Alex George, PhD

Scientist D Jubilee Centre for Medical Research Jubilee Mission Medical College & Research Institute Thrissur 680 005 Mobile #: +91-95449-08706 e-mail: alexgeorge@jmmc.ac.in

Professional Profile

Experienced Scientist with a demonstrated history of working in the hospital & health care industry. Skilled in Cytogenetics and molecular genetics with a particular interest in molecular diagnostics, Telomere Genetics, Bioinformatics, Industry Related Clinical Research, Liquid Biopsy Research and Translational Research. Strong research professional with a Doctor of Philosophy (Ph.D.) focused on Human/Medical Genetics from Vellore Institute of Technology.

Educational Qualifications

- Post Doc- Specific focus on Cancer Biology and Extra Cellular Vesicle Research Canterbury Christ Church University (CCCU), Kent, The United Kingdom ICMR-DHR International Fellowship (2019)
- PhD Specific focus on Human Genetics (2010-2014) Thesis Title -*Micronuclei frequencies and its structural variations in precancerous, fragile chromosome and cancerous syndromes (2014)* Vellore Institute of Technology, Vellore, Tamilnadu
- M.Sc. Biomedical Genetics 2008-2010, Vellore Institute of Technology, Vellore, Tamilnadu

Technical Skills

	Karyotyping, Chromosome staining, Banding Techniques, FISH
Genetics and Genomics	Techniques, Chromosomal Aberration Analysis, Sister chromatid
	exchange Analysis, CBMN Cyt Assay, Comet Assay, DNA and
	RNA sequence analysis
Molecular Biology	Extra cellular vesicles isolation and characterisation, Nanopore
	based DNA Sequencing, Northern and southern blot, Wound
	healing Assay (Scratch assay), Size Exclusion Chromatography,
	Human DNA, RNA, cfDNA, cfRNA and Protein isolation from
	blood, Urine and tissues, SSCP, PAGE and RFLP.
Cell Culture/ Cell line	Human Leukocyte Culture, Culturing, and maintenance of cell lines
preparation	(including stable cell lines), Isogenic cell line preparation (pVector
	and ShRNA), DNA transfection
Protein biochemistry	Protein electrophoresis, ELISA, Western blotting,
	immunoprecipitation, IHC, development of in vitro assays, cell
	fractionation, glycerol and sucrose gradients, protein purification,
	column chromatography (size-exclusion, affinity, and
	immunoaffinity).

Areas of interest- #Genetics and Molecular Biology, #Genetic Counselling, #Clinical Research, #Liquid Biopsy Research, #Congenital Anomalies, # Ayurveda Biology and, #Cancer

Fellowships, Certification and Courses

- ICMR-DHR international Fellowship for the year 2019-2020, Ministry of Health and Family Welfare. Government of India.
- Certified 3T-IBHSc training for health science faculty (certificate number 1267) from the **UNESCO Chair of Bioethics (Haifa)**
- Completed **Research to publication** course conducted by **British Medical Journals** in collaboration with the University of California, San Francisco (UCSF). 2019

Research experience

• ICMR-DHR International Fellow - Investigating the role of sortilin in lung progression where the results from this study will feed into a global analysis of sortilin function in different types of lung cancer under the supervision of Dr. Cornelia M Wilson, Academic Laboratory Director at Canterbury Christ Church University, School of Human and Life Sciences, Life Sciences Industry Liaison Lab, Sandwich, UK (September 2019- September 2020). The research work was a part of Liverpool Cancer Research in collaboration with Liverpool University, UK

Highlights of work conducted:

i) Technique/expertise acquired:

a) Preparation of Isogenic cell lines using gene-specific transfection, pTarget vector transfection into SK-MES-1 cell line to express the sortilin and shRNA transfection into CALU-1 cell line to down-regulate sortilin

b) Extracellular Vesicle Isolation and Characterisation- Using Polyethene glycol and ultracentrifugation method characterisation using Size

