CBMS842

Advanced Medicinal Chemistry

S2 Day 2017

Dept of Chemistry & Biomolecular Sciences

Contents

General Information

Unit convenor and teaching staff
Lecturer
Joanne Jamie
joanne.jamie@mq.edu.au

Lecturer in charge
Peter Karuso
peter.karuso@mq.edu.au
Contact via 9850 8290
F7B232
Monday 6-9PM

Lecturer, Tutor and Adminitrator
Andre Hallen
andre.hallen@mq.edu.au
Contact via 04359 28260
F7B214
Monday 6-9PM, contact via e-mail

Credit points
4

Prerequisites
(Admission to MBiotech or MBioBus or MLabQAMgt or MRadiopharmSc or MSc) and
permission by special approval

Corequisites

Co-badged status

Unit description
This unit builds on the fundamentals of medicinal chemistry, including the discovery, design
and development of new medicines. The aim of the unit is to integrate chemical biology and
organic chemistry to reveal how these are used in medicinal chemistry to design and
synthesise new drugs and to understand their mode of action. The unique aspect of this unit is
the focus on computational chemistry in the field of drug design and development. This
includes aspects of molecular modelling, molecular dynamics, docking, pharmacophore
modelling and QSAR as they relate to the understanding of drug action and design of new
drugs.

Important Academic Dates

Information about important academic dates including deadlines for withdrawing from units are available at https://www.mq.edu.au/study/calendar-of-dates

Learning Outcomes

On successful completion of this unit, you will be able to:

Apply the principles of rational drug design for the creation of drug libraries

Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)

Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

General Assessment Information

On line quizzes are multiple choice questions on the previous 2 weeks work.

The report and presentation is a major work that you will start preparing in week 5 and complete in week 13. It involves a written report and a powerpoint presentation (15 minutes)

The final exam is a 3 hr written exam

Your marks (in-class and online quizzes, report and presentation) will be placed on the CBMS842 web site.

Your final grade will be based on the mark from the aggregation of the individual assessments, **with 50% or greater needed overall for a pass.**

Medical certificates or official documents must be lodged as part of a disruption to studies request at ask.mq.edu.au as soon as possible if you are absent for any of the assessment tasks or miss the due date for any of the on-line tasks. If your reason is regarded as valid for missing the in-class quizzes, you will be given an average of the other quizzes done; with the on-line quizzes an extension of time will be provided if the disruption to studies request is approved. If you miss the mid-session test or final exam for a valid reason, a supplementary test/exam will be provided. An extension for submission of the lab reports/lab books will also be provided if the disruption to studies approval is obtained. Any assessment tasks not submitted on time that does not get approval through the disruption to studies request will get a 10% deduction of marks for every weekday late.

Final Examination Details: The examination timetable will be available in Draft form approximately eight weeks before the commencement of the examinations and in final form approximately four weeks before the commencement of the examinations. You are expected to present yourself for examination at the time and place designated by the University in the Examination Timetable. This could be any day after the final week of semester and up until the

final day of the official examination period. It is Macquarie University policy to **not set early examinations** for individuals or groups of students. All students are expected to ensure that they are available until the end of the teaching semester, that is, the final day of the official examination period.

The only exception to sitting an examination at the designated time is because of documented illness or unavoidable disruption. Absence from the final exam will result in a grade of F except in the case of a genuine medical emergency or misadventure as defined by the University (see below). In these circumstances you should apply for a supplementary exam at ask.mq.edu.au.

NOTE: If you apply for a supplementary examination, you must make yourself available for the week of **December 11 – 15, 2017**. If you are not available at that time, there is no guarantee an additional examination time will be offered. Specific examination dates and times will be determined at a later date.

Assessment Tasks

Name	Weighting	Hurdle	Due
Five on-line assessments	25%	No	Weeks 3, 5, 7, 9, 11
Final Exam	50%	No	Week 15
research presentation	25%	No	Week 13

Five on-line assessments

Due: **Weeks 3, 5, 7, 9, 11**
Weighting: **25%**

5 on-line quizzes, worth 5% each

On successful completion you will be able to:
- Apply the principles of rational drug design for the creation of drug libraries
- Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)
- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

Final Exam

Due: **Week 15**
Weighting: **50%**

this is a 3 hr final exam

On successful completion you will be able to:

- Apply the principles of rational drug design for the creation of drug libraries
- Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)
- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

research presentation

Due: **Week 13**

Weighting: **25%**

Using what you have learn, pick a drug target, research what is known about this target and summarize the relevant literature and design your own library of compounds to test. Present this review and design task to the rest of the class in week 13 and hand in a written report.

