Year of signing MoU	Name of the organization with whom MOU/Collaboration being signed	Duration	Purpose of MOU/Collaboration	List the actual activities under each MOU year-wise	Date of the activity conducted
2021 (20th October 2021) (Prof. Suman Kundu) ("Pathophysiological investigations of Sickle Cell Disease and Interventions to improve associated Hemorheological Abnormalities")	M/s Sai Phytoceuticals Pvt. Ltd., registered under Companies Act 1956 (no. 5570148 of 1995-96) having its registered office at S-553, Greater Kailash Part II, New Delhi 110048	5 years	Research		
2021 (20th October 2021) (Prof. Suman Kundu) ("Pathophysiological investigations of Sickle Cell Disease and Interventions to improve associated Hemorheological Abnormalities")	M/s Sai Phytoceuticals Pvt. Ltd., registered under Companies Act 1956 (no. 5570148 of 1995-96) having its registered office at S-553, Greater Kailash Part II, New Delhi 110048	5 years	Research		
2021 (7th May 2021) (Prof. Suman Kundu) (Material transfer agreement for BL21(DE3)/pH80.0hug plasmid (developed by Dough Henderson)	University of Texas Permian Basin, 4901 East University Boulevard, Odessa, Texas 79762-8122, USA.	-	Research		
2020 (11th December 2020) (Prof. Suman Kundu) ("New Drug Candidates to Combat Hypertension and Cardiac Hypertrophy Designed against an Unconventional Target and Pathway")	M/s Sai Phytoceuticals Pvt. Ltd., registered under Companies Act 1956 (no. 5570148 of 1995-96) having its registered office at S-553, Greater Kailash Part II, New Delhi 110048	5 years	Research		

2020 (11th December 2020) (Prof. Suman Kundu)	M/s Sai Phytoceuticals Pvt. Ltd., registered under Companies Act 1956 (no. 5570148 of 1995-96) having its registered office at S-553, Greater Kailash Part II, New Delhi 110048	5 years	Research		
2021 (9th December 2021) (Prof. Suman Kundu) ("Pathophysiological investigations of Sickle Cell Disease and Interventions to improve associated Hemorheological Abnormalities")	Sri Sri College of Ayurvedic Science and Research Hospital, Sri Sri University, Cuttack, Odisha	5 years	Research		
2017-20 (Prof. Suman Kundu) ("Screening lead molecules identified by structure based rational drug design methods against cytochrome b5 reductase 3 and dopamine beta hydroxylase in spontaneously hypertensive rat modesl for antihypertensive effects"	Prof. C.C. Kartha, Rajiv Gandhi Centre of Biotechnology, Kerela	4 years	Research	Research project completed	
2020 onwards (Prof. Alo Nag)	Prof. Chandi Mandal, Central University of Rajasthan	Ongoing	Research	Published few papers in collaboration	
2020 onwards (Prof. Alo Nag)	Dr. Kulbhushan Sharma, INMAS, DRDO New Delhi	Ongoing	Research	Published few papers in collaboration	
2023 (April 2023) (Dr. Vijay Kumar Prajapati)	Prof. Yvon Sterkers, University of Montpellier, France	Ongoing	Research	Visit of Dr. Vijay planned in November 2023	-

2018 onwards (Dr. Garima Khare)	Dr. Anupam Das Talukdar, Assam University, Silchar, Assam	2018-21 (completed)	Research	Research work completed	
2012 onwards (Dr. Dau Dayal)	Prof. Abraham B Korol, University of Haifa, Israel	Ongoing	Research	Published few papers in collaboration	
2012 onwards (Dr. Dau Dayal)	Prof. Pawel Michalak, Edward Via College of Osteopathic Virgina, USA	Ongoing	Research	Published few papers in collaboration	
2023 onwards (Dr. Dau Dayal)	Dr. Vijendra Sharma, University of Windsor, Ontario, N9B 3P4, Canada	Ongoing	Research	Published few papers in collaboration	

University of Delhi South Campus
Benito Juarez Road, New Delhi - 110 021.
Accounts Branch (Projects)

UDSC

Phone: 91-11-24111788
Fax : 91-11-24117772

वित्त / अनु परि./20-21/Biochemistry/ तिथि :15/01/2021

परियोजना प्रभारी PI : Prof. Suman Kundu
परियोजना Project : **FRP IoE Scheme, DU**
विभाग Department : Biochemistry

महोदया/महोदय

Kindly refer to your proposal for constitution of MoU/MoA Committee for collaboration Agreement with Sai Phytoceuticals.

