TECHSIGHTING
NEURAL REGENERATION

Some Nerve!

Old dogmas seem to die hard, and science is one field where it seems to take many different approaches to disprove long-held beliefs. One such belief is that nerves and neural tissue are essentially static. An insult such as a lack of blood flow (stroke) or a crush injury can cause nerve death and paralysis. Possible treatments for these kinds of injuries could involve creating new neurons or making old neurons work overtime. To tackle the first approach, we have to kill some old dogmas about neural regeneration.

Lately, some exciting work has shown that neural progenitor cells exist in vivo. In one study, researchers showed that the brain contains cells so pluripotent that they can actually give rise to bone marrow cells. This is perhaps overkill for the treatment of neural disorders, where you are simply trying to find a robust source of neurons and myelinating cells. Where do you look for these progenitors? A group from the California Institute of Technology (*1*) turned their attention to neural crest cells for a possible answer.

They chose to study cells derived from the sciatic nerve of late-gestational fetal rats. The idea was that since this nerve is still undergoing rapid development, it could harbor significant amounts of a neural stem cell population. They did a quick experiment in which they looked at the different cell types that came from the sciatic nerve tissue when it was placed in culture. After 14 days, they identified neurons, Schwann cells, and smooth muscle–like myofibroblasts. Mixed colonies were formed, indicating a multipotent progenitor. Subculturing experiments showed that this progenitor could renew itself during clonal expansion. This type of progenitor is referred to as a neural crest stem cell (NCSC).

They next set out to isolate a subpopulation of the sciatic nerve that would be enriched in NCSCs. They used cell sorting techniques in conjunction with antibodies to the neurotrophin receptor p75 and to the peripheral myelin protein P_0. By combining the antibodies, they identified five subpopulations on the basis of staining intensity. For example, one population (12%) were $p75^+$ and P_0^-. They then performed experiments using agents that induced differentiation. With BMP2 (bone morphogenetic protein) to instruct differentiation to neurons and NGR1 (glial growth factor) to instruct differentiation to glia, they could show that the $p75^+$ P_0^- fraction could yield neurons or glia.

Using this $p75^+$ P_0^- fraction, they then showed that these cells could also differentiate and propagate in vivo. They injected the purified cells into the ventral neural crest pathway of chick embryos at an early developmental stage, when neural crest cells are still undergoing their well-known migrations. After 3 days, they stained with rat-specific probes to look for the donor cells. They found that the cells engrafted efficiently and gave rise to glia and neurons at various locations in the chick peripheral nervous system.

Taken together with some labeling studies that show the turnover of these NCSCs in vitro, it seems that there may be a rich source of neuronal progenitor cells in the developing long nerves. Further experiments will shed light on the human system and whether small pockets of these cells persist beyond early development. The implications of such findings are of critical importance to those who are devising ways to regenerate neurons for therapeutic use.

—ROBERT SIKORSKI AND RICHARD PETERS

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TECHSIGHTING
LAB MANAGEMENT

Time Is Data

Whether you are running a laboratory in the academic or industrial sector, there are two ways that you can increase the amount of data that is generated by your laboratory: Get more resources through an increase in funding or maximize the use of your existing resources (or both). This month, we focus on ways that laboratory directors can maximize the use of their resources by using project management software tools.

Laboratory projects are often very complicated: they can last years, involve multiple people, and draw on many different techniques. Yet the vast majority of labs do not have a clear project management strategy in place. Part of this contradiction stems from the fact that basic science research goals change over time. This, after all, is the very essence of basic research. The tendency is to think that the lab will adapt over time to the change of direction that is guided by the results of experiments. But come grant or budget review time, many lab directors often are disappointed by the amount of progress that has been accomplished despite a significant investment of time and resources. While keeping creativity intact, project management tools might be able to help use limited resources more efficiently.

Project management basically consists of keeping scope, schedule, and resources in balance. In other words, the process consists of defining and tracking tasks and scheduling resources to accomplish those tasks. By investing some time in project management, one tends to use resources—including equipment, chemicals, and most importantly, people—in a more efficient way.

If the project is very simple, keeping track of tasks and use of a time-line will suffice. This can simply be done by writing on a board or keeping a flow sheet handy. If the project becomes more complicated, however, there are a number of software tools that can be helpful. You may wish to invest in scheduling programs. These software packages keep track of recurring and nonrecurring tasks with a calendar. Whenever tasks are accomplished, you update the file. The packages Act! (Symantec Corp.) or Now Up-to-Date (Qualcomm, Inc.) are popular choices. Act! is both a contacts database, that is, address book, and a scheduling program. Now Up-to-Date is a scheduling program that integrates seamlessly with Now Contact, a contacts database.

If you are trying to track multiple projects or if you have multiple people working on several projects, Project 98 (Microsoft Corp.) for the Windows operating system is an excellent solution. The software package lets you enter any number of tasks and schedule them. You can have multiple views into the data for a better understanding of the status of all your projects. For instance, you can produce Gantt charts (a graph consisting of horizontal bars that depict the start date and duration of each task) or PERT diagrams (charts depicting tasks as a network of dependencies). Project 98 won the Editor's Choice Award from *PC Magazine* last year and is seamlessly integrated with Microsoft Office. Project 98 has the added advantage of letting you assign specific resources to tasks. Those who are more detail-oriented can even enter the cost for each resource; the software will then help track the spending or "burn rate" of the project.