Exclusion Chromatography (SEC), Nano Particle analysis (Nanosight 300) and TEM.

c) Cell viability analysis using resazurin assay. - The metabolic activity of the isogenic cell lines different treatments was noted using Resazurin assay

d) Wound healing assay- Wound healing assay or scratch assay will be used to determine the rate of migration of cells in the conditioned media with or without treatment

e) Western blot

The expression of marker proteins in -/- sort, +/- sort and +/+ sort cell lines were studied using western blot.

ii) Results

a) The sortilin deregulation (upregulation or downregulation) affects the (Calu1 and SKMES-1) cells, which indicates that balancing sortilin is a suggestible mechanism to control the cancer progression

b) Sortilin is involved in the cell migration and invasion of lung cancer cell lines (Calu1 and SKMES-1)

c) Sortilin is significantly increased in the low stage cancer patients where it tends to decrease during the progression

d) The study shows a relation between EGFR and Sortilin expression, where EGFR decrease while Sortilin increase in the cancer patients

• **Co-I in ICMR project** titled- Influence of demographic, clinical, genetic and pattern of management in maintaining long term abstinence among patients of alcohol use disorders who received treatment from De-addiction centres in Thrissur district: A prospective follow up study (2019-2022)

Oxford nanopore-based DNA sequencing for selected trait markers

- Genetics of cleft lip and Palate- this is an ongoing project which includes several genes related to cleft lip pathogenesis and syndrome 2015- till date
 - DNA sequencing of IRF6 genes CRISPLD2 genes
 - Karyotyping and FISH for the syndromic CLP
 - -
- Gene polymorphisms in Age-related Macular degeneration- The gene polymorphisms were studied to establish an early diagnosis and better treatment 2015-2017
 - DNA sequencing for HTRA1, CFH and ARMS2 genes
- Genotoxic effects of thymoquinone, a Nigella sativa active compound, in human peripheral lymphocytes and K562 Cell line 2015- 2017 CBMN Cyt Assay
- One month training in **Cytogenetics and Genetic counselling** in St.Johns National Academy of Health Sciences, Bangalore as a part of establishing the research activities in Jubilee Centre for Medical Research (2015 Jan)
- Completed **doctoral degree** thesis titled 'Micronuclei frequencies and its structural variations in precancerous, fragile chromosome and cancerous syndromes' under the guidance of **Dr. Radha Saraswathy**, Senior professor at VIT university (December 2010-August 2014)
 - Karyotyping
 - CBMN Cyt Assay
 - PNA FISH for Telomeres
 - PCR-SSCP
 - DNA sequencing
- Undergone six-month Project on 'CYP1B1 Gene Mutation Analysis in Primary Congenital Glaucoma Patients' (January 2010- July 2010)

- PCR-SSCP
- DNA Sequencing
- .
- DBT Sponsored student research titled "Gene-environment interactions in ocular diseases" in the sector BIOLOGICAL SCIENCES (INCLUDING BIOTECHNOLOGY) UNDER STUDENT RESEARCH PROJECT SCHEME Sponsored by DBT and State Council during the academic year 2009-2010
 - PCR-SSCP
 - DNA Sequencing

External Academic activities

- External examiner for the final project viva voce examination of M.Sc. Biomedical Genetics Students with GC and Non-GC specialisation, **VIT University** Vellore, 28/06/18
- External examiner for II Sem Applied Zoology theory paper Cytogenetics and evolution (ZOO2 C 07), Calicut University (Main Campus)- 21/05/2019
- Reviewer for Archives of Gynecology and Obstetrics (ARCH)- Q2, Life Sciences-Q2, Journal of Epilepsy
- Assigned as **Institutional Research Committee Member** from January 2021 to December 2024 (JMMC&RI)

