

**Government of India
Bhabha Atomic Research Centre
Radiation Biology & Health Sciences Division**

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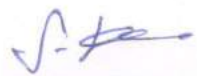
28th August 2023

Sub: Nomination of Ms. Archita Rai, DAE PhD Fellow for the "Sun Pharma Science Foundation Science Scholar Awards-2023"


It is my pleasure to nominate Ms. Archita Rai for the prestigious Sun Pharma Science Foundation Science Scholar Awards-2023. Ms. Archita is pursuing PhD in Life Sciences discipline under Homi Bhabha National Institute. She is currently in 5th year of doctoral studies under my supervision. As a part of PhD work, she has been working on identification of a novel radio-sensitizer by inhibiting Nrf-2 in human lung adenocarcinoma cells that harbour Keap-1 mutations. Radio-resistance is a major impediment in the therapy of Nrf-2 overexpressing lung cancers, which can result in relapse and recurrence. Ms. Archita has used Clobetasol Propionate, a known Nrf-2 inhibitor, to sensitize A549 human lung cancer cells to radiation induced killing. She has extensively investigated the molecular mechanism of action of Clobetasol Propionate which is approved by US-FDA for clinical use as an anti-psoriatic drug.

Her thesis work has contributed significantly in identifying a novel radio-sensitizer and contributed in the fundamental understanding of the role of Nrf-2 in ferroptosis. She is highly motivated, hardworking and a meticulous researcher. I very strongly recommend her for the Sun Pharma Science Foundation Science Scholar Awards-2023. Sun Pharma Science Foundation is an independent non-profit organisation registered under the Societies Registration Act.

Sincerely,

 28/8/2023

Dr. Santosh Kumar Sandur,
Head, Radiation Biology & Health Sciences Division
Bhabha Atomic Research Centre, Trombay
Mumbai-400085


28/8/2023

Director, Bio-Science Group may kindly approve

डॉ. टी. के. घाँटी / Dr. T. K. Ghanty

निदेशक, जैव-विज्ञान वर्ग
Director, Bio-Science Group

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Bhabha Atomic Research Centre
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29th August 2023

Justification letter

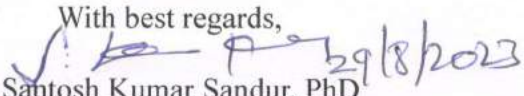
It is my great pleasure to nominate Ms. Archita Rai for the Sun Pharma Science Foundation Science Scholar Awards 2023. Ms. Archita is a PhD student of Homi Bhabha National Institute and is currently pursuing her 5th year of PhD in Life Sciences under my supervision at Radiation Biology and Health Sciences Division, Bhabha Atomic Research Centre. As I understand that the intent of the Sun Pharma Science Foundation Science Scholar Awards is to support the brilliant and upcoming new generation of scientists and researchers of India, Ms. Archita Rai's research work falls in the scope of this prestigious award.

Ms. Archita has taken up a very challenging project of sensitizing human lung cancer cells to radiation-induced cytotoxicity. Lung cancer accounts for approximately 8% of cancer-related deaths in India. Due to the socio-economic status of the patient and burden on clinical infrastructure, therapy resistance is a major roadblock. Role of Nrf-2 in management of oxidative stress has been widely studied and its central role in maintaining cellular redox homeostasis and cytoprotection has been well understood. While activators of Nrf-2 have found application in management of inflammatory and oxidative stress related disorders, the project undertaken by Ms. Archita addresses the mitigation of negative side of Nrf-2 in cancer cells. The hyperactivation of Nrf-2 in 20-25% lung cancers renders them resistant against radiotherapy, which warrants the need for clinically available Nrf-2 inhibitors. Currently, there are no bonafide radio-sensitizers available in the clinic to overcome constitutive and inducible radio-resistance in lung cancers. Ms. Archita identified a reported Nrf-2 inhibitor, Clobetasol propionate (CP) as a radio-sensitizer and carried out extensive in vitro studies to demonstrate its efficacy through multiple endpoints. She has deciphered detailed mechanism of action of CP mediated radio-sensitization. CP inhibited expression and nuclear translocation of Nrf-2 in A549 human lung cancer cells and in spheroid model. She has employed genetic manipulation to validate the causal role of Nrf-2 in CP induced radio-sensitization. CP mediated radio-sensitization was also translated in human lung xenograft tumor bearing mice. The most noteworthy highlight of her work is that CP is a FDA approved anti-psoriatic drug and hence it has promising potential for 'bench to bed' translation.

Subsequently, Ms. Archita has worked extensively to understand the mechanism of action of CP in mediating radio-sensitization. She used the information from transcriptomics to identify ferroptosis as a potential pathway for radio-sensitization. She has carried out numerous studies including morphological features, biochemical parameters and expression levels of key mediators to explore the role of ferroptosis in CP mediated radio-sensitization. She also demonstrated that iron chelator and ferroptosis inhibitor reversed CP mediated radio-sensitization. In her pursuit to understand the mechanism of ferroptosis and radio-sensitization, she meticulously established the role of mitochondrial ROS in inducing ferroptosis. Her work resulted in identification and validation of Nrf-2 inhibitor mediated radio-sensitization and contributed in understanding the intricate pathway of mitochondrial ROS mediated ferroptosis. Her project has significantly added to the knowledge about novel ferroptosis inducers as potential radio-sensitizers. A part of the work embodied in this project garnered appreciation at the 5th Asian Congress for Radiation Research (ACRR-2022) held at Mumbai, India and she won the **Best Poster Award** for the same. This part of the work is under Revision in the Journal '**Acta Pharmacologica Sinica**' (Publisher: Springer Nature) with **Impact Factor of 8.2**.

Ms. Archita has a good aptitude for acquiring new skills and she is a quick learner. Her passion for translational as well as fundamental research is commendable. Her research goals to contribute to the therapeutic challenges in cancer treatment align with the aims of Sun Pharma Science Foundation to promote research activity in India in the field of pharmaceutical sciences. Ms. Archita is talented, hardworking and sincere PhD candidate. Ms. Archita has excellent communication skills and actively advocates for science popularisation. Recognition of her research will definitely act as a boost for young minds like her to pursue research and make efforts towards addressing pertinent health issues of our country. I very strongly recommend her for the prestigious Sun Pharma Science Foundation Science Scholar Awards 2023 in the field of Pharmaceutical Sciences.

With best regards,


Santosh Kumar Sandur, PhD

Head, Radiation Biology & Health Sciences Division,
Bhabha Atomic Research Centre,
Professor, Homi Bhabha National Institute
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