341P A COMPUTER-BASED INTERACTIVE TUTORIAL TO INTRODUCE THE PRINCIPALS OF THE DRUG DISCOVERY PROCESS

D. G. Dewhurst, S. Oswald[1], M.H. Todd[1] & A. D. Williams, School of Applied Sciences, Faculty of Health & Social Care, Leeds Metropolitan University, Calverley Street, Leeds LS1 3HE and [1]Zeneca Pharmaceuticals, Alderley Park, Macclesfield SK10 4TF, UK.

Computer-based learning (CBL) programs are now widely used to enhance and support traditional forms of student learning. Until recently pharmacology has not been prominent in the high school curriculum but some exam boards are now introducing modules containing pharmacology at advanced level. Here we demonstrate an interactive CBL package designed to introduce students to the principles of the drug discovery process. It is suitable for high school students and may also be useful for first year undergraduates from a range of biological science, medical and health-related courses.

The program was developed using Multimedia Toolbook® (Asymetrix) to run on IBM PC compatibles (minimum delivery platform: 486 PC running Windows™ version 3.1 or better (Microsoft), a 256 colour VGA monitor and a mouse).

The main menu has seven options, which may be accessed in any order: *The Pharmaceutical Industry - setting the scene*, an introduction to the industry, some histrorical aspects of drug discovery, different functions of medicines: *Selecting a Disease Area*, describes the sort of issues which the industry will consider in deciding what sort of drug they wish to develop; *Selecting the target*, introduces potential drug targets (enzymes, receptors and ion channnels) and uses examples of common diseases to illustrate how different drugs act; *Initial Screening*, describes techniques (high throughput screening) and principles of using an assay to test large libraries of potential compounds; *The Screening Cascade*, covers the methods (enzyme assay, cell assay, mode of action test, selectivity test and optimization) used to identify a small number of potential compounds with which to proceed into development; *Safety Testing and Clinical Trials*, describes methods of toxicity testing, and phase I, II and III of clinical trials; *Self-assessment Section*, contains a number of largely multiple-choice questions covering each of the sections.

High quality colour graphics are used extensively throughout the program and features such as animation and a hotword facility are used to enhance student learning. The program is highly interactive and uses several features to promote this. For example the main sections all have associated student tasks/self-assessment questions e.g. true/false questions with feedback, drag-and-drop exercises, data interpretation exercises, calculations, case histories, group activities. These are designed to consolidate knowledge and to allow students to self-assess their understanding of the section they have completed. They are also used to present additional information and explanations through the feedback. Glossary (definitions of terms) and hotword/hypertext links (fuller explanations of terms and concepts) are used throughout.

The learning package is intended to be used either to support existing teaching of modules containing pharmacology or for independent study. Brief trials with high school students have indicated that it would occupy students for one to two hours of study and that it works best when students study in pairs.

342P THE ZENECA TEACHING DAY: TEACHING ABOUT DRUG DISCOVERY AND SUPPORTING THE PRACTICE OF GENERIC SKILLS

I.E. Hughes[1], M. Todd, J. Major & C. Wilson, [1]Dept. of Pharmacology, University of Leeds, Leeds LS2 9JT & Zeneca Pharmaceuticals, Alderley Park, Macclesfield SK10 4TG.

