

Course Title: Cancer Therapy Through Targeting Mammalian DNA Repair Pathways

Overview

The mammalian cells utilize DNA repair pathways to remove different types of DNA damages caused by physical and chemical agents and help restore the genome to its native state. Unfortunately cancer cells use the same repair pathways to survive after chemo- or radiotherapy-induced DNA damage. While bacteria and yeast have served as invaluable tools in revealing the core steps of DNA repair, we are still deciphering different repair proteins implicated in the mammalian repair pathways. Mammalian repair pathways not only require more proteins than bacteria but also use unique proteins not present in lower organisms, such as the DNA damage-responsive nuclear enzyme poly(ADP-ribose) polymerase-1 (PARP1). Recent studies have also revealed unique DNA repair deficiencies in some cancer cells. This course will deal with different DNA repair pathways in normal and cancerous cells, mechanism of actions of PARP1 in DNA damage responses including DNA repair, and the concept of synthetic lethality in therapy of BRCA mutant cancer cells by simultaneous targeting two different DNA repair pathways. This will course be given by Professor Girish Shah of Laval University (Quebec City, Canada), who has an extensive experience with various roles of PARP1 in DNA damage responses.

Course Objectives

- Comprehensive understanding of mammalian DNA repair pathways in normal cells
- Contribution of DNA repair pathways in the resistance of cancer cells to therapy
- DNA repair and other roles of PARP1 and other DNA repair proteins.
- Targeting of PARP1 in cancer therapy

Course Details: (40 hours over 10 days from 23rd October -1st November 2017)

Day 1: Monday 23 Oct 2017 (3 hours)

- **Registration of Participants:** 9:00 am – 11.00 am
- **Inauguration Ceremony:** 11:00 am – 12.00 noon
- **Introduction to the Course & interaction with Foreign Faculty:** 2:30 pm – 4.30 pm
Overview of the course, distribution of teaching materials and logistics of the course, feedback surveys.

Day 2: Tuesday 24 Oct 2017 (5 hours)

- **Lecture 1:** 10:00 am – 11.30 am
 - **DNA repair pathways-I:** Overview of DNA damages and DNA repair pathways; post-translational modifications, chromatin remodeling and other processes required for efficient DNA repair
- **Lecture 2:** 11:45 am – 1.15 pm
 - **DNA repair pathways-II: Direct Repair (DR) and Base Excision Repair (BER)**

- **Tutorial 1:** 2:30 pm – 4:30 pm
 - Sharing research experience on Cancer therapy-I

Day 3: Wednesday 25 Oct 2017 (5hours)

- **Lecture 3:** 10:00am – 11.00am
 - **DNA repair pathways-III: Mismatch Repair (MMR)**
- **Lecture 4:** 11:15 am – 1.15 pm
 - **DNA repair pathways IV: Nucleotide Excision Repair (NER)**
- **Tutorial 2:** 2.30 pm- 4:30 pm
 - Presenting a model research paper on the subject

Day 4: Thursday 26 Oct 2017 (5 hours)

- **Lecture 5:** 10:00 am – 11.30 am
 - **DNA repair pathways-V: Homologous Recombination Repair (HRR)**
- **Lecture 6:** 11:45 am – 1.15 pm
 - **DNA repair pathways-VI: Non-Homologous End-Joining (NHEJ)**
- **Tutorial 3:** 2.30 pm- 4:30 pm
 - Open Discussion on DNA repair pathways and other factors affecting DNA repair

Day 5: Friday 27 October 2017 (4 hours)

- **Exam 1:** 10:00 am - 12:00 noon: DNA repair pathways
- **Tutorial 4:** 2.30 pm- 4:30 pm
 - Exposure of participants to Cancer Research facilities at JMI

Day 6: Saturday 28 October 2017 (3 hours)

