

Course Name	: Gene silencing and genome editing: principles and applications
Course Number	: BY527
Credits	: 3-0-0-3
Prerequisites	: IC136 or consent of the faculty member
Intended for	: UG (IDD Bioengg, 4 th year) / M.Sc./M.Tech./ Ph.D.
Elective or Core	: Elective

Preamble: The main objective of this course is to introduce the concepts, developments and applications of gene silencing & genome editing technologies. This course provides a comprehensive understanding of RNAi mediated gene-silencing and CRISPR-Cas9 gene-editing technologies and potential applications to genetically modify organisms for commercial, agriculture, medical purposes. The students will learn how RNAi works, how it can be utilized to modulate gene expression and perform genetic screens in various model systems. Similarly, the students will learn discovery of CRISPR-Cas9 system, its mechanism and regulatory aspects of genome editing. As a result of this course, the students will have strong foundations and first-hand scientific understanding of current trends in gene silencing and genome editing.

Learning Outcome:

By the end of this course, students will be able to understand principles and mechanisms of RNAi and CRISPR-Cas9 technologies and their potential applications in biomedical research, agriculture, and healthcare industries. They will learn to use online tools to design RNAi (siRNAs) and CRISPR (sgRNA) constructs to knockdown and edit genes of interests. They will be able to design experiments to silence gene expression in various organisms and learn the ethical implications of genetic manipulation.

Course modules:

Module 1 *Introduction to gene structure and regulation* **[6 hours]**

Basic principles of genome organizations, gene structure, chromatin structure, gene silencing by histone modifications, gene silencing by DNA methylation (epigenetics and genome imprinting). Eukaryotic gene structure, eukaryotic transcription, transcriptional gene silencing.

Module 2 *RNA biology* **[6 hours]**

Post-transcriptional gene silencing. Introduction to RNAi (brief history and endogenous roles). Discovery of siRNAs and microRNAs. Molecular mechanisms RNAi. Genetic manipulations and RNAi in *C. elegans*, *Drosophila*, mammalian systems and plants.

Module 3 *Small silencing RNAs* **[6 hours]**

Classification, biogenesis and gene-regulatory mechanisms of small RNAs. Cellular functions of small RNAs. Functions of small RNAs in developmental biology, diseases and agriculture. RNAi screens (reverse genetic screens) in cell culture and model organisms.

Module 4 *Applications of RNAi* **[3 hours]**

RNAi-induced innate immunity and antiviral siRNAs. RNA-based therapeutics, vaccines and delivery of siRNAs. Examples of candidate RNAi drugs (Givosiran, Patisiran etc)



Module 5 *Genome editing methods-1* **[6 hours]**

Transgenesis, site-specific chromosomal integration by Cre-LoxP, phiC31-integrase, and Mos1-transposon.

Module 6 *Genome editing methods-2* **[6 hours]**

Genome engineering with TALENs and ZFNs. Discovery and mechanisms of CRISPR-Cas9 mediated genome editing. Different CRISPR systems and their uses in genome editing.

Module 7 **[3 hours]**

Designing of sgRNAs and repair templates. Next generation cloning technologies. Genome engineering methods for model organism. Construction of transgenics and knockouts using *C. elegans* model organism.

Module 8 *Applications of CRISPR mediated genome editing* **[6 hours]**

Cas9 for gene regulation: CRISPR interference (CRISPRi), CRISPR activation (CRISPRa) and CRISPRon. Genome-wide CRISPR knockout screens. Applications in agriculture, food and fuel industry. Ethical concerns of genome editing by CRISPR.

Text books

1. Genome Engineering via CRISPR-Cas9 System. Edited by Vijai Singh, Pawan K. Dhar, 2020 Academic Press, ISBN 978-0-12-818140-9.
2. RNAi: A Guide to Gene Silencing. Edited by Gregory J. Hannon, 2003, Cold Spring Harbor Laboratory Press, ISBN 978-0879696412.

Reference Books

1. RNA Interference in Practice: Principles, Basics, and Methods for Gene Silencing in *C. elegans*, *Drosophila*, and Mammals. Edited by Ute Schepers, 2005, Wiley-VCH Verlag GmbH, ISBN 978-3527310203.
 2. MicroRNAs: From Basic Science to Disease Biology, Krishnarao Appasani, 2008, Cambridge University Press, ISBN 9780521865982.
 3. Regulation of Gene Expression by Small RNAs. Edited by Rajesh K. Gaur, John J. Rossi. 2009, CRC Press, ISBN 978-1138111738.
 4. Genome Editing and Engineering: From TALENs, ZFNs and CRISPRs to Molecular Surgery. Edited by Krishnarao Appasani, 2018, Cambridge University Press, ISBN 978-1-107-17037-7.
 5. CRISPR-Cas: A Laboratory Manual. Edited by Jennifer Doudna, 2016, Cold Spring Harbor Laboratory Press, ISBN 978-1-621821-31-1.
- Relevant research articles/reviews will be advised related to the topic being taught.



Similarity Content Declaration with Existing Courses:

S.No	Course code	Similarity content	Approx. % of content
1	Molecular Biotechnology (BY515)	Transcriptional Control of Gene Expression	< 10%

Justification for new course proposal if cumulative similarity content is > 30%: N.A.

Approvals:

Other Faculty who may be interested in teaching this course: *Dr. Prosenjit Mondal*

Proposed by Prasad Kasturi

School: SBS

Signature: _____

Date 30/09/2020

Recommended/Not Recommended, with Comments:

Chairman, CPC

Approved / Not Approved

Date: _____

Chairman, Senate

Date: _____

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