

Principles of Ligand-Targeted Drug Delivery: Design and Development of 'Smart Drugs'

Under the aegis of MHRD—Global Initiative of Academic Networks

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Overview

With most non-targeted investigational drugs failing in the clinical trials due to unanticipated toxicities, there is an unmet need to deliver drugs selectively to the diseased tissue. This has led to a growing interest in the field of targeted drug delivery. Along with physicians and academic researchers, many industries have fallen in line to focus research in this area. Consequently, many targeted therapies have been developed over the last two decades and made their way into the clinic.

Drug delivery operates at the interface of chemistry, biology and medicine. Beyond the conventional aspects of medicinal chemistry, this field requires extensive understanding of the fundamental differences between diseased cell and healthy cell. While there are multiple approaches currently exist for making this distinction, one of the most promising strategy is to recognize the difference in the expression levels of certain cell surface receptors on diseased cell vs healthy cell. Exploiting this difference to discriminate a pathologic tissue from its healthy counterpart is an efficient strategy for drug delivery. In this class, high affinity ligands targeting these upregulated cell surface receptors were exploited to carry otherwise non-targeted drugs. Thus, hundreds of antibody-based and small-molecule-based ligand-drug conjugates are being investigated and several of them are already approved for cancer applications.

Recently, numerous pharmaceutical industries have realized this potential of ligand-targeted drug delivery and started looking for new avenues for collaboration. Because there is a growing academic interest in pharmaceutical research, these industries have turned to academia for novel ideas for drug delivery. While training in medicinal chemistry has become prevalent in academia worldwide, there is a dearth of similar trainings or courses in drug delivery. With growing number of academic institutions willing to collaborate on industrial projects, it is an appropriate time to expose students and faculty to this developing field. To keep up with these advances in medicinal chemistry, it is prudent to provide drug delivery courses, training and research facilities to groom the next generation researchers with required tools to perform research and develop 'smart' drugs.

Accordingly, this ligand-targeted drug delivery course is designed to provide students a 10,000-foot view of drug delivery in general, and ligand-targeted drug delivery in specific. Targeted to reach students and faculty with a basic understanding of organic chemistry and biochemistry, the course will overview theoretical principles and practical aspects of ligand-targeted drug delivery. The main objective of this course is to shed light on how to translate basic research in this field to the clinic.

Schedule of the Course

Schedule of the course	: May 5-16, 2020
Total Number of days/lectures	: 10-days/20-lectures and 10 tutorials

Registration Fee

Participant from outside India	: USD 300
Industry/ Business organization	: Rs. 5,000
Scientists/Academic Institutions	: Rs. 4,000
Students/College teachers	: Rs. 3,000

The fee includes all instructional materials, computer use for tutorials, internet facility and GST. The participants will be provided with accommodation at IIT Indore hostel on payment basis.

Topics Covered

Smart Drugs: Introduction to ligand-targeted drug delivery: why targeting? Pros and Cons of targeting, Design of ligand-targeted drug system: general aspects, The so called 'Magic Bullet', Selection of targeted cell- cell types and phenotypes of disease, Identification of targeted receptor-expression profiles, Selection of targeting ligand-the effect of size on drug properties, Selection of targeting ligand- Small molecule vs antibody, Selection of targeting ligand-affinity and selectivity, Identification of optimal drug: mechanism of action and potency, Design of linker-a critical factor to control pharmacokinetics (PK), Targeted receptors in cancer, Targeted drugs in cancer, Translation of targeted therap Targeting inflammatory diseases from bench-to-the clinic, Potential pitfalls of targeted therapy, Targeting tumor microenvironment, Ligand-targeted imaging agents-role of peptides & small molecules, Ligand-targeted imaging agents-role of imaging agents, Fluorescence-guided surgery, Conclusion.

Faculty Information



Teaching Faculty

The course will be delivered by Dr. Madduri Srinivasarao, Scientist, at Purdue University, West Lafayette, USA. Dr. Madduri Srinivasarao is a scientist and researcher at Purdue University, Indiana, USA. After receiving PhD (2010) in organic chemistry from Purdue University, he started his postdoctoral research in drug delivery in the same institution, with Professor Philip S Low (2011-2013). After a brief industrial stint in India, he moved back to academic research and continued ever since to work on targeted drug delivery (2015-to date). He is also a teaching faculty at the Ivy Tech Community College, Indiana, USA.

In the laboratory of Dr. Low, as lab manager, Dr. Srinivasarao is actively pursuing translational research in development of targeted therapeutic and imaging agents for cancer and other inflammatory diseases. A major focus of his research is aimed at the design and development of novel drug delivery strategies with small molecule targeting ligands that target overexpressed cell surface receptors on cancer and other diseased tissues. He is also developing targeted chimeric antigen

receptor (CAR) T-cell therapies for brain cancers with small molecule adaptor molecules.

He has published several peer-reviewed articles in the field of organic chemistry and medicinal chemistry. Some of his papers were published in prominent journals such as *Nature Reviews Drug Discovery*, *Chemical Reviews*, *Nature Communications*, *Journal of Organic Chemistry*, *Chemical Communication*, *Bioconjugate Chemistry*, etc. He has filed several US patents on his novel drug delivery research.

Dr. Srinivasarao has taught several undergraduate and graduate level courses in general and organic chemistry at Wayne State University and Purdue University. Currently, as a faculty at Ivy Tech, he is also teaching chemistry courses to both pre-med and pre-dental undergraduate students.



Coordinating Faculty

Dr. Venkatesh Chelvam, an Organic Chemist and Chemical Biologist is an Associate Professor in the Discipline of Chemistry and Biosciences and Biomedical Engineering at IIT Indore. His long-term goal is to establish a centre of excellence in the field of biosciences especially for detection and treatment of cancer and inflammatory diseases at IIT Indore. He has more than 10 years of experience in imaging and microscopic techniques for diagnosis and therapy of diseased condition from Purdue University, USA. He was also a postdoctoral fellow in the laboratory of Prof. Hans-Ulrich Reissig at Freie University Berlin, Germany in 2006-2008, where he was awarded Alexander von Humboldt fellowship and worked on total synthesis of natural products for cancer. He has published more than 42 peer reviewed journal papers in highly reputed international journals along with 4-USA and 5-Indian patents and some of his outstanding discoveries were published in prominent journals such as *Current Protocols in Chemical Biology*, *Nanomedicine*, *Journal of Nuclear Medicine*, *Journal of Cell Sciences*, *Journal of Medicinal Chemistry*, *Molecular Pharmaceutics*, *Bioconjugate Chemistry*, *Journal of Organic Chemistry*, *European J. Organic Chemistry*, *Organic Letters*, etc. His revolutionary work on diagnosis and therapeutic applications of cancer and inflammatory diseases are US patented, and currently in clinical trials. Moreover, he had appeared in ABC news for developing technology for intra-operative guided surgery of ovarian cancer in patients.

Who should attend this course?

1. Chemists from Pharmaceutical Industry
2. Researchers from Industry and government organizations including R&D laboratories.
3. Students at all levels (BTech/MSc/MTech/PhD) or Faculty from reputed academic institutions and technical institutions.

Course Coordinator

For any further information and registration, please contact:

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Relevant Readings for the proposed course:

- ✓ Srinivasarao, M.; Low, P. S. Ligand-targeted drug delivery, *Chemical Reviews* **2017**, 19, pp12133.
- ✓ Srinivasarao, M.; Galliford, C. Low, P. S. Principles in the design of ligand-targeted cancer therapeutics and imaging agents. *Nature Reviews Drug Discovery* **2015**. 14, pp203.