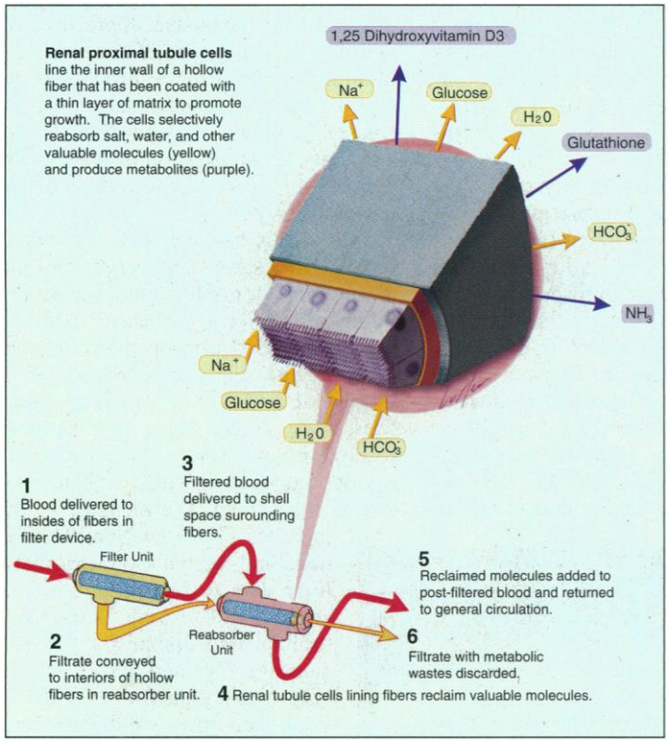
TECHSIGHTING
BIOMEDICINE

Test Tube Kidneys

Anyone who has ever treated patients with end-stage renal failure will immediately recognize the value of the research described below. While most people are aware that hemodialysis will keep people with failing kidneys alive, many do not know the significant morbidity and mortality associated with this procedure. For instance, patients in their early 50s who are undergoing chronic hemodialysis have less than a 50:50 chance of surviving for 5 years. Why? The answer has to do with the exact role played by the functioning kidney cells.

The kidney is an amazing organ that functions as both an endocrine gland (secreting a version of vitamin D), and a filtration unit (removing the bloodstream's many toxic waste products). Toxins such as blood urea nitrogen, ammonia, and organic ions will rise to toxic levels in the blood if not for the function of specific cells in the kidney. These key cells are located in the proximal renal tubules. A group in Michigan has now tested whether these cells could augment hemodialysis and yield a better treatment for patients with renal failure.

The investigators used a coupled system that relies on standard ultrafiltration technology to remove small molecules, like blood urea nitrogen, in concert with a novel, cell-based technology to perform the metabolic processes of the kidney. The latter technology is based on the ability to grow porcine proximal renal tubules in culture after harvest from 4- to 6-week-old Yorkshire pigs. These renal cells can be grown as confluent monolayers on the inner surface of hollow fibers. These fibers can then be packed into bioreactor cartridge devices, termed renal tubule assist devices (RAD), that contain up to 2.5×10^9 cells.



To test the function of a such a bioreactor kidney, they chose to use dogs that were put into renal failure by bilateral nephrectomies. By creating a closed perfusion circuit that went from jugular vein to hemofilter to RAD cartridge to jugular vein, they created a system in which to study the biochemical changes produced by the live cells.

First, they did a mock experiment to find whether the porcine cells would be harmed by the toxic metabolites in the blood of human renal failure patients. They took a culture of porcine renal tubules and bathed it in the uremic ultrafiltrate obtained from patients with end-stage renal disease. After culturing these cells with the ultrafiltrate for 1 week, they did not see any significant cell death. The pig renal cells seemed well adapted to functioning in a uremic environment.

