Medicinal Chemistry (Yr2) Ancillary Arrangements 0809

This ancillary is compulsory for F124 and F125 students. The first-year medicinal biology ancillary course is a prerequisite.

Course organiser: Prof Robin Leatherbarrow (RJL) (r.leatherbarrow@imperial.ac.uk)

Other lecturers: Prof Alan Spivey (ACS) (a.c.spivey@imperial.ac.uk), Prof Andrew Miller (ADM) (a.miller@imperial.ac.uk), Prof Tony Gee (TG) (a.gee@imperial.ac.uk), various Lecturers from Pfizer, Sandwich co-ordinated by Dr Lyn Jones (Pfizer) (Lyn.Jones@pfizer.com).

Autumn term:

1. ***ACS - 8 lectures:*** *Biosynthesis – inspiration for drug discovery*: Review of primary metabolism and enzyme co-factor chemistry examining the formation of the major classes of secondary metabolites: shikimate derivatives, alkaloids, fatty acids, polyketides and isoprenoids. Chemical mechanisms of some of important transformations and illustrations of how intervention to block strategic transformations provides a rational basis for both drug and agrochemical discovery.
2. ***RJL – 8 lectures:*** *Enzymes:* Why Study Enzymes?: General Properties of Enzyme-Catalysed Reactions, Comparison Between Enzyme-Catalysed and Solution Reactions. Kinetics of Enzyme Catalysed Reactions: Allosteric Kinetics, Enzyme Inhibition, Irreversible Inhibitors, IC50 Measurements, Tight-binding Inhibitors, Slow-binding Inhibitors. General Features of Enzyme Catalysis: pH Dependence, Temperature Dependence, Unfolding. Use of Binding Energy in Catalysis: Binding Between Enzyme and Reactants, Utilization of Binding Energy, Transition-state Analogues. Enzyme Mechanisms: Lysozyme, Ribonuclease, Protein Engineering, Mechanism of Subtilisin, Catalytic Antibodies

Spring term:

3. ***ADM – 8 lectures:*** *Drug interactions in biology*: a) Drug discovery, Classical Drug Discovery, Sources, Druglikeness, Lipinski's rules, Pharmacophores, Drug Discovery in the post-genome era, New Sources, CAD-QSAR, HTS, Combichem, Chemical Genetics, Drug design. Interdisciplinary Approaches to Drug Design. Drug Development, Administration-distribution, Metabolism–excretion, Pharmacokinetics. Discovery and development of Biopharmaceuticals, Proteins peptides, Genetic drugs; pDNA, siRNA, mRNA, miRNA artificial chromosomes, aptamers.
4. ***Pfizer*** – ***8 lectures:*** *Modern case studies in drug discovery:* 1. History of Drugs (Don Middleton): Set the scene – what's to come in the 8 lectures, What is medicinal chemistry and what are we trying to do, History – where did it all start, Nobel Prize winners and other key figures e.g. Paul Janssen (a famous Belgian!), Illustrate the story with plenty of examples, particularly from the outset. Classics in drug design (Corey book for inspiration). 2. Molecular Interactions (Alan Stobie): Basic concepts. Binding thermodynamics. Hydrophobic effect, Van der Waals. H-bonding. Dipole. Pi-pi. Cation-pi. Halogen bonding. 3. The Drug Discovery Process (David Fox): From idea to launch. Follow the path of a Sandwich drug (Maraviroc?), The central importance of chemistry. The role of medicinal chemistry and design, Include high throughput screening and parallel chemistry, Put key scientific themes (from other courses in chemistry) into context. 4. Molecular Interactions (David Pryde): Conformation. Chirality. Atropisomers. Exploiting bound water. 5. Physicochemistry in Drug Design (Karl Gibson): Acid/base/neutral, LogP, Stability, solubility and solid form. 6. ADME (Mark Bunnage): What happens to a drug in the body. Include brief discussion of drug delivery, Sildenafil and TAFi as examples. 7. Drug Safety (Graham Maw): Link between structure and toxicity. Structural alerts. 8. Thermodynamics and kinetics (Lyn Jones): Biophysical techniques to measure these, Use in drug discovery: thermodynamic signatures; tiotropium, Incorporate key themes in the previous lectures, Summary.
5. ***TG*** – ***2 lectures/visit to cyclotron:*** *Imaging in Medicine:* PET, MRI, CT (+ site visit to Hammersmith): *not examined*

Summer term:

EXAM: 2.5 h (4Qs, 35 min each). *NB.* 4 lectures = 0.5 of a question