I am to convey the approval of the competent authority for constitution of committee comprising of the following members to prepare a Memorandum of Understand/Agreement (MoA/MoA).

Prof. Srinivasan, Jamia Hamdard
Prof. Zahid Ashraf, JMI
Prof. Prasanjit Guchhait, RCB
Prof. Amit Tyagi, INMAS
Prof. Sunil Khare, IIT Delhi
Prof. Y Singh, Dean Research (Life Sciences) Delhi University
Dr. Amulya Pande, NII
Dr. K. Ratnabali, Legal
Mr. A. K. Prakash, Joint Registrar, UDSC

सहायक कुलसचिव (वित्त)

Department of Biochemistry

University of Delhi South Campus
Benito Juarez Road, Dhaula Kuan, New Delhi - 110 021, India

Phone: +91-11 24112081
+91-9899007460 (Mob.)
Fax: (+91-11) 24115270
E.mail: sumankundu7@gmail.com
suman.kundu@south.du.ac.in

UDSC

Suman Kundu, *Ph.D.*
Professor & Head

RC/87-88
26/4/19
9.5.19

DD(LA)/2292
3/5/19
6/5/19

April 22, 2019

To
The Chairperson
Research Council
University of Delhi, Delhi 110007

Submitted for legal vetting.
Pami Dua
1/5/19

Deputy Dean Legal, Dr. Raman Mittal.
The attached agreement is legally in order
Prof. Raman
3/5/2019

Through: Head

Chairperson, RC.

Subject: Endorsement of Collaborative Research Agreement with Sai Phytoceuticals Pvt Ltd

Dear Prof. Pami Dua,

In the last few years we initiated research on **novel drug discovery against cardiovascular diseases like systemic hypertension, pulmonary hypertension, cardiac hypertrophy**, etc. We have **identified and designed potential small molecules** that may lead us to **novel drugs** in the near future. In our laboratory they are yielding promising results and a few of them have been screened successfully in multiple animal models appropriate for hypertension and cardiac hypertrophy. Now these molecules need to be synthesized in large quantities and screened for their toxicology and pharmacokinetic and pharmacodynamic characteristics, which involves high expenses and goes into the domain of industry. **Lately, I had applied for a grant from DBT-BIRAC-PACE for such translational research, which may give us hope for a drug made in India. DBT wanted me to have an industry collaborator, without which they cannot issue grant to me** (letter attached from DBT). In my search I came up with a company named **Sai Phytoceuticals Pvt. Ltd, New Delhi,** who is ready to collaborate and help me take the drug discovery work forward. To collaborate with this company, we need to put in place a **Collaborative Research Agreement** (CRA), for future research activities, intellectual property rights and commercialization. The CRA is proposed to be titled as: **"New Drug Candidates to Combat Hypertension and Cardiac Hypertrophy Designed against an Unconventional Target and Pathway"**

Based on CRA that we had with AIIMS in the recent past, I have drafted a document, which is similar to the one endorsed earlier by Delhi University (signed copy attached for your kind reference). The document is endorsed by Sai Phytoceuticals already. **We believe that we have promising compounds with us that can lead us to new drugs, which can go to the level of commercialization. These molecules have already been patented through Delhi University** (details in Annexure I of CRA). Hence we request a quick endorsement from authority in Delhi University so that we can proceed with our work.

Forwarded by HOD.
22/4/19

Thanking you,
With regards,

Suman Kundu 22/4/19

डा० सुमन कुन्डु / Dr. SUMAN KUNDU
प्राध्यापक / Professor
जैव रसायन विभाग
Department of Biochemistry
दिल्ली विश्व विद्यालय दक्षिण परिसर
University of Delhi South Campus
नई दिल्ली-११००२१ / New Delhi-110021

विभागाध्यक्ष / Head
जैव रसायन विभाग
Department of Biochemistry
दिल्ली विश्वविद्यालय दक्षिण परिसर
Delhi University South Campus
नई दिल्ली-११००२१
New Delhi-110021

No. BT/PR13531/MED/30/1523/2015
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

Block 2, 6-8th Floors
CGO Complex, Lodhi Road,
New Delhi- 110 003
Dated: **22/06/2017**