- **Lecture 7:** 10:00 am – 11.30 am
 - **PARP1 (part I): Biochemistry and Genetics of PARP1**
- **Lecture 8:** 11:45 am – 1.15 pm
 - PARP1 (part II) DNA repair roles of PARP1 after DNA damage

Day 7: Sunday 29 October 2017 (3 hours)

- **Lecture 9:** 10:00 am – 11.30 am
 - **Targeting PARP in cancer therapy: synthetic lethal approach for BRCA-mutant cancers and potentiation of chemo-/radio-therapy for other cancers**
- **Lecture 10:** 11:45 am – 1.15 pm
 - **Methodologies to study PARP1 in vitro and in vivo in relation to DNA repair**

Day 8: Monday 30 October 2017: (5hours)

- **Exam 2:** 10:00am – 12.00noon:
PARP1 in DNA damage responses and cancer therapy
- **Lecture 11:** 1:30pm –2.30pm
 - Other roles of PARP1: cell death and other processes
- **Tutorial 5:** 2.30 pm- 4:30 pm
 - Sharing research experience on Cancer therapy-II

Day 9: Tuesday 31 October 2017 (4 hours)

- **Lecture 12:** 10:00 am – 12.00 am
 - **Contribution of DNA repair pathways in resistance of cancer cells to therapy and targeting of other DNA repair related proteins in cancer therapies**
- **Tutorial 6:** 1.30 pm- 3:30 pm
 - Open discussion on the Frontiers in Cancer therapy

Day 10: Wednesday 1st November 2017

- **Results and Awards Ceremony:** 9.30am-12:30 pm
 - Certificates of participation in the course and awards for top ranked students to be given by the appropriate highest authorities of JMI

Teaching Faculty

Prof. Girish Shah is a tenured full professor at Laval University in Quebec City (Canada), and a “Senior Researcher” at the CHU de Quebec Laval University Hospital Research Centres. A major focus of his studies is to understand the mechanisms by which PARP1 participates in DNA repair, cell death and cancer in the cells exposed to genotoxic stress. He has identified two novel roles of PARP1 in DNA repair in the nucleotide excision repair pathway (PNAS, 2013; PNAS 2017), and more recently in the non-homologous end-joining repair pathway (Molecular Cell 2016). He has published two reviews in 2013 on therapeutic targeting of PARP1 in cancer. His team has published 60 peer-reviewed papers (cited 2,721 times) with an h-index of 26, 4 book chapters and 125 abstracts, indicating widespread acceptance of his team’s work by the peers. It is also reflected in him being invited to write 1st chapter for Methods in Molecular Biology on PARP (2011) and invitations to speak at prestigious International meetings, such as European Soc. Photobiol (09/2013) and Gordon Research Conference on DNA Repair (03/2014). His research has been supported by numerous competitive grants from Canadian and US funding agencies.

Prof. Shah has received numerous national and international recognition, honours and awards, such as, an honour plaque and citation for “Outstanding Achievement in Carcinoid/Neuroendocrine Tumor Research” in 2006 from the Carcinoid Cancer Foundation Inc. of USA. His has been nominated to the Board of Directors of the Carcinoid NeuroEndocrine Tumor Society of Canada and was appointed as the Chair of its Scientific and Medical Advisory Board in 2014. In 2012, he was appointed by the Italian National Agency ANVUR as a “Foreign member for the committees that grant Professorship in Italian Universities”. In 2012, he also received the Visiting Professorship award in the International Short Visit-category from the

Swiss National Science Foundation (SNSF) for conducting collaborative work with Professor GP Dotto at the University of Lausanne, Switzerland.

Who Can Attend

- Students at all levels and Faculty from reputed academic institutions.

Registration Fees

Participants from abroad : US \$500

Industry/ Research Organizations: 10,000/-

Academic Institutions

Faculty members: Rs. 5000/-

Master/PhD students: Rs. 1000/-

The above fee includes all instructional materials, computer use for tutorials, 24 hr free internet facility.

Course Coordinator

Prof. Jawaid Ahmad Khan

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