Guest Lectures and Invited Talks

- Guest Lecture on "Cytogenetic techniques and diagnostics" St. Aloysius College, Thrissur 15/04/2015
- Delivered a lecture in Second Hands-on Workshop on Cell Culture Techniques organised by Pushpagiri Research Centre, Pushpagiri Institute of Medical Sciences and Research, Tiruvalla. 24/06/2016
- Delivered a talk on the topic 'Telomere Loss and Gain: A progressive mode of Genomic Instability' at National symposium on genetics in clinical medicine (NSGCM-2017) 16/09/2017
- Industrial Expert Guest Lecture on "Basic genetic laboratory skills need to practice as professionals", VIT, Vellore. 02/11/2017
- Industrial Expert Guest Lecture on "Medical Genetics: Diagnostics and research in hospitals" VIT, Vellore. 02/11/2017
- Industrial Expert Guest Lecture on "Genotoxicity Assays" VIT, Vellore. 04/10/2018
- Industrial Expert Guest Lecture on "Diagnosis and Genetic Counseling for Syndromic and Non-syndromic Cleft Lip and Palate" VIT, Vellore. 04/10/2018
- Delivered a talk on Molecular Aspects of Ageing at CME on Ageing -Current Concepts, conducted by the Department of Biochemistry, JMMC&RI, Thrissur. 02/03/2019
- Industrial Expert Guest Lecture on "GxE interactions: impacts, adaptation and diseases" VIT, Vellore. 03/11/2020

Directly supervised PhD and MD students in the Jubilee Centre for Medical Research (Not as an official guide)

Completed

- Genotoxic effect of selected nanoparticles: An in vitro study (PhD- University of Calicut 2015- 2019)
- Genotoxic effects of Diisononyl phthalate (DINP) and Di (2ethyl hexyl) phthalate (DEHP) on human peripheral blood in vitro (PhD-University of Calicut 2016-2020)
- Assessment of genotoxicity effects of fullerene C₆₀ by CBMN assay *in vitro* (PhD-University of Calicut 2016-2020)
- Frequency of CYP2C19*2 alleles and its effects on response to Clopidogrel in patients with the acute coronary syndrome (MD. Biochemistry, Govt. Medical College Thrissur 2016-2019)
- Genotype profiling of advanced non-small cell lung carcinoma patients and their treatment response rates to platinum-based chemotherapy (MD. Biochemistry, Govt. Medical College Thrissur 2016-2019)
- Genotoxicity studies in cement dust workers (Meenakshi Academy of Higher Education and Research 2016-2020)
- Telomere Length analysis in low birthweight babies (Meenakshi Academy of Higher Education and Research 2016-2020)
- Asthma ADAM33 gene polymorphisms and dermatoglyphics (Meenakshi Academy of Higher Education and Research 2016-2020)
- Gestational diabetes and MTNR1B gene association (Meenakshi Academy of Higher Education and Research 2016-2020)

Ongoing

- Asthma ADRB2 gene polymorphisms (JSS University Mysore 2017-Ongoing)
- Haplotyping of IRF6 gene in cleft lip trio (MG University, Kottayam 2018-ongoing)
- Genotyping of CRISPLD2 and IRF6 genes (University of Calicut 2016- ongoing)
- Epidemiological study & Screening of MSX1 genetic variants in orofacial clefts (NIT Calicut 2016- ongoing)
- Regulatory effects of sortilin and extracellular vesicle trafficking in lung cancer progression (MG University, Kottayam 2020- ongoing)
- Regulatory role of miRNAs in sortilin mediated extracellular vesicles and triple-negative breast cancer progression (MG University, Kottayam 2022- ongoing)
- Parent of origin effect of Forkhead Box F2(FOX F2) gene in orofacial cleft a case parent trio study (MG University, Kottayam 2022- ongoing)

Clinical Trials

• Does Sevoflurane Induce Genomic Instability in Patients Undergoing General Anaesthesia? ClinicalTrials.gov Identifier: NCT03109119 (2017-ongoing)