ORDER

Sanction of the President is hereby accorded, under Rule 18 of the Delegation of Financial Powers Rules ,1978 , for the implementation of the project entitled: "**Screening lead molecules identified by structure-based rational drug design methods against cytochrome b5 reductase 3 and dopamine beta hydroxylase in spontaneously hypertensive rat models for antihypertensive effects**" for a period of 3 Year 0 Month at a total cost of Rs. **8752800** (Rupees Eighty Seven Lakhs Fifty Two Thousand Eight Hundred Only) on the terms and conditions detailed here under:-

2 **The Project :**

2.1 Title : **"Screening lead molecules identified by structure-based rational drug design methods against cytochrome b5 reductase 3 and dopamine beta hydroxylase in spontaneously hypertensive rat models for antihypertensive effects"**

2.2 Details of the Investigators:

Project Cordinator

Dr. Suman Kundu
Professor
Department of Biochemistry
Delhi University, South Campus
Department of Biochemistry, University of Delhi South Campus
Benito Juarez Road, Delhi 110021

Principal Investigators:

Prof. Suman Kundu
Professor
Department of Biochemistry
Delhi University, South Campus
Department of Biochemistry, University of Delhi
South Campus, Benito Juarez Road, Delhi 110021

Prof. C C Kartha
Professor of eminence
Cardiovascular Disease Biology
Rajiv Gandhi Centre For Biotechnology
Division of Cardiovascular Disease Biology, Rajiv Gandhi Centre for Biotechnology, Thycaud Post, Poojappura, Thiruvananthapuram, Kerala, Trivandrum, Kerala 695014

CO-PI:

Dr. Surya Ramachandran
Program Scientists
Cardiovascular Disease Biology

Memorandum of Understanding
(MoU)
For Collaborative Research on
"Pathophysiological Investigations of Sickle Cell Disease and Interventions to Improve Associated Hemorheological Abnormalities"

BETWEEN

Learn Lead Serve

Sri Sri College of Ayurvedic Science and Research Hospital,

Sri Sri University, Sri Sri Vihar, Bidyadharpur,

Arilo, Ward No.3, Cuttack – 754006, Odisha

And

Department of Biochemistry

University of Delhi South Campus

Benito Juarez Road, New Delhi – 110021

Collaborative Research Agreement

This Collaborative Research Agreement ("Agreement") is made on this 9th Day of December, 2021 ("Effective Date")

BY and BETWEEN

Sri Sri College of Ayurvedic Science and Research Hospital,
Sri Sri University (SSCASRH, SSU),
Sri Sri Vihar, Ward No. – 3, Godi Sahi, Cuttack – 754006, Odisha, India
hereinafter referred to as **"SSU"** or the **First Party.**

AND

Department of Biochemistry
University of Delhi (DBiochem, DU),
a University established under the Delhi University Act, 1922
having its registered office at University Campus, Delhi - 110007, India
hereinafter referred to as **"DU"**
or the **Second Party.**

WHEREAS all the parts are hereinafter referred to as **"Parties"**.

AND WHEREAS the Parties have conceived a proposal to work jointly on the theme of **"Pathophysiological investigations of sickle cell disease and interventions to improve associated hemorheological abnormalities"** as per **Annexure I**.

AND WHEREAS, the Parties to this Agreement desire to establish common framework to facilitate in terms of exchange of information, material, to carry out research and to execute such other agreements as may be necessary for the Proposal.

NOW THEREFORE, in consideration of the promises and mutual covenants hereinafter contained, the Parties hereto agree as follows:

SRI SRI UNIVERSITY CUTTACK

Received: 18 December 2022 | Revised: 29 March 2023 | Accepted: 16 April 2023

DOI: 10.1002/jcb.30417

RESEARCH ARTICLE

Journal of Cellular Biochemistry WILEY

Oncogenic role of an uncharacterized cold-induced zinc finger protein 726 in breast cancer

Shreetama Bandyopadhayaya[1] | Pooja Yadav[1] | Ankit Sharma[1] | Sanjay Kumar Dey[2] | Alo Nag[3] | Rekha Maheshwari[4] | Bridget M. Ford[5] | Chandi C. Mandal[1]

[1]Department of Biochemistry, School of Life Sciences, Central University of Rajasthan, Ajmer, Rajasthan, India

[2]Dr. B. R. Ambedkar Centre for Biomedical Research (ACBR), University of Delhi, Delhi, India

[3]Department of Biochemistry, University of Delhi South Campus, New Delhi, India