Besides the software packages mentioned above, there are a number of other worthwhile tools. These include CA-SuperProject (Computer Associates International, Inc.); Project Scheduler 7 (Scitor Corp.); Sure Trak Project Manager (Primavera Systems, Inc.); TurboProject Professional (IMSI, Inc.); Time Line (Time Line Solutions, Inc.); Milestones, Etc. (Kidasa Software, Inc.); ActionPlan (Netmosphere, Inc.); and FastTrack Schedule (AEC Software). Some of these tools have been reviewed on ZDNet (www.zdnet.com/products/businessswuser/manage.html). Information about such tools is indeed often found under the business software section of computer magazines (either print or online versions).

Some might think that project management tools are overkill for a laboratory director, but let's work through the following scenario: Imagine a lab where three postdoctoral fellows and one graduate student are each trying to purify proteins for their own projects. If you are tracking the progress of each member of your lab, you might find out that they are wasting an inordinate amount of time waiting for the availability of the liquid chromatography system, for instance. Let's assume that all of the proteins being purified in your lab require a chromatography step of about 2 days duration. If your lab members are all competing for access to the apparatus at the same time, that purification step will take 1 to 2 weeks to complete if the four members have to wait for their turns. By monitoring the tasks on all the projects, you might be able to guide some postdocs to tackle other tasks while the chromatography system is busy. As a matter of fact, with good project planning, you would have been able to tell ahead of time that there would be some conflict for accessing the column and would have been able to put the projects on different tracks to avoid unnecessary down time. Although this scenario does not appear disastrous by itself, repeat it a number of times throughout the year, and weeks, if not months, of productivity can be lost. Because lab work involves many different tasks, there are probably a number of other scenarios in your lab where time and resources are unnecessarily wasted.

Project management tools are also very helpful in analyzing past experience with projects. If you are disciplined enough to update the project file frequently, you should be able to analyze retrospectively your project management skills. You might indeed be able to identify tasks that are "bottlenecks" in your laboratory and either allocate more resources for those tasks or come up with an alternative strategy to avoid that task completely.

In conclusion, use of project management software tools might very well help your lab save time and resources in the long run. As an aside, we only discovered these tools after we left our careers as laboratory scientists to run a business. Who knows what great things might have happened if we had had them at the bench?

Links to the resources mentioned above are available on our website at http://mednav.com/zone/science.

—RICHARD PETERS AND ROBERT SIKORSKI

TECHSIGHTING

IMAGE ENHANCEMENT

The Eyes Have It

A new computer-based approach to processing images, called Super Resolution, accomplishes the seemingly impossible—increasing a digital image's resolution so that elements which cannot otherwise be seen become visible. Such topics, appearing to border on magic but based on sound mathematical and physical principles, were discussed at a 23 February 1999 meeting organized by Malur Sundareshan at the University of Arizona.

Originally developed as tools for such tasks as restoring blurred images from the flawed lens of the Hubble Space Telescope, the new algorithms are being used for everything from detecting previously unseen oil slicks on the surface of the ocean to extracting information from blurry old photographs. Image enhancement by Super Resolution could conceivably enable researchers to track bullet paths on frames of the famous Zapruder film of the Kennedy assassination.

To understand how Super Resolution works, consider a digital image (for example, computerized scan of a photograph). It is composed of a tiny grid of dots called pixels that, when put together, recreate the image. Simple resolution-increasing techniques (such as duplicating neighboring pixels) do not, however, add more information to the image. Super Resolution, on the other hand, attempts to reconstruct the original scene that gave rise to the image. In doing so, the technique effectively rebuilds the picture at a new, higher resolution than the parent image.

As an example, imagine one blurred photo showing two faces and a second sharply focused photo showing one of the same faces. Super Resolution algorithms would identify the mathematical transformations necessary to convert the blurred face in the first photo to the sharp image of the same face in the second photo. These operations, when applied to the entire blurred photo, define a means of reconstructing the second face as well. Thus, researchers who know the detailed optical properties of a telescope and the basic composition of the objects in its field of view can apply the technique to visualize objects beyond the telescope's resolving power. This is merely one simple application of Super Resolution. Researchers have combined numerous sophisticated mathematical operations to give the technique tremendously powerful restoration and resolution-enhancing capabilities.

Knowledge about the visual properties of the objects in the image is essential for the process to work. The limitations of the original imaging system must also be taken into account. Logical constraints, such as limiting an object's apparent brightness, are employed in building the algorithm. Further considerations may include an object's size, color, motion, composition, reflectance, or texture. The more detailed these data and assumptions are, the better the image can be reconstructed. The processing algorithms employ Fourier transformation, noise filtering, and other mathematical tools. The product of their analysis is a reconstructed scene with the maximum likelihood of having been the source for the original image.

Super Resolution is applicable to all types of spectral data, not just visible light. One area of current interest is for frequencies from 30 to 120 GHz, generally called the millimeter-wave band of the spectrum. Imaging resolution from this range of frequencies is low, but has the advantage of penetrating clouds, smoke, clothing (showing concealed weapons), or even buildings.

Emissions around 95 GHz have tremendous potential for acting like a sophisticated kind of "x-ray vision" because of their ability to penetrate coverings that block the passage of visible light. There are two ways to image an object in this frequency range. The first method relies on beaming 95 GHz frequencies at an object and analyzing the results with a detector. The more desirable, passive imaging technique collects 95 GHz emissions from objects using a device called a radiometer and provides image data without the need for externally applied radiation.

One limitation to using 95 GHz radiation in conjunction with Super Resolution for practical purposes, such as airport security, is the relatively slow time (approximately one minute) for acquiring and processing images. Current work is focused on using Super Resolution to improve the quality of these images and to reduce the computing time required for processing them.

—KEVIN AHERN

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