Ongoing Funded Projects

1. Area- Orofacial Clefts

Funding Agency- Smile Train India (2021-2024)

Project Title: Epidemiological and Genetic Research among the Orofacial cleft patients from Central Kerala: A hospital-based Case Control Study

Budget: Rs. 7,860,000/-

Principal Investigator

Dr. Alex George Scientist C Jubilee Centre for Medical Research, MMC&RI, Thrissur

Co-Principal investigators

- Dr. P V Narayanan Chief Surgeon and Head of the Department Charles Pinto centre for Cleft lip, Palate and Craniofacial Anomalies JMMC&RI
- Dr. P R Varghese Research Coordinator Jubilee Centre for Medical Research JMMC&RI
- Area- Psychiatry and State (biochemical) and Trait (genetic) markers in alcoholism Funding Agency: ICMR, Govt. of India (2019-2021) Project Title: Influence of demographic, clinical, genetic and pattern of management in maintaining long term abstinence among patients of alcohol use disorders who received treatment from De-addiction centres in Thrissur district: A prospective follow up study Budget: Rs. 5,300,000 /-

Principal Investigator

• *Dr. Praveenlal Kuttichira* Principal (Prof. of Psychiatry) JMMC&RI, Thrissur

Co-Principal investigator (Role- Trait Markers identification and Sequencing)

 Dr. Alex George Scientist C Jubilee Centre for Medical Research, JMMC&RI, Thrissur **3.** Area-SARS Cov2 Variants among PLHIV

Funding Agency: **ICMR, Govt. of India** (2022-2023) Project Title: Effectiveness of Covid Vaccine and identification of SARS Cov2 Variants among PLHIV in Central Kerala – An Ambi-directional Cohort Study Budget: **Rs. 3,974,770/-**

Principal Investigator

- Dr.Joe Thomas Professor, Department of Community Medicine JMMC&RI, Thrissur Co- investigator
- Dr. Alex George (Role _SarsCov-2 Sequencing) Scientist C
 Jubilee Centre for Medical Research, JMMC&RI, Thrissur

Completed Funded Projects

1. **ICMR-DHR** International Fellowship for the year 2019-2020, **Ministry of Health and Family Welfare**. Government of India.

Publications

Book Chapters

Kannampuzha, S., Ravichandran, M., George, A., Vellingiri, B., Valsala Gopalakrishnan, A. (2023). Kanzaki Disease. In: Rezaei, N. (eds) Genetic Syndromes. Springer, Cham. <u>https://doi.org/10.1007/978-3-319-66816-1_1762-1</u>

Journal Articles

- Padinharayil H, Rai V, George A. Mitochondrial Metabolism in Pancreatic Ductal Adenocarcinoma: From Mechanism-Based Perspectives to Therapy. Cancers. 2023 Feb 8;15(4):1070. (Q1, IF-6.575)
- Mukherjee AG, Renu K, Gopalakrishnan AV, Veeraraghavan VP, Vinayagam S, Paz-Montelongo S, Dey A, Vellingiri B, George A, Madhyastha H, Ganesan R. Heavy Metal and Metalloid Contamination in Food and Emerging Technologies for Its Detection. Sustainability. 2023 Jan;15(2):1195. (Q1, IF-3.889)
- Kannampuzha S, Ravichandran M, Mukherjee AG, Wanjari UR, Renu K, Vellingiri B, Iyer M, Dey A, George A, Gopalakrishnan AV. The mechanism of action of non-coding RNAs in placental disorders. Biomedicine & Pharmacotherapy. 2022 Dec 1;156:113964. (Q1, IF-7.419)
- Mukherjee AG, Wanjari UR, Gopalakrishnan AV, Bradu P, Sukumar A, Patil M, Renu

K, Dey A, Vellingiri B, George A, Ganesan R. Implications of cancer stem cells in diabetes and pancreatic cancer. Life Sciences. 2022 Nov 19:121211. (Q1, IF-6.78)

