
Executive Director's Report – George Owen

As promised 2011 is going to be a special year. We have every reason to believe that we can push ahead with our well targeted research programs that will integrate the translation of any advances in neuroscience into an outstanding clinical trial.

The replication study of Stephen Davies work at Yale is well under way and we should, within a matter of months, have some indication of how that is going. As we have said in previous communications, replicating what appears to be ground breaking research is necessary and we are looking forward with great excitement to seeing the results from this study. If we prove that this cellular therapy is reproducible, it is a great step forward in further studies that will form the basis of a clinical trial. I might remind you that this is a single component study and we are very hopeful that Stephen Davies GDAbmp cells will combine very well with his other area of study that is with Decorin.

StepAhead has also provided funding for a bridge of self assembling nano-fibre constructs that were described by Fabrizio Gelain at our December meeting last year. This study will be done in Argentina in partnership with Prof. Gustavo Moviglia.

A report from Kathy Traianedes, on a further study we are supporting is printed below. It is important to stress that this collaboration is to treat injured or diseased dogs only. No dogs will be subjected to any experimental spinal injury. We believe in this partnership we can bring a positive outcome for these unfortunate animals but in that process can learn a lot about the surgical technique, cell dosage, other agents in combination and the role of rehabilitation.

A report on work in Florida from Brent Reynolds is also included. It is very interesting as it focuses on the human cells that will be critical to a human treatment of SCI.

Efforts to raise funding for these various activities continues. Barbara and I will both be attending the National Lions Convention in Launceston next month. Lions have been outstanding in their support for our projects. Despite the huge demands made upon them during the recent national and international disasters to which Lions always and traditionally give most generously, they were still able to maintain support for our projects.

Finally preparations are already underway for this year's scientific meeting which will once again be a show stopper with an excellent faculty of researchers who are at the cutting edge of the research that has direct application to clinical trials. We will keep you informed of the program and again it will be open to those with spinal cord injuries along with their family and friends and to the general scientific community of this country.

Keep up the good work and any way in which you can support our program would be most welcome.

Mr George Owen
Executive Director, SAA

News from Brent Reynolds' laboratory

My lab has had a long-standing history in studying and working with neural stem cells. Our ability to isolate and expand these cells in culture provides an almost unlimited source of donor material for tissue repair and cell replacement therapies. We have recently developed a new approach to purifying or enriching for a particular type of brain cell -- neurons. Neurons are the functional units of the nervous system and it is the loss of these types of cells that are often responsible for deficits following injury or disease. One of the difficulties has been obtaining large quantities of neurons in a purified form to be used as a source of cells for replacement. Our new method allows us to obtain a pure population of neurons and we have been implanting these cells into the chronic injured cord. To date we find good survival of the donor cells and have seen recovery of function. We are continuing the studies, working with one of the most experienced and talented spinal cord injury labs in the world, Dr. Paul Reier's lab. Over the next 6 to 12 months we will continue these studies and begin to initiate experiments using human neural stem cells as the donor population. If all goes well this should put us in the position of initiating early-stage clinical testing in the near future.

Kathy Traianedes report

Worldwide, hundreds of thousands of people are victims of Spinal Cord Injury (SCI), mainly occurring in active young adults. In Australia, there are approximately 300 new cases of SCI every year with approximately 14,000 total SCI cases. The healthcare cost of SCI in Australia is approximately \$2 billion and the lack of any effective therapy emphasizes the massive burden to global healthcare systems. Even partial restoration of damaged spinal cord following SCI could result in major improvements in breathing, upper/lower limb function (including simple chores such as eating, drinking, reading and personal hygiene) and bowel/bladder function. A small change in the extent of SCI could dramatically increase the injured person's quality of life, and independence.

Despite more than 50 years of research using rodent (mainly rats) models, no effective treatment aimed at reversing SCI in humans has been achieved. To develop a clinically relevant animal model of chronic SCI so we can test new forms of treatment, the model of choice is that of spontaneous complete paraplegia in the dog. It is a very common, naturally occurring SCI presentation in dogs, representing up to 1% of all presentations to veterinary general practitioners. In the canine there are distinct parallels to human SCI. Specifically some of these include, the size of the lesion and mechanism of injury is similar to humans, the pathology of the injury is similar, control mechanisms for bladder and bowel functions are similar to humans, and dogs are amenable to the same rehabilitation and behavior analysis that is used in humans.