[4]Department of General Surgery, JLN Medical College, Ajmer, Rajasthan, India

[5]Department of Biology, University of the Incarnate Word, San Antonio, Texas, USA

Correspondence
Chandi C. Mandal, Department of Biochemistry, School of Life Sciences, Central University of Rajasthan, NH-8, Bandar Sindri, Kishangarh 305817, Ajmer, Rajasthan, India.
Email: chandicmandal@gmail.com and ccmandal@curaj.ac.in

Funding information
Department of Biotechnology, Ministry of Science and Technology, India, Grant/Award Number: 6242 P9/RGCB/PMD/DBT/CCML/2015; DST-SERB, Grant/Award Number: DST/CRG/2021/002963; Department of Science and Technology, Ministry of Science and Technology, India, Grant/Award Number: INT/RUS/RFBR/P-256

Abstract

The unobtrusive cold environmental temperature can be linked to the development of cancer. This study, for the first time, envisaged cold stress-mediated induction of a zinc finger protein 726 (ZNF726) in breast cancer. However, the role of ZNF726 in tumorigenesis has not been defined. This study investigated the putative role of ZNF726 in breast cancer tumorigenic potency. Gene expression analysis using multifactorial cancer databases predicted overexpression of ZNF726 in various cancers, including breast cancer. Experimental observations found that malignant breast tissues and highly aggressive MDA-MB-231 cells showed an elevated ZNF726 expression as compared to benign and luminal A type (MCF-7), respectively. Furthermore, ZNF726 silencing decreased breast cancer cell proliferation, epithelial–mesenchymal transition, and invasion accompanied by the inhibition of colony-forming ability. Concordantly, ZNF726 overexpression significantly demonstrated opposite outcomes than ZNF726 knockdown. Taken together, our findings propose cold-inducible ZNF726 as a functional oncogene demonstrating its prominent role in facilitating breast tumorigenesis. An inverse correlation between environmental temperature and total serum cholesterol was observed in the previous study. Furthermore, experimental outcomes illustrate that cold stress elevated cholesterol content hinting at the involvement of the cholesterol regulatory pathway in cold-induced ZNF726 gene regulation. This observation was bolstered by a positive correlation between the expression of cholesterol-regulatory genes and ZNF726. Exogenous cholesterol treatment elevated ZNF726 transcript levels while knockdown of ZNF726 decreased the cholesterol content via down-regulating various cholesterol regulatory gene expressions (e.g., SREBF1/2, HMGCoR, LDLR). Moreover, an underlying mechanism supporting cold-driven tumorigenesis is proposed through interdependent regulation of cholesterol regulatory pathway and cold-inducible ZNF726 expression.

KEYWORDS

breast cancer, cholesterol regulatory pathway, cold stress, epithelial-to-mesenchymal transition, oncogene, zinc finger protein 726 (ZNF726)

frontiers in Genetics

ORIGINAL RESEARCH

Peroxisome Proliferator Activated Receptor Gamma Sensitizes Non-small Cell Lung Carcinoma to Gamma Irradiation Induced Apoptosis

*Simran Kaur[1,2], Alo Nag[2], Gurudutta Gangenahalli[1] and Kulbhushan Sharma[1]**

[1] Division of Stem Cell and Gene Therapy Research, Institute of Nuclear Medicine and Allied Sciences, New Delhi, India, [2] Department of Biochemistry, University of Delhi, New Delhi, India

The nuclear receptors known as peroxisome proliferator activated receptor gamma (PPARG) are lipid-activated transcription factors that have emerged as key regulators of inflammation. PPARG ligands have been shown to have an anti-proliferative effect on a variety of cancers. These ligands can induce apoptosis via TP53 (Tumor protein p53) or ERK1/2 (Extracellular signal-regulated kinases 1/2) (EPHB2) pathways. However, the exact mechanism is not known. PPAR, a type II nuclear hormone receptor deserves attention as a selective target for radiotherapy. Our study examines the potential of selective agonism of PPARG for radiation therapy in non-small cell lung carcinoma (NSCLC). We found that the overexpression of PPARG protein as well as its induction using the agonist, rosiglitazone was able to stimulate radiation-induced cell death in otherwise radio resistant NSCLC A549 cell line. This cell death was apoptotic and was found to be BAX (BCL2 associated X) mediated. The treatment also inhibited radiation-induced AKT (Protein Kinase B) phosphorylation. Interestingly, the ionising radiation (IR) induced apoptosis was found to be inversely related to TP53 levels. A relatively significant increase in the levels of radiation induced apoptosis was observed in H1299 cells (TP53 null) under PPARG overexpression condition further supporting the inverse relationship between apoptosis and TP53 levels. The combination of PPARG agonist and radiation was able to induce apoptosis at a radiation dose at which A549 and H1299 are radioresistant, thus confirming the potential of the combinatorial strategy. Taken together, PPARG agonism was found to invigorate the radiosensitising effect and hence its use in combination with radiotherapy is expected to enhance sensitivity in otherwise resistant cancer types.

