

The Miami Project Research Faculty, part of the University of Miami Miller School of Medicine, is a multidisciplinary team of investigators with a common goal - to conduct neuroscience research that addresses traumatic injury to the central nervous system and that ultimately leads to new or improved treatments for spinal cord injury and other neurological disorders. Its research team is made up of basic and clinical scientists with expertise in critical areas of neuroscience.

The Miami Project to Cure Paralysis has a dedicated laboratory devoted to high-content screening (HCS) of neurons. The laboratory is run by Dr Vance Lemmon and Dr John Bixby and is known as the LemBix Laboratory. The laboratory adopted a laboratory information management system (LIMS) to help manage and automate the vast amount of data. The result is that the LemBix laboratory has improved efficiencies, productivity and sample integrity by implementing integrated laboratory workflows and automating data management. The LIMS implementation encompasses an on-demand solution that serves the needs of the project's goals - to manage its workflows and operations in the most efficient and effective way to turn data into knowledge.

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## Finding a Cure for Spinal Cord Injury

### On-Demand LIMS for CNS Regeneration: The Benefits of Integrating Informatics and High-Content Screening to Accelerate Discovery



The Miami Project to Cure Paralysis is the world's most comprehensive spinal cord injury research centre, housed in the Lois Pope LIFE Centre, a Centre of Excellence at the University of Miami Miller School of Medicine. The Miami Project's international team of more than 200 scientists, researchers and clinicians take innovative approaches to the challenge of spinal cord injury.

Injury to the central nervous system (CNS) has devastating effects on the structure and function of the brain and spinal cord. Since the early 1980s, immense research progress has been made and has given hope that injuries to the CNS will one day be repairable. Still, there is much that researchers need to learn about the complex processes that occur in the brain and spinal cord after injury, and how those processes can be changed or reversed. Miami Project investigators carry out a broad scope of research to address the consequences of neurological injuries.

The goal of the LemBix laboratory is to uncover signal pathways, genes, compounds, or drugs that can be used to promote nerve growth. HCS of various libraries on primary neurons requires that the team of scientists follow a variety of process steps and employ complex manipulations of cells and libraries to obtain meaningful results. The approach of HCS itself produces vast amounts of data in the form of images and well-based and cell-based phenotypic measures. A single experiment can generate data from 300,000 neurons with 120 parameters per cell. Managing sample workflow and library data, along with the extensive amount of experimental results is a considerable challenge. The laboratory needed an informatics solution to meet the ever growing data deluge and to turn data into knowledge.

#### THE BENEFITS OF HIGH CONTENT SCREENING

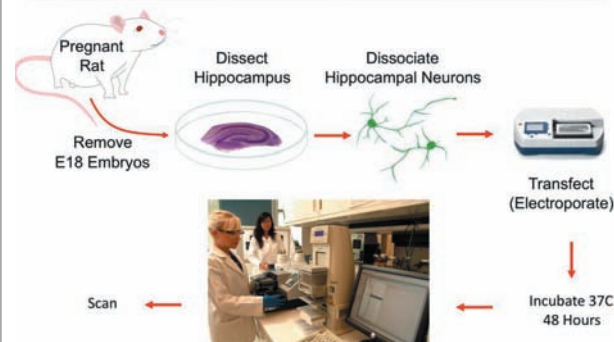
Traumatic injury to the central nervous system (CNS) usually results in irreversible loss of function. There are two main reasons for this: one is due to the death of nerve cells and their support cells; the second is due to the severing of very long processes (called axons) that transmit electrical signals from one nerve cell to others. Transected CNS axons do not re-grow or reestablish connections with their targets. Consequently, individuals with injured spinal cords can be irreversibly paralysed.

High content screening offers an ideal way to identify genes; molecular pathways, and, ultimately, drugs that can promote the regeneration of CNS axons. HCS permits the quantification of cell morphology, including the lengths and numbers of axons, of neurons in culture. The LemBix laboratory has screened 3,000 different genes in primary neurons and measured 120 different parameters in over 6 million neurons in the span of one year. In the LemBix HCS workflow, CNS neurons are isolated as single cells before being transfected with expression vectors coding for potential regeneration-associated genes and green fluorescent protein.

Then, neurons are plated into 96-well plates and cultured for 48 hrs before being fixed and stained to permit visualisation of nuclei and neuronal morphology. The plates are then imaged and analysed using a Thermo Scientific Cellomics™ VTI ArrayScan and Cellomics BioApplications.

