) and Coagulase positive (213) (58.4%) *S.aureus* strains were isolated from hospital. The following test such as gram stain, catalase test and Coagulase test (slide/tube) were carried down. Antibiotic susceptibility test were carried down by agar diffusion method using following discs vancomycin (30µg), erythromycin (15µg), Ampicillin (20µg) etc.., It shows that MRSA species are resistant to amoxicillin and cefoxitin. They showed high resistant to ampicillin (94.7%) clindamycin and erythromycin (85.7%) and vancomycin (17.6%). Minimum Inhibitory Concentration (MIC) for vancomycin was determined by Muller – Hinton Agar plate method. *S.aureus* strains were used as vancomycin susceptible control and *Enterococcus faecalis* were used as vancomycin resistant control (van A/van B/van C). According to MIC, vancomycin resistance in relation to MRSA were classified into susceptible, intermediate and resistance. mecA gene commonly shows resistance to methicillin and other

antibiotics. Hence, mecA gene was found in MRSA. It was detected by PCR. DNA was prepared by suspending 25µl of sterile water in the culture and kept in a water bath for 12 minutes at 100˚ C. One micron of suspension is used to perform the PCR. Multiplex PCR are used for detection of vancomycin gene by using primers. After amplification it was subjected to 1% agarose gel and EtBr is used for visualization. Coagulase negative *S.aureus* vancomycin resistant gene was not found. Four van A genes was found in VISA in *S.aureus* (N=13) whereas two van A gene in S.aureus (N=5). Six van B genes were found in intermediate susceptible and one van B gene in resistance to *S.aureus*. van C gene was not isolated in Coagulase negative and VISA and VRSA. Thus the study was concluded as van A & van B is involved in the resistance mechanism.

Further reading: Maysaa El-Sayed Zaki, Aalaa Abouelnour, Sherif MH El-Kannishy and Rasha Hassan. Molecular Study of Vancomycin Resistance in Hospital Acquired Staphylococcus Infection, Inter. J. Drug Devel. Res., 11(3):11-14, 2019.

http://www.ijddr.in/drug-development/molecular-study-of-vancomycin-resistance-in-hospital-acquired-staphylococcus-infection.pdf

***Author correspondence: Mr. Mohamed Suhail Nawabjohn.,** Department of Biochemistry, School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India. E.Mail: suhaildgl@gmail.com

JOURNALS /WORKSHOPS/ CONFERENCE/ INTERNSHIPS

D. MubarakAli*

School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India.

Special Issues:

Physiological and Molecular Plant Pathology (Elsevier): IF: 1.678

Special Issue on Molecular and multi-omics in plants under stress, Submission dateline: **March 2020**

Guest Editors: M. Wang, S. Hemalatha, Saravanakumar, K

Biocatalysis and Agricultural Biotechnology (Elsevier): CireScore: 2.28

Special Issue on Marine Natural Products, Submission dateline: **March 2020**

Guest Editors: Ganeshkumar, M., Praveenkumar, R

Workshop:

Awareness Program on Life Skills and Counselling to be held on January 28, 2020 at School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India

National Workshop on Medicinal Mushroom Technology to be held on January 30-31, 2020 at School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India

Conference:

This 19th European Congress on Biotechnology is organised by the European Federation of Biotechnology, ECB 2020 will be in Maastricht, Netherlands from June 28 - July 1, 2020 at Maastricht, Netherlands

International Symposium on Biodiversity, Biology and Biotechnology of Algae to be held on January 8-10, 2020 at University of Madras, Chennai, Tamil Nadu, India

***Author correspondence: Dr. D. MubarakAli**, Assistant Professor, School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India. E.Mail: mubarakali.sls@crescent.education

❖ INSTRUCTIONS TO CONTRIBUTORS

SLS newsletter, a biannual publication by the School of life science intends to enlighten the readers with research articles, reviews, reports, research highlights, news and facts, concerned to the advancing field of biotechnology.

In order to acknowledge recent advancements and potential knowledge, bringing it to the notice of the science community through the newsletter, SLS welcomes original research, review and reports and details of the forthcoming events (conferences, seminars, symposia, trainings and workshops.)

❖ GUIDELINES FOR SUBMISSION:

✓ The article submitted must be an own write up on the selected article.

✓ References: The research paper referred must be assessed from renowned publishers (science, nature etc.,) and the references must be mentioned in the article.

✓ No Plagiarism will be entertained.

✓ The article should be typed in double space in word format limited to > 1000 words with font “Cambria” and font size 12 with 1.5 line spacing.

✓ Illustration and tables: Illustrations must be reduced to one – third of the page. Typed tables should be provided with tittles. Authors are specially requested to reduce the number of tables, illustrations and diagrams to a minimum (maximum 2).

✓ The SLS newsletter assumes no responsibility for statements and opinions advanced by the contributors to the journal.

SLS NEWSLETTER - MEMBERSHIP FORM

S.No.	Particulars to be filled		
1.	**Name of the applicant**	:	
2.	**Designation**	:	
3.	**Date of Birth**	:	
4.	**Affiliation**	:	
5.	**Permanent Address** (Newsletter to be sent)	:	
6.	**E. Mail id**	:	
7.	**Mobile Number**	:	
8.	**Membership mode**	:	**Annual** ☐ **Life** ☐
9.	**Membership type**	:	**e-Newsletter** ☐
		:	**p-Newsletter** ☐
10.	**Signature with date**	:	

***Conditions apply**