The Zeneca Teaching Day is a teaching resource which consists of video taped material (UK or US formats), slides (Powerpoint), text material (Word6) and hardcopy which was prepared with the support of Zeneca Pharmaceuticals and of the Department for Education and Employment's Discipline Network scheme. The resource pack is designed to facilitate teaching about drug discovery and development in a way which lets students practice and develop their communication, group working, data interpretation and problem-solving skills. The material is designed to be presented over a 1 or 2 day teaching session and is suitable for 2nd or 3rd year students.
The objectives are: to gain an appreciation of the time scales and activities involved in the process of discovering, testing, obtaining approval for, and marketing, a new prescription medicine; to understand the mix of factors that need to be brought into the decision as to in which disease area a pharmaceutical business might invest research resources; to use a rating system to select a disease area in which to develop a drug; to understand the technical issues behind a potential research programme; to appreciate the role of rational drug design and high throughput screening as tools for drug discovery; to practice working as a group, decision making in a group and data interpretation within the context of a complex, inter-related and multifactorial information base and to practice and develop communication skills as well as to enjoy the teaching session. There is a comprehensive tutors guide which sets out one way the material can be use by pharmacology teachers without special knowledge or expertise in this area to enable students to achieve the objectives given above. However, it is anticipated that tutors may wish to adapt the material to their own interests and to fit local constraints.
The material is divided into a number of sections covering: Introduction and objectives; Overview of the drug development process; Drug discovery - WHY discover WHAT drugs and HOW to do it; Use of criteria and a rating system to select a disease area; Pharmacological approach to a target - the endothelin story; High throughput screening - how it's done by the best in the world; Selecting between the candidate compounds.
The material could be extended to incorporate toxicological information or information on clinical trials. For example, it could be used in conjunction with the pharma-CAL-ogy CAL package "Clinical Trials and Drug Development".
To run the session as designed you will need: facilities to display material provided in the form of PowerPoint files; an OHP; several (1-10) groups of students 6-10 per group; space where the groups can work and talk independently as well as an area where material can be presented to all the students at the same time; a fair amount of stamina to last the day. The teaching package has been evaluated by students and is highly rated. It is available for purchase through the pharma-CAL-ogy consortium and can be modified to suit local preferences as required.

343P INTRODUCTION TO PHARMACOGENESIS: TEACHING THE PRINCIPLES OF INTERACTION OF MEDICINES WITH MOLECULES, ORGANS AND THE HUMAN BODY WITH THE HELP OF CD-ROM TECHNOLOGY

[1]A.Sj. Koster, [2]N.J. de Mol, [3]G. Storm, [1]D. van Heuven-Nolsen, [1]F.P. Nijkamp, [4]G. van den Brink and [3]J. Perquin, Departments of [1]Pharmacology, [2]Medicinal Chemistry, [3]Biopharmacy and [4]Pharmacotherapy, Faculty of Pharmacy, Utrecht University, P.O. Box 80.082, 3508 TB Utrecht, the Netherlands.

In our Faculty, the principles of interaction between drugs and biomolecules (enzymes, receptors, plasma proteins), organs (elimination, pharmacodynamics) and the animal body (pharmacokinetics, pharmacotherapy) are treated in an integrative course at the end of the first year. New educational insights, in combination with a large number of students (over 200 every year), made it necessary to redesign this course in such a way that interactive and self-directed, self-paced individual learning is stimulated. Large-scale lectures will be replaced by 5 small-scale meetings between teacher and students. The students have to prepare themselves for these meetings using written assingments, which can be worked out with the help of a specially designed multimedia programme: "Introduction to Pharmacogenesis".

The programme consists of 10 modules (physicochemical properties, protein binding, biopharmacy, absorption, distribution, elimination, receptor action, aspecific action, pharmacokinetics, pharmacotherapy), each consisting of screens (in total 130). Measurable qualities and experimental findings are described under FACTS, theoretical aspects and models under CONCEPTS. The concepts will help to integrate a large number of facts into a unified way of thinking. A self-test is included in each module. In every session these test questions are presented in other random sequences. In addition, an entrance- and final-test of the programme is supplied. All screens can be viewed in audio-mode (visuals explained by spoken word) or text-mode. By multisensorial stimulation (eyes and ears) the impact of the message is enhanced. All screens are directly linked to screens with related subjects. This makes it possible to wander through the programme and to discover unsuspected relations between subjects. Intuitive learning is facilitated in this way. A total of 10 simulations, related to drug transport, metabolism, excretion, concentration in plasma, dose response curves, and therapeutic plasma levels, are included. More than 450 keywords can be searched alphabetically or by direct links from the screens in text-mode. Pharmacochemical, pharmacological, pharmacokinetic and therapeutic data of ca. 20 medicines are included in a compendium.