Screening campaigns using primary neurons are uncommon due to the expense of culturing cells that require complex defined media and the variability between preparations of nerve cells. The LemBix laboratory tackles the variability between preparations, in part, by including a number of control treatments that are used for normalising data across experiments. But it is clear that much of the variability between different experiments is due to variability in reagents and cell preparation. In order to rapidly identify sources of variability, it is essential to have a LIMS that tracks supplies, reagents and workflows that automate these activities.

#### Screen Pipeline



#### SOLUTION REQUIREMENTS AND BENEFITS ACHIEVED

The Miami Project to Cure Paralysis sought a LIMS for the LemBix laboratory that would facilitate its laboratory workflows and automate its previously manual data management processes. Prior to implementing a Thermo Scientific LIMS the laboratory used paper-based worksheets and manual notebooks. The nature of the work conducted in the laboratory, using numerous compound libraries and gene libraries, resulted in the laboratory becoming overwhelmed with all the data it had to oversee.

Furthermore, the laboratory was moving away from traditional academic research activities, such as hypothesis testing, where it was relatively easy to keep track of information manually using notebooks. Instead, the laboratory was performing complicated screening campaigns involving several people. Keeping track of what each person was doing through the processes of preparing the cells and perturbations, staining and analysing the data was a challenge. The laboratory determined that a manual, paper-based process was not efficient and that a more automated electronic method was required.

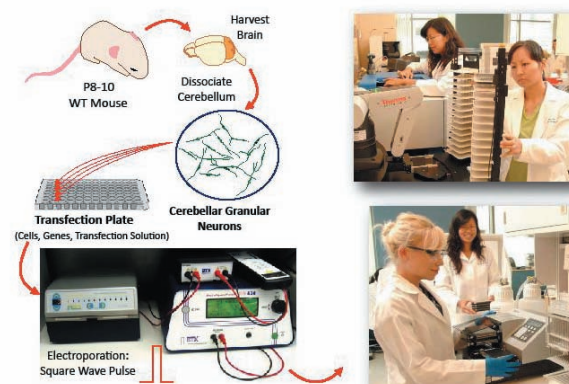


Figure 1

Workflow, reagent and stock tracking are an imperative for the lab. In cell culture they use complicated media and different types of reagents and many of their experiments fail due to problems with the reagents and stocks. Within the laboratory's workload, hundreds of different reagents are used for a particular experiment and there are dozens of different steps to document the processes, such as recording the number of cells that are inserted into a particular well, how they were treated, when they were put into the incubator, etc. It is crucial that the laboratory keeps track of every detail of these processes. Furthermore, with so many people being involved in the workflow of a particular experiment, a simple solution that could be used by all the people who need to enter information was needed. The LIMS keeps track of stocks and reagents throughout the different workflows and facilitates the lab's ability to identify which reagents are worth progressing or need to be discarded. For the LemBix laboratory the LIMS improves productivity by providing improved quality control and more efficient triaging of bad reagents.

Another key driver for implementing a LIMS was the chance to reduce turnaround time, improve planning of new experiments and ensure that standard operating procedures (SOPs) would be adhered to. It was vital that the solution would enforce business rules and be able to capture details about workflow to identify problems or optimal conditions.

Scientists also needed to be able to readily retrieve and analyse the data at any time to facilitate data acquisition and knowledge sharing that was previously difficult and timely to acquire. The LIMS centralises all of the information into a single database.

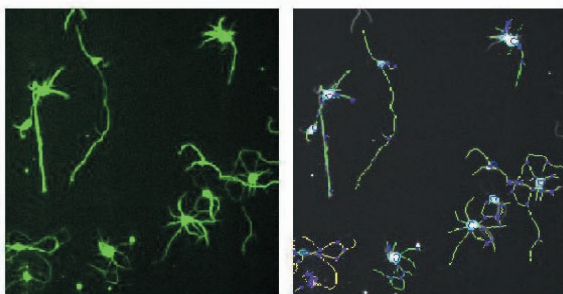


Figure 2

### CHANGING DEMANDS OF THE PROJECT

Companies such as Thermo Fisher Scientific are focused on delivering the most appropriate tools to their customers as their needs change, as their businesses grow and as the market requires. An on-demand internet LIMS solution enables laboratories to have access to their data anywhere, at any time, from any web browser. The Miami Project to Cure Paralysis realised that an on-demand LIMS solution would be ideal in helping to reduce overhead for dedicated and specialised IT resources to maintain and support the system. With full featured LIMS functionality available on-demand, the laboratory has all the data reliability and security benefits that come from an installed LIMS but without the added hassle of maintaining an implemented client-server application. Thermo Scientific LIMS-on-Demand has made it possible for the laboratory to control its data more easily, freeing up valuable resources in the laboratory.