Next, they looked at the stability of the porcine cells in the RAD cartridge. The uremic filtrate must flow over the cells in the system, a situation that produces some amount of shear stress on the cell layer. They investigated whether the cells could remain firmly attached during the cleansing run. During the first hour of the run there was some cell loss, but it decreased to near zero for the last part of a 24-hour run. Of the 2.5×10^9 cells, only $<6 \times 10^4$ cells were lost in total.

The researchers then measured critical elements in the plasma of dogs before and after treatment with the RAD system and compared the results to control dogs that were in renal failure but were left untreated. They found a significant decrease in the levels of potassium and blood urea nitrogen in the treated dogs. Potassium fell from an average of 5.7 meq/l in the untreated dogs to 3.8 meq/l in the treated dogs during the approximately 24-hour treatment procedure. The blood urea nitrogen level fell from 90 to 57 mg/dl in the same treated dogs.

To ask whether metabolic activity was robust in the RAD system, they looked at the processing of ammonia in the filtrate. Ammonia constitutes about 15% of all nitrogenous waste produced in the body. It is also a key player in the removal of acid from the peripheral blood. From analysis of both acid and filtered ammonia levels, the RAD cartridge was shown to be active. In addition, the group measured the level of 1,25-$(OH)_2D_3$ an active version of vitamin D produced by functioning kidneys. Amazingly, they found that animals repeatedly treated with RAD had levels of the hormone nearly equivalent to those of normal subjects.

The results of the RAD studies are encouraging, and show nicely how the fruits of cell culture and bioreactor technology can be applied to a medical problem. The next steps may involve experiments to immortalize the porcine renal tubule cells to make it easier to obtain significant supplies for large-scale clinical trials in the future.

—ROBERT SIKORSKI AND RICHARD PETERS

References

1. H. D. Humes, D. A. Buffington, S. M. MacKay, A. J. Funke, W. F. Weitzel, *Nature Biotechnol.* **17**, 451 (1999).

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TECHSIGHTING
NET TIP

Electronic Lab Suppliers

Some 9.4 billion dollars per year are spent for the purchase of scientific instruments and supplies worldwide. A laboratory scientist probably orders various lab supplies on a weekly basis and a piece of equipment every few months. A typical routine would be to first try to locate the product catalogs: In a large laboratory, this may not be a trivial task, because these catalogs tend to end up on many different benches. Then, you would need to scan through these catalogs to find

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which supplier is carrying the product of interest. A given product might be offered by more than one supplier, and you need to decide which is the best buy. Next, you typically call the customer service line to find out if the product is in stock. Finally, you fill out your purchase order.

The Internet is revolutionizing every aspect of the economy, and it was just a matter of time before online scientific supplies stores were available. This month, we review two such "stores" on the Web. Both have a similar business model: for every item you purchase, the supplier pays a commission fee to the virtual store. The convenience for you is that you can search product catalogs online and order the products you want with a few clicks of the mouse. You can pay by credit card or by purchase order. In each case, you need to be a registered user of the site to be able to purchase items.

The first store we reviewed is Chemdex (www.chemdex.com). The company states that 150,000 to 240,000 products (depending of which area of the site you read) are offered on its site from more than 110 suppliers.

When accessing the site, you can search products by suppliers (such as Amersham or Calbiochem) or by category (such as antibody or DNA products). Also, you can build a list of the favorite products that you order often. You can read more about the product you search for by clicking on its name. A drawback of the site is that you have to register in order to view the prices of the items that are available.

The other online store is SciQuest (www.sciquest.com). This site features more than 100,000 products from 100 suppliers. It, too, lets you organize supplies into favorite items that you frequently reorder. You can search the site by products or suppliers, or both. For each product, there is information that appears in a pop-up window.

A definite plus of this site is that prices are published openly, so you only need to register if you want to buy something. The site also features a link to another site that is owned by SciQuest: LabDeals (www.labdeals.com). There, discounted equipment and supplies are available either as fixed-price items or through online auctions. (We did not try buying any items from these sites, so we cannot comment on their speed for fulfilling orders or their customer service.)