- Padinharayil H, Alappat RR, Joy LM, Anilkumar KV, Wilson CM, George A, Valsala Gopalakrishnan A, Madhyastha H, Ramesh T, Sathiyamoorthi E, Lee J. Advances in the Lung Cancer Immunotherapy Approaches. Vaccines. 2022 Nov 19;10(11):1963. (Q1, IF-4.961)
- Renu K, Mukherjee AG, Wanjari UR, Vinayagam S, Veeraraghavan VP, Vellingiri B, George A, Lagoa R, Sattu K, Dey A, Gopalakrishnan AV. Misuse of Cardiac Lipid upon Exposure to Toxic Trace Elements—A Focused Review. Molecules. 2022 Jan;27(17):5657. (Q1, IF-4.927)
- Renu, K.; Vinayagam, S.; Veeraraghavan, V.P.; Mukherjee, A.G.; Wanjari, U.R.; Prabakaran, D.S.; Ganesan, R.; Dey, A.; Vellingiri, B.; Kandasamy, S.; Ramanathan, G.; Doss C, G.P.; George, A.; Gopalakrishnan, A.V. Molecular Crosstalk between the Immunological Mechanism of the Tumor Microenvironment and Epithelial– Mesenchymal Transition in Oral Cancer. *Vaccines* 2022, *10*, 1490. https://doi.org/10.3390/vaccines10091490(Q1, IF-4.961)
- Padinharayil H, Varghese J, John M C, Rajanikant G K, Wilson C M, Al-Yozbaki M, Renu K, Dewanjee S, Sanyal R, Dey A, Mukherjee A G, Wanjari U R, Gopalakrishnan A V, George A. Non-small cell lung carcinoma (NSCLC): Implications on molecular pathology and advances in early diagnostics and therapeutics. Genes and Disease (Q1, IF-7.243)
- Ramgir SS, Renu K, Vellingiri B, George A, Tirupapuliyur D, Thiagarajan P, Valsala Gopalakrishnanan A. Phytomedicinal therapeutics for male infertility: critical insights and scientific updates. Journal of natural medicines. 2022 Apr 4:1-28. (Q1, IF-3.192)
- Rai S, Badarinath AR, George A, Sitaraman S, Bronson SC, Anandt S, Babu KT, Moses A, Saraswathy R, Hande MP. Association of telomere length with diabetes mellitus and idiopathic dilated cardiomyopathy in a South Indian population: A pilot study. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 2022 Feb 1;874:503439. (Q2, IF-3.189)
- Renu K, Panda A, Vellingiri B, George A, Valsala Gopalakrishnan A. Arsenic: an emerging role in adipose tissue dysfunction and muscle toxicity. Toxin Reviews. 2021 Oct 20:1-0. (Q4, IF-5.075)
- Mukherjee, A.G., Wanjari, U.R., Chakraborty, R., Renu, K., Vellingiri, B., George, A., CR, S.R. and Gopalakrishnan, A.V., 2021. A review on modern and smart technologies for efficient waste disposal and management. *Journal of Environmental Management*, 297, p.113347. (Q1, IF-8.910)
- Belkozhayev, A.M., Al-Yozbaki, M., George, A., Sharipov, K.O., Byrne, L.J. and Wilson, C.M., 2021. Extracellular vesicles, stem cells and the role of miRNAs in neurodegeneration. *Current Neuropharmacology*. (Q1, IF-7.708)
- Renu, K., Chakraborty, R., Haritha, M., Rajeshwari, K., Famurewa, A.C., Madhyastha, H., Balachandar, V., George, A. and Abilash, V.G., 2021. Molecular mechanism of heavy

metals (Lead, Chromium, Arsenic, Mercury, Nickel and Cadmium) induced hepatotoxicity–A review. Chemosphere, p.129735. (Q1, IF-8.943)