Another challenge in medical research is that often the source of seed money for new research endeavors in academic research institutions are justified to fund buildings and equipment rather than software projects that can appear intangible and have unspecified outcomes or timelines. Thus, obtaining sufficient resources to purchase, install and provide ongoing support of a traditional client-server LIMS for a single or multiple laboratory environment can be a daunting task. The monthly payment structure for LIMS-on-Demand is better suited for this type of funding versus a large upfront capital expenditure and scales nicely for laboratories that need to dial their user base up or down with their workload. Furthermore, since the on-demand model means that the backend IT infrastructure is managed and maintained at the vendor site, laboratories with minimal or no IT staff do not need to take on this added burden.



### LIMS IN USE AT LEMBIX – USE CASE

A scientific workflow was developed in the Thermo Scientific LIMS for the lab's specific application and incorporated a typical screening pipeline with many steps (Figure 1). First, brain regions are harvested and these brain pieces are then dissociated and transfected in 96-well plates with DNA. Neurons are then allowed to grow in 96 wells for 2-3 days before being fixed and stained for imaging (Figure 2). Sometimes the neurons are treated with chemicals or drugs instead of or in addition to DNA.

This example shows how the desired goals of implementing a LIMS such as improved tracking of data, plate management and workflow documentation were successfully achieved. The laboratory now had real-time reporting capabilities that allowed laboratory members and supervisors to have immediate access to information on collaborative projects. Furthermore, it facilitated tracking reagents in multiple-well plates, linking digital information with workflows and documenting stocks and lots used in experiments.

### CONCLUSION

High content screening is being counted on to uncover signaling pathways, genes, compounds and drugs that can be used to promote nerve growth. The screening pipeline includes solid experimental techniques combined with instrumentation and analytical tools.

The process produces enormous amounts of data. Thermo Scientific LIMS-on-Demand is ideal for routine laboratories that need to manage this data, increase efficiencies by automating their operations and track their samples with little or minimal IT resources. It is a full featured LIMS that can be accessed anywhere at any time from any web browser.

LIMS-on Demand solved a critical problem for the LemBix Laboratory. Scientists no longer have to rely on the university's IT team to maintain the servers and no longer have database licensing issues. They can focus on the core business of finding a cure for spinal cord injury rather than working as database managers and server experts.

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### LIMS-ON-DEMAND OFFERS ATTRACTIVE ALTERNATIVE FOR SMALL AND MEDIUM SIZED LABS

Paula Hollywood of ARC writes about the changes occurring in the LIMS business: "The cost of acquiring a LIMS in the traditional license delivery model can run between \$100,000 for an entry level solution to upwards of \$750,000 for a sophisticated enterprise package. These prices can put a commercial LIMS out of reach for small and medium sized laboratories, in effect compelling these organisations to develop home-grown systems. Approximately 75% of homegrown system costs can be directly attributed to human resources and capital equipment expenditures that may in fact cause such systems to be more expensive to develop, maintain, and validate.

A new alternative for small to medium labs is LIMS-on-Demand. Hosted by an application service provider, users can access a fully functional, validated solution via a web browser for a monthly subscription fee. The primary benefits of the on-demand model are low total cost of ownership and ease of use."

Thermo Scientific LIMS-on-Demand provides all the benefits of a fully installed LIMS, such as built-in workflows, a powerful database, the ability to capture, store and analyse lab data, monitor resources and integrate with instrumentation, and reporting templates, while minimising the need for IT resources and eliminating expensive hardware and software. LIMS-on-Demand provides scientists with automated data reporting (eliminating the time-consuming tasks associated with manual or paper-based processes) and enables them to make faster, more informed decisions.

Scientists using LIMS-on-Demand simply connect to their system over the Internet - from anywhere and from any web browser - when they want and for as long as they want.

Thermo Fisher Scientific has been in the Informatics business servicing customers from all industries for over thirty years. Recognised by market analysts as market and thought leaders, they have twice received Microsoft Corporation Innovation Awards for providing next generation solutions that enable customers to advance science, and multiple awards from Frost & Sullivan in Market Leadership and Competitive Strategic Leadership. Their solutions have been built on the latest technologies from Microsoft and Oracle and their dedication to increasing laboratory efficiency while lowering the total cost of LIMS ownership has earned the company a dominant leadership position in the LIMS market.

Thermo Fisher Scientific has equipped laboratories around the world and across a range of industries with innovative and purpose-built LIMS solutions. Their breadth and depth of expertise and solutions demonstrates their commitment to serving the needs of customers.

Thermo Scientific LIMS-on-Demand is the latest example of the company's commitment to innovation and ability to deliver solutions that meet changing market demands and the most challenging needs of its global customer base.