In summary, we were impressed by the breadth of products offered at both sites and the ease with which a busy scientist can navigate through them. By ordering through these online stores, you simply sit at your computer and do a little comparison shopping. In the end, you may save time and money. That's why we love the Net.

—RICHARD PETERS AND ROBERT SIKORSKI

TECHSIGHTING
SOFTWARE

Back to the Basics?

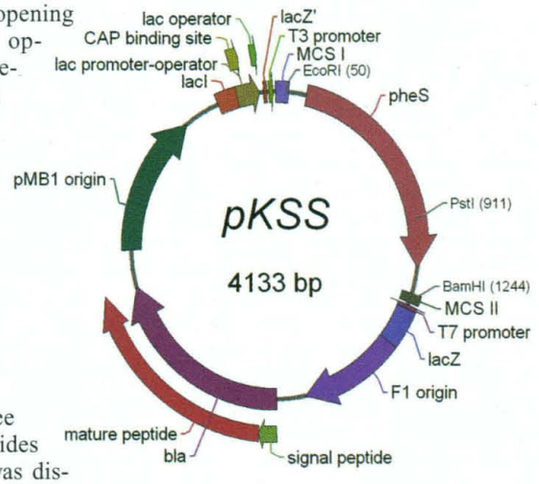
In the age of computer technology and automation, access to basic information should be only be a mouse click or two away. This is the philosophy behind The Mona Group's interactive CD-ROM called *Understand! Biology: Molecules, Cells & Genes* (version 1.0). The software contains more than 1700 biology-related topics in 40 mini-courses, complete with pictures, movies, and spoken pronunciation for selected terms. In addition, the CD contains chapter reviews from 11 different introductory biology texts, as well as interactive self-quizzing sections, complete with answers and hints.

Understand! Biology: Molecules, Cells & Genes (version 1.0)
The Mona Group LLC
Sunderland, MA.
$29.95.
413-548-3955.
www.monagroup.com

The program runs from a single CD. Users are greeted with a screen fixed in the center of the monitor. The opening window presents the user with options for minicourses, textbook review chapters, test sections, and the index. Maneuvering in the program requires only the clicking of the mouse. Minicourses and textbook review sections cover many biological topics, from classical experiments to immunological principles, with each topic described in a series of informative screens with graphics or movies in logical progression. The visual aids are colorful (see figure), and a mouse click provides a larger display, although this was disappointing in places, because some graphics are presented in low resolution. Some topics have textbook references, so that if the given description is not satisfactory, it can be easily located in the textbook. The hypertext design of the software is simple, but effective. A click on a technical term presents the user with a definition of the term, accompanied by visual aids. Certain terms are also coupled to a speech function. If the user is not familiar with the pronunciation, a button click will provide the spoken word. Although this is a very interesting concept, the speech function unfortunately does not pronounce all words clearly.

The product has the appeal of a new computer game, and one can easily become lost browsing through the wealth of information. For this reason, the index section is a very practical place to begin a search and is a feature that caters to users who are not certain of the correct spelling of technical terms. As the user types, words that are similar to the entered spelling are listed, and further spelling narrows the list. Upon completion of this step, the user clicks on the desired term and is presented with a description of the selected item. The program also has integrated questions and answers independent from the "thought problems." If one wishes to have a printed copy of selected screens, this must be done with the screen dump feature (standard on Macintosh computers).

The Mona Group home page provides access to basic product information, an application for a free demonstration, and information concerning forthcoming modules. Hardware requirements are quite modest. Most Macs with CD-ROM drives using at least System 7, or PCs with CD-ROM drives using at least Windows 3.1, will work with the software.



DNA structure module.

The *Understand! Biology: Molecules, Cells & Genes* module is an innovative software product that uses hypertext effectively. It is a useful and basic reference tool for the researcher and a good educational supplement for the student. An instructor version is also available. The product is reasonably priced, considering both Macintosh and PC versions are contained on the same CD.

—FRANK HOOVER

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