Only dogs with injury or disease causing spinal paralysis will be in this treatment study. Dogs will be selected that are clinically diagnosed as non-recoverable. The treatment will be offered to the dog owner, and with their consent and agreement to participate in the rehabilitation, then the treatment will be provided free of any charge. Information on the progression of recovery will be obtained through medical imaging and clinical neurological outputs such as sensation and motor recovery, just as would occur in a human study. Should any dog die, only with the consent of the owners would an autopsy be conducted.

Annual Scientific Conference 2010 – Summary

We had an outstanding meeting last year. Speakers came from all over the world, including North America, South America, Europe, Asia, New Zealand and Australia. As in other years the focus of the meeting was on treating the chronic injured spinal cord, and in line with our 5th annual meeting last year, the theme was directed towards engineering repair of the injured spinal cord. The purpose behind this focus reflects our understanding of spinal cord injury and where the biomedical research community sits in regards to its knowledge of what occurs following damage to the cord. Remarkable advances have been made in the last decade towards our understanding of the structural, biomedical and genetic changes that occur after injury to the mature brain and spinal cord. This now puts us in the envious position to intervene to improve outcomes and develop meaningful treatments and even eventually cures. We now feel that we are able to approach this complex problem in the same manner in which an engineer approaches an engineering problem. The tools and knowledge have accumulated to the point where we now have the means to design and apply approaches that will allow us to re-engineer the damaged spinal cord. Following this train of thought, the problem can be broken into bite size or manageable pieces. Each of these pieces can be attacked in isolation, plans drawn up to overcome the hurdles, and experiments carried out to determine the most efficacious approach. Once solved the components are recombined to provide a solution to the overall problem.

Our meeting was broken into five sessions, ranging from understanding the basic biology of spinal cord injury through to clinical interventions. The meeting started with an overview of StepAhead's history and its mission by our Chairman of the Board Tony Benbow and President/Founder George Owen. This was followed by a very thoughtful presentation by Prof. Loane Skene from the University of Melbourne who highlighted the difficulties regulating human stem cell research in Australia and the potential that exists for stem cell approaches to disease. Ms. Chante Masset then gave one of the most heartbreaking and enlightening talks. Chante is 11 years old and injured her spinal cord less than one year ago in a pool accident. She spoke from her heart about the impact this injury has had, not only on her life but, on her family and friends as well. Our keynote speaker, Dr. Stephen Davies (University of Colorado), has been a collaborator of StepAhead for several years and spoke to us on some of his latest research aimed at breaking down and overcoming the glial scar that occurs following injury. Dr. Davies has been using an agent that can be infused into the spinal cord and dissolves the scar, allowing damaged spinal cord nerve fibres to re-grow. The data was compelling and indicated that even single intervention treatments aimed at fixing one of the many barriers to spinal cord regeneration, can have relevant functional outcomes.

After a short break, Drs. Jesse Owens (University of Alaska) and Brent Reynolds (University of Florida) spoke about the challenges that exist to developing new therapeutics. Dr. Owens has been an inspiration to StepAhead over the years and is irreplaceable, not only in his outlook and energetic approach to life but he is also a spinal cord injured patient and researcher. This provides him with the perspective that few have. Dr. Owens' approach has been embraced by StepAhead and involves addressing the three main barriers to spinal cord injury: (1) overcoming the glial scar, (2) bridging the gap that is often present at the site of injury and (3) enhancing neuron regeneration and conductivity. Dr. Reynolds followed by outlining some of the practical difficulties that face biomedical researchers today in moving new innovative and promising therapies from the lab to the clinical testing phase. While difficulties do exist, none of these are insurmountable and none are problems that we do not have the tools or the will to surmount.