On successful completion you will be able to:

- Apply the principles of rational drug design for the creation of drug libraries
- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

Delivery and Resources

This is a self taught unit using the "molecular conceptor" software. Each week a set number of tasks are assigned and assessed. There is no text book set for this unit but the material in the CBMS306 text book (Patrick, "Medicinal Chemistry", 5th Ed) is assumed knowledge.

Unit Schedule

Week 1 introduction

A1. INTRODUCTION TO DRUG DISCOVERY

A2. PRINCIPLES OF RATIONAL DRUG DESIGN

A2.3 Receptor-Based Design

A2.4 Integration in a Global Perspective

A2.5 Challenge of the Genomics Era

A2.6 Typical Projects

Week 2 Molecular basis of drugs

J1. MOLECULAR GEOMETRY

J4. MOLECULAR ENERGIES

J6.3 Visualization

J6.4 Editing & Manipulation

J6.5 Surfaces & Volumes

J6.6 Visualizing Interactions

Week 3 Library design

C1 Introduction

C2 Basis of a good scaffold

C3 Scaffold selection and design

C4 Focussed and diverse strategies

C5 measuring distances

C8 Increasing quality of the library

C9 Example of library analysis

C3. CASE STUDIES IN LIBRARY DESIGN

C3.2.1 Case Study-Diaminopyrimidines DHFR inhibitors

C3.1 Case Study-1 : CDK2 Inhibitors

Week 4 Protein structure function & MD

E1. STRUCTURAL BIOINFORMATICS

E2. PROTEIN STRUCTURE

E3. MOLECULAR DYNAMICS

Week 5 SAR

A3.1 Introduction   A3.2 Probing H-Bond Interactions

A3.3 Probing Ionic Interactions

A3.4 Probing Hydrophobic Interactions

A3.5 Probing Other Interactions

A3.6 Modifications to Alter the Geometry of the Ligand

A3.7 Complexity of SAR Analyses

A3.8 Example of Good Exploitation of SAR Complexity

Week 6 SAR case studies

A1.1 Case Study-1 : Banyu Example

A1.2 Case Study-2 : Dioxobenzothiazole Example

A1.3 Case Study-3 : EGF-R Kinase Inhibitors

A1.4 Case Study-4 : Nifedipine Example

A1.5 Case Study-5 : Carbonic Anhydrase Example

A1.6 Case Study-6 : β-Lactam Antibiotics

A1.7 Case Study-7 : Anilino-Quinazoline Example

B3.8 Case Study-8 : Salicylamide Mimics

Week 7 Structure based design

E1. INTRODUCTION TO PROTEIN-LIGAND BINDING

E1.2 Analytical Process

E1.3 Principles of Analysis

E1.4 Example of Tight Interactions

E1.5 Receptor & Ligand Flexibility

E1.6 Role of the Solvent

E1.7 Prediction of Binding Modes

E1.8 Methods for Analyzing Binding

2. PRINCIPLES OF STRUCTURE-BASED DESIGN

E2.1 Introduction

E2.3 The Four Design Methods

E2.4 Analog Design

E2.5 Database Searching

E2.7 Manual Design

E2.8 Another Iteration

E2.9 A Success Story

E2.10 Conclusion

Week 8 Molecular docking

Week 9 case studies - structure based design & molecular docking

Week 10 Ligand based design

Week 11 case studies - Ligand based design

Week 12 QSAR and case studies

Policies and Procedures

Macquarie University policies and procedures are accessible from Policy Central. Students should be aware of the following policies in particular with regard to Learning and Teaching:

Academic Honesty Policy http://mq.edu.au/policy/docs/academic_honesty/policy.html

Assessment Policy http://mq.edu.au/policy/docs/assessment/policy_2016.html

Grade Appeal Policy http://mq.edu.au/policy/docs/gradeappeal/policy.html

Complaint Management Procedure for Students and Members of the Public http://www.mq.edu.au/policy/docs/complaint_management/procedure.html

Disruption to Studies Policy (in effect until Dec 4th, 2017): http://www.mq.edu.au/policy/docs/disruption_studies/policy.html

Special Consideration Policy (in effect from Dec 4th, 2017): https://staff.mq.edu.au/work/strategy-planning-and-governance/university-policies-and-procedures/policies/special-consideration

In addition, a number of other policies can be found in the Learning and Teaching Category of Policy Central.