Keywords: PPARG, radiosensitization, NSCLC, BAX, TP53, Hedgehog signaling

OPEN ACCESS

Edited by:
Kaushlendra Tripathi,
The University of Alabama at Birmingham, United States

Reviewed by:
Rafa Amal,
The University of Alabama at Birmingham, United States
Giulia Cantini,
University of Florence, Italy

****Correspondence:***
Kulbhushan Sharma
kulsharma@gmail.com

Specialty section:
This article was submitted to Stem Cell Research, a section of the journal Frontiers in Genetics

Received: *15 March 2019*
Accepted: *24 May 2019*
Published: *13 June 2019*

Citation:
Kaur S, Nag A, Gangenahalli G and Sharma K (2019) Peroxisome Proliferator Activated Receptor Gamma Sensitizes Non-small Cell Lung Carcinoma to Gamma Irradiation Induced Apoptosis. Front. Genet. 10:554. doi: 10.3389/fgene.2019.00554

Abbreviations: AKT, protein kinase B; BAX, BCL2 associated X, apoptosis regulator; BCL2, B-cell lymphoma 2, apoptosis regulator; C4-2, human papillomavirus-related cervical squamous cell carcinoma; CASP3, caspase 3; CDKN1A, cyclin-dependent kinase inhibitor 1A, p21; CDKN1B, cyclin-dependent kinase inhibitor 1B, p27; EPHB2, ephrin type B receptor 2, PARP, poly ADP ribose polymerase; PC3, prostate cancer cell line; PI3K, phosphoinositide 3-kinase; PI, propidium iodide; SW-48, SW human colon adenocarcinoma; TP53, tumor suppressor p53; TZD, thiazolidinediones.

UNIVERSITÉ MONTPELLIER
FACULTÉ DE MÉDECINE

CENTRE HOSPITALIER
UNIVERSITAIRE

MiVEGEC
UMR CNRS5290-
IRD224-UM

Laboratoire de Parasitologie-Mycologie
Cheffe de service : Professeure LAURENCE LACHAUD
UMR "Maladies Infectieuses et Vecteurs : Ecologie, Génétique, Evolution, Contrôle"
CNRS 5290 - IRD 224 - Université Montpellier
Directeur : Frédéric SIMARD
Directeur-Adjoint : Sylvie HURTREZ-BOUSSES & ANA RIVERO

PR. YVON STERKERS

Montpellier, June, 21st 2023

To whom it may concern

It is with great pleasure that I am writing this letter of invitation to support the application of Dr Vijay Kumar PRAJAPATI to the Scientific High Level Visiting Fellowships (SSHN) 2023- Short Research Trip to France-SRTF of the French Institute in India (IFI). We propose that Dr PRAJAPATI comes to my laboratory between 15 and 29 November 2023. Dr PRAJAPATI is a talented Indian researcher who is developing original research aimed at developing new therapeutic approaches to Leishmaniasis. Leishmaniasis is a neglected disease that is endemic in many parts of the world, particularly in the south of France and in India. My laboratory, which houses the French National Reference Centre for Leishmaniasis, also developes fundamental research axes and participates in the development of tools to decipher the biological mechanisms of *Leishmania*. In particular, we were the first to implement the CRISPR-Cas9 genome-editing technique in this parasite. I knew Dr PRAJAPATI through EMBO funding for one of his PhD students, Ketan KUAR, for a three-month stay at the end of 2022. We have set up a qRTPCR and genome editing skills transfer project entitled "Targeting apoptotic pathway to develop leishmania therapeutics". The work went very well and the experiments produced promising initial results. I obtained funding for an additional 6 months between June and December 2023 so that Ketan could return and continue his training and obtain results on his thesis project. Transferring skills from North to South is a difficult task, particularly for a PhD student. Dr PRAJAPATI's stay in my laboratory will enable him to acquire genome editing techniques (obtaining tagged lines) as proposed in the proposal which will be very useful for the project and which he will be able to use and to implement the technic on his return to India.
We therefore have a nascent but robust collaboration on a public health disease of interest to both our countries. Your support for Dr PRAJAPATI's visit is timely and important.
Yours sincerely.