The newly designed course has been tested with a relatively small number of 1st-year pharmacy students (50). Our first experience is that students can indeed be stimulated to individual self-directed learning. However, carefully written assignments and small-scale meetings between students and teachers are essential to guide all students succesfully through the course. Although the CD-ROM programme is specifically designed for the 1st-year curriculum, several aspects will make it a useful addition to teaching programmes in other disciplines.

"Introduction to Pharmacogenesis" was produced in collaboration between the Faculty of Pharmacy, Utrecht University and OMI Multimedia/NOB Interactive. The CD-ROM will run on a 486 DXII PC, 66 MHz processor, 4 MB internal memory, 2-speed CD-ROM player, SVGA video card (1 MB, 640x480, 256 colours). Windows 3.x or Windows95 and Quicktime for Windows (version 2.02 or higher) are required. A Pentium 133 MHz PC with 6-speed CD-ROM player is recommended.

344P GENOMICS AND PHARMACOLOGY

J Craig Venter, The Institute for Genomic Research, Rockville, Maryland, USA

The Institute for Genomic Research (TIGR) is a nonprofit research institute with interests in structural, functional, and comparative analysis of genomes and gene products. Researchers at TIGR developed Expressed Sequence Tag (EST) sequencing and were first to apply high-throughput, automated techniques to the collection of EST data. TIGR has contributed more than 170,000 sequences, from 300 cDNA libraries constructed from 37 distinct tissues, to the public EST collection. To identify the unique transcripts within the nearly 700,000 ESTs generated world-wide, we assembled them as elements of shotgun sequence assembly project, producing nearly 65,000 distinct tentative human consensus (THC) sequences, a first approximation of human genomic coding potential.

TIGR was first to sequence and publish a complete microbial genome. The *Haemophilus influenzae* genome (1.83 Mb) contains 1741 predicted coding regions; nearly 60% can be assigned a putative biological role based on matches to proteins from other species. We have since sequenced five additional genomes. *Mycoplasma genitalium* with 470 genes, has the smallest genome of any free-living organism. *Methanococcus janaschii*, a deep-sea, hyperbaric, thermophilic methanogen is the first sequenced *Archaea*. *Helicobacter pylori* is the causative agent of gastric ulcers and a contributes to development of stomach cancer. *Archaeoglobus fulgidus* is the first sulfate-reducing organism and second *Archaea* sequenced. *Borrelia burgdorferi*, which causes Lyme disease, is the first spirochete sequenced and may provide insight into the eukaryotic evolution.

TIGR is also involved in eukaryotic sequencing. *Plasmodium falciparum* is the most deadly of the four *Plasmodium* species known to cause malaria. TIGR is sequencing chromosomes 2, 10, 11, and 14 as part of an effort to complete the 30 Mb genome within five years. Our approach to sequencing *Arabidopsis thaliana*, a plant model organism, relies on shotgun sequencing of bacterial artificial chromosome (BAC) clones and identification of new targets using an innovative BAC end sequencing strategy.

TIGR human sequencing focus on chromosome 16p. One of six NIH funded large-scale pilot Human Sequencing Centers, we will finish nearly 30 Mb of genomic sequence before March 1999. We plan to be a major contributor to the sequencing of the human genome and have worked to develop laboratory protocols and software to facilitate sample management, quality control, closure, finishing, and annotation of BAC projects.

Sequence data is the first step in developing an understanding of fundamental processes underlying life. Determination of the function each gene is the target for the next generation of whole-genome analysis, "functional genomics." A number of techniques have been developed, including cDNA microarraying and the Affymetrix GeneChip™ technology, that may allow whole-genome expression monitoring. The challenge for the future is to develop these techniques and integrate their results with existing data to develop a picture of cellular metabolism and gene function. TIGR aims to be one of the leaders in developing these functional genomic approaches to address fundamental biological questions.