Student Code of Conduct

Macquarie University students have a responsibility to be familiar with the Student Code of Conduct: https://students.mq.edu.au/support/student_conduct/

Results

Results shown in *iLearn*, or released directly by your Unit Convenor, are not confirmed as they are subject to final approval by the University. Once approved, final results will be sent to your student email address and will be made available in eStudent. For more information visit ask.mq.edu.au.

Student Support

Macquarie University provides a range of support services for students. For details, visit http://students.mq.edu.au/support/

Learning Skills

Learning Skills (mq.edu.au/learningskills) provides academic writing resources and study strategies to improve your marks and take control of your study.

- Workshops
- StudyWise
- Academic Integrity Module for Students
- Ask a Learning Adviser

Student Services and Support

Students with a disability are encouraged to contact the Disability Service who can provide appropriate help with any issues that arise during their studies.

Student Enquiries

For all student enquiries, visit Student Connect at ask.mq.edu.au

IT Help

For help with University computer systems and technology, visit http://www.mq.edu.au/about_us/offices_and_units/information_technology/help/.

When using the University's IT, you must adhere to the Acceptable Use of IT Resources Policy. The policy applies to all who connect to the MQ network including students.

Graduate Capabilities

PG - Capable of Professional and Personal Judgment and Initiative

Our postgraduates will demonstrate a high standard of discernment and common sense in their professional and personal judgment. They will have the ability to make informed choices and decisions that reflect both the nature of their professional work and their personal perspectives.

This graduate capability is supported by:

Learning outcome

- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

Assessment task

- Five on-line assessments

PG - Discipline Knowledge and Skills

Our postgraduates will be able to demonstrate a significantly enhanced depth and breadth of knowledge, scholarly understanding, and specific subject content knowledge in their chosen fields.

This graduate capability is supported by:

Learning outcomes

- Apply the principles of rational drug design for the creation of drug libraries
- Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)

Assessment tasks

- Five on-line assessments
- Final Exam

PG - Critical, Analytical and Integrative Thinking

Our postgraduates will be capable of utilising and reflecting on prior knowledge and experience, of applying higher level critical thinking skills, and of integrating and synthesising learning and

knowledge from a range of sources and environments. A characteristic of this form of thinking is the generation of new, professionally oriented knowledge through personal or group-based critique of practice and theory.

This graduate capability is supported by:

Learning outcomes

- Apply the principles of rational drug design for the creation of drug libraries
- Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)

Assessment tasks

- Five on-line assessments
- Final Exam

PG - Research and Problem Solving Capability

Our postgraduates will be capable of systematic enquiry; able to use research skills to create new knowledge that can be applied to real world issues, or contribute to a field of study or practice to enhance society. They will be capable of creative questioning, problem finding and problem solving.

This graduate capability is supported by:

Learning outcomes

- Apply the principles of rational drug design for the creation of drug libraries
- Exploit structure activity relationships (SAR) and quantitative structure activity relationships (QSAR) principles to understand drug modes of action (MoA)

Assessment task

- research presentation

PG - Effective Communication

Our postgraduates will be able to communicate effectively and convey their views to different social, cultural, and professional audiences. They will be able to use a variety of technologically supported media to communicate with empathy using a range of written, spoken or visual formats.

This graduate capability is supported by:

Learning outcome

- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

Assessment tasks

- Final Exam
- research presentation

PG - Engaged and Responsible, Active and Ethical Citizens

Our postgraduates will be ethically aware and capable of confident transformative action in relation to their professional responsibilities and the wider community. They will have a sense of connectedness with others and country and have a sense of mutual obligation. They will be able to appreciate the impact of their professional roles for social justice and inclusion related to national and global issues

This graduate capability is supported by:

Learning outcome

- Design the structure of small molecules by combining the principles of drug design to create potential new drugs (NCE)

Assessment task

- research presentation

Changes from Previous Offering

This is a completely new version of CBMS842, run for the first time this year. It has no overlap with any previous offering of CBMS842 and requires CBMS306 (or equivalent) as a prerequisite.