- Wilkin PJ, Al-Yozbaki M, George A, Gupta GK, Wilson CM. The undiscovered potential of essential oils for treating SARS-CoV-2 (COVID-19). Current Pharmaceutical Design. 2020 Oct 15. (Q2, IF- 3.310)
- Al-Yozbaki M, Acha-Sagredo A, George A, Liloglou T, Wilson CM. Balancing neurotrophin pathway and sortilin function: Its role in human disease. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer. 2020 Sep 18:188429. (Q1, IF- 11.414)
- Woodman C, Vundu G, George A, Wilson CM. Applications, and strategies in nanodiagnosis and nanotherapy in lung cancer. Seminars in Cancer Biology 2020 Feb 20. (Q1, IF- 17.012)
- Krishna L, Sampson U, Annamala PT, Unni KM, Binukumar B, George A, Sreedharan R. Genomic Instability in Exfoliated Buccal Cells among Cement Warehouse Workers. The Journal of Occupational and Environmental Medicine. 2020 Jan;11(1):33. (Q3, IF-1.644)
- Raveendran SK, Ramachandran L, Joseph L, Asokan AK, Raj S, George A, James J. A novel SRY gene mutation c. 266 A> T (p. E89V) in a 46, XY complete gonadal dysgenesis patient. Andrologia. 2019 Oct;51(9): e13377. (Q3, IF-2.532)
- George A, Venkatesan S, Ashok N, Saraswathy R, Hande MP. Assessment of genomic instability and proliferation index in cultured lymphocytes of patients with Down Syndrome, Congenital Anomalies and Aplastic Anaemia. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 2018 Jun 8. (Q2, IF- 3.189)
- Vijayaraghavan D, Joseph C, George A. Clinical and Cytogenetic Analysis of a Baby with Vestigial Tail and Limb Defects. Journal of medical science and clinical research. Volume 06 Issue 07 2018 July
- Vidya PV, George A, Chitra KC. An in vitro study on the induction of micronuclei and other nuclear anomalies in peripheral blood lymphocyte culture by metal oxide nanoparticles. Int. J. Adv. Res. Biol. Sci. 2017;4(1):1-8.
- Mukul Prasad, S. Charles Bronson, Tushar Warrier, ARS. Badarinath, Shivam Rai, Kaushal Baid, Sneha Sitaraman, Alex George, C.R. Anand Moses, Radha Saraswathy, R. Vasuki, A. Shanmugam (2015). Evaluation of DNA damage in Type 2 diabetes mellitus patients with and without peripheral neuropathy: A study in South Indian population. Journal of Natural Science, Biology and Medicine, 6(1), 80. (Q3)
- George, A., R. Dey, V. Bhuria, S. Banerjee, S. Ethirajan, A. Siluvaimuthu and R. Saraswathy, (2014). Nuclear Anomalies, Chromosomal Aberrations and Proliferation Rates in Cultured Lymphocytes of Head and Neck Cancer Patients. Asian Pacific Journal of Cancer Prevention. 15, 1119-1123 (Q2 IF-1.9-2014)
- George, A., M. Jayasankar and R. Saraswathy, (2012). Genomic instability in peripheral blood lymphocytes of cancer prone syndromes. Int J Pharm Bio Sci. 3, 128-135 (Q2, IF-1.5 2012)
- Saraswathy, R., G. Alex, B. Basil, A. Badarinath, R. Girish, G. Ribu, V. Abilash, G. Cruz

and K. Marimuthu, (2011). Clinical and Cytogenetic Effects in Habitants under Large Duration Exposure of Endosulfan. Asian Journal of Medical Sciences. 3, 17-22

Saraswathy, R., V. Abilash, G. Manivannan, A. George and K.T. Babu, (2010). Four novel mutations detected in the exon 1 of MBL2 gene associated with rheumatic heart disease in South Indian patients. International Journal of Genetics and Molecular Biology. 2, 165-170