Pr Yvon Sterkers
CHRU Site Antonin BALMES
Laboratoire de Parasitologie
39 Avenue Charles Flahault
34295 Montpellier cedex 5 - France
Tél : 33(0)4 67 63 00 / 27 51
Fax : 33(0)4 67 63 00 49

Pr. Yvon Sterkers
Equipe "Biologie, Génétique et Pathologie des Pathogènes Eucaryotes"
Laboratoire de Parasitologie-Mycologie
MiVEGEC UMR 224 IRD / 5290 CNRS / Université Montpellier
UFR Médecine/CHU/Université Montpellier

Adresse : Laboratoire de Parasitologie-Mycologie, C.H.R.U. de Montpellier (Site Antonin Balmès),
39 Avenue Charles Flahault, 34295 MONTPELLIER cedex 5 (France)
Tel : + (33) (0)4 67 63 27 51 (Secrétariat) ou + (33) (0)4 67 33 23 74
Fax: + (33) (0)4 67 63 00 49; e-mail : yvon.sterkers@umontpellier.fr

App No. MED/2017/70

No. BT/PR25123/NER/95/1027/2017
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY
(NER-BPMC)

Block 2, G-8th Floors
CGO Complex, Lodhi Road,
New Delhi- 110 003
Dated: 19/09/2018

ORDER

Sanction of the President is hereby accorded, under Rule 18 of the Delegation of Financial Powers Rules ,1978 , for the implementation of the project entitled: **"Drug discovery approaches for the effective control of tuberculosis – target based virtual screening and whole cell screening of medicinal plants"** for a period of 3 Year 0 Month at a total cost of Rs. **11888800** (Rupees One Crores Eighteen Lakhs Eighty Eight Thousand Eight Hundred Only) on the terms and conditions detailed here under:-

2 The Project :

2.1 Title : **"Drug discovery approaches for the effective control of tuberculosis – target based virtual screening and whole cell screening of medicinal plants"**

2.2 Details of the Investigatiors:

Project Cordinator

Dr. Anupam Das Talukdar
Assistant Professor
Department of Life Science & Bioinformatics.
Assam University
Department of Life Science & Bioinformatics,
Assam University Silchar, Silchar, Assam, 788011

Principal Investigators:

Generated through eProMIS

Dr. Anupam Das Talukdar
Assistant Professor
Department of Life Science &
Bioinformatics,
Assam University
Department of Life Science &
Bioinformatics,
Assam University Silchar,
Silchar,Assam, 788011

Dr. Garima Khare
Assistant Professor
Biochemistry
University of Delhi, South Campus
Room No. 103, Department of
Biochemistry, B.K. Bachhawat
Block, University of Delhi South
Campus, Benito Juarez Road, New
Delhi, New Delhi,Delhi, 110021

Dr. Pankaj Chetia
Assistant Professor
Life Sciences
Dibrugarh University
Dibrugarh, Assam, India,
Dibrugarh,Assam, 786004

CO-PI:

Prof. Manabendra Dutta Choudhury
Professor
Life Science and Bioinformatics
Assam University
Assam University, Silchar, , Assam, Silchar -
788011, Assam

Dr. Devid Kardong
Associate Professor
Life Sciences
Dibrugarh University
Department Of Life Sciences
Dibrugarh University
P.O. Rajabheta
Dibrugarh (Assam), Dibrugarh - 786004,
Assam

Vandali

the geneticssociety

ARTICLE

Seasonal changes in recombination characteristics in a natural population of *Drosophila melanogaster*

Dau Dayal Aggarwal[1,2,9✉], Sviatoslav Rybnikov[3,4,9✉], Shaul Sapielkin[3,4], Eugenia Rashkovetsky[3], Zeev Frenkel[3], Manvender Singh[5], Pawel Michalak[3,6,7] and Abraham B. Korol[3,4✉]

Environmental seasonality is a potent evolutionary force, capable of maintaining polymorphism, promoting phenotypic plasticity and causing bet-hedging. In *Drosophila*, environmental seasonality has been reported to affect life-history traits, tolerance to abiotic stressors and immunity. Oscillations in frequencies of alleles underlying fitness-related traits were also documented alongside SNPs across the genome. Here, we test for seasonal changes in two recombination characteristics, crossover rate and crossover interference, in a natural *D. melanogaster* population from India using morphological markers of the three major chromosomes. We show that winter flies, collected after the dry season, have significantly higher desiccation tolerance than their autumn counterparts. This difference proved to hold also for hybrids with three independent marker stocks, suggesting its genetic rather than plastic nature. Significant between-season changes are documented for crossover rate (in 9 of 13 studied intervals) and crossover interference (in four of eight studied pairs of intervals); both single and double crossovers were usually more frequent in the winter cohort. The winter flies also display weaker plasticity of both recombination characteristics to desiccation. We ascribe the observed differences to indirect selection on recombination caused by directional selection on desiccation tolerance. Our findings suggest that changes in recombination characteristics can arise even after a short period of seasonal adaptation (~8–10 generations).

Heredity (2021) 127:278–287; https://doi.org/10.1038/s41437-021-00449-2

INTRODUCTION

Environmental seasonality plays an important role as an ecological factor, and its significance as a potent evolutionary force is becoming increasingly evident. The evolutionary consequences of within-year oscillations in selection directions and intensities considerably depend on the generation time. In perennials, exposure to environmental seasonality as lifespan-long regular background may select for pleiotropy and phenotypic plasticity. In annuals, whose developmental stages are distributed throughout a year, it may additionally select for fine-tuning of life-history traits and bet-hedging (Williams et al. 2017). Yet, seasonality effects in multivoltine species, having several generations per year, can be even more complex, leading to far-reaching population-level effects, including maintenance of balanced polymorphism (Haldane and Jayakar 1963; Korol et al. 1996; Wittmann et al. 2017), complex dynamics of allele frequencies (Kirzhner et al. 1995, 1996) and evolving dominance (Otto and Bourguet 1999; Connallon and Chenoweth 2019), in addition to those mentioned above. Moreover, multivoltine species seem to be the most appropriate models for addressing the intriguing interplay between different adaptations to seasonality, including the interaction between plastic and heritable responses to periodical environmental stressors.

Fruit flies are particularly informative models in seasonality studies. The population size of various *Drosophila* species has long been known to fluctuate during a year (Goldschmidt et al. 1955; Prakash and Reddy 1979). Later studies have also shown seasonal oscillation in several important fitness-related phenotypic traits, including desiccation tolerance (McKenzie and Parsons 1974; Parkash et al. 2011; Aggarwal et al. 2013), the activity of metabolic enzymes (Knibb 1986), life-history traits, resistance to heat, cold and starvation (Behrman et al. 2015) and innate immunity (Behrman et al. 2018). In a recent extensive genome-wide analysis, Bergland et al. (2014) identified hundreds of SNPs whose frequency oscillates among seasons; the authors related them to variation in adaptive phenotypic traits, first of all cold- and starvation tolerance.

In contrast to stress tolerance and other fitness-related traits considered in the above-mentioned studies, changes in recombination have never been studied in the context of seasonal adaptation, to the best of our knowledge. Typically, recombination does not directly affect the survival of the individual. However, it does affect the diversity of its progeny and, thereby, the genetic structure of the whole population in the next generation. This suggests that variation in recombination can be adaptive (Korol

[1]Department of Zoology, Banaras Hindu University, Varanasi, India. [2]Department of Biochemistry, University of Delhi South Campus, New Delhi, India. [3]Institute of Evolution, University of Haifa, Haifa, Israel. [4]Department of Evolutionary and Environmental Biology, University of Haifa, Haifa, Israel. [5]Department of Biotechnology, UIET, MD University, Rohtak, India. [6]Edward Via College of Osteopathic Medicine, Monroe, LA, USA. [7]Center for One Health Research, Virginia-Maryland College of Veterinary Medicine, Blacksburg, VA, USA. [9]These authors contributed equally: Dau Dayal Aggarwal, Sviatoslav Rybnikov. Associate editor: Louise Johnson. ✉email: daudayal@south.du.ac.in; sviatoslav.rybnikov@gmail.com; korol@evo.haifa.ac.il

Received: 13 November 2020 Revised: 7 June 2021 Accepted: 7 June 2021
Published online: 23 June 2021

Collaborations Proof.