Following a brief lunch, Dr. Rob Kapsa, a principal scientist at St. Vincent's Hospital in Melbourne, gave an informative lecture on the use of biomaterials for building regenerative scaffolds in the injured spinal cord. Dr. Fabrizio Gelain (MIT trained bioengineer from the University of Milan, Italy) followed this explaining some of his most recent results using a bio-inspired nano-structured scaffold that is composed of self-assembling peptides. He detailed their use and practical application in the chronic injured cord. Rounding out our session on scaffold biology was Dr. Kathy Traianedes from St. Vincent's Hospital who spoke about a promising and practical approach; the use of a cellular tissue for enhancing spinal cord repair. She has been working with the matrix that is currently in clinical use and has been successfully used in millions of patients (not for spinal cord injury) and therefore represents a favorable matrix that could see clinical

application once we can learn how to apply it specifically to the spinal cord.

Our afternoon session closed out with two stellar lectures by a collaborative team based in North America who have pooled their unique skills and expertise to form a team that is developing one of the unique therapies for chronic spinal cord injury. Dr. Jeannette Davies (the second half of the husband and wife team of Stephen Davies and Jeannette Davies, University of Colorado) presented some of the team's most recent data on using a specific type of human brain cell called an astrocyte. These cells have long been thought to play a supportive role in the function of the nervous system and to have an inhibitory or negative effect on regeneration. Based on the groundbreaking work of one of our other speakers, Dr. Mark Noble (University of Rochester, NY), who had discovered a particular type of astrocyte precursor cell nearly 25 years ago, Drs. Noble and Davies have developed a way to turn astrocytes that may have a negative role on spinal cord regeneration into astrocytes that promote regeneration. Dr. Davies presented some of the most remarkable data that these particular types of cells can be used to enhance regeneration. What was most exciting about the presentation was these cells were human in origin, moving us one step closer to clinical application. Dr. Noble finished out the session by giving a historical overview of the application of cellular therapies for spinal cord injury and touching on a number of the hurdles that scientists face in repairing the injured cord and how these can be overcome. Dr. Noble's talk was inspirational and confirmed why he is one of the world's leading experts in this area.

Our second day began with a lecture by Dr. Karl Johe, founder and chief scientific officer of NeuralStem Ltd. (a biotechnology company focused on using human neural stem cells for repairing the injured brain and spinal cord). Dr. Johe has been pioneering this approach for over a decade and has developed the technology to the point where it is now being tested in clinical trials. He detailed the design and implementation of a recently approved trial for implanting human neural stem cells into the injured spinal cord of patients with ALS. NeuralStem Ltd. is now planning a human trial for chronic spinal cord injury and is considering Australia as one of its clinical testing sites. This was outstanding news to learn that cellular therapies for spinal cord injury are now entering the human testing phase. Our next speaker was Dr. Keith Crutcher who gave one of the most thoughtful lectures of the meeting, pointing to the need to provide proper tissue geometry for regenerating spinal cord nerve fibres. The importance of this cannot be understated, Dr. Crutcher presented compelling data that aligning fibres correctly, with the appropriate signals to direct growth, can make the difference between success and failure.

Our second last session of the morning was focused on the development and use of appropriate animal models for translational research. Dr. Sam Long, a veterinarian and researcher at the University of Melbourne, spoke about the use of dogs that have been injured by accidents or normal degeneration and how these animals can be treated to not only relieve their pain and suffering but also to provide useful information regarding human therapeutics. Dr. Stephen Livesey gave an informative overview of the use of animal models in spinal cord injury. His lecture was sobering in that it brought home the point that we have made little progress in the past 20-30 years in regards to improving outcomes in spinal cord injured patients. This contrasts the large gains that have been made in our understanding of what happens at a cellular level post-injury and further emphasizes that we are at a time when all the great basic biology is bearing fruit for the difficult task of translational research. His lecture highlighted the notion that new approaches are needed, approaches that are innovative, aggressive and step outside of the dogmas and convention that exist in this area. Dr. Livesey is a member of our Board of Directors and has a strong biotechnology background (having founded a tissue matrix company in the USA and directed its research towards successful development of a therapeutic product). His insight and practical experience is allowing StepAhead to take a lead in this area, supporting and partnering with some of the most innovative research groups in the world.

After a short lunch break we returned for our final session of the meeting focused on clinical application of cellular therapies for chronic spinal cord injury. The session opened with a talk by Dr. Samsen, (a neurosurgeon and Director of the Passat Neurological Institute in Bangkok). Dr. Samsen attended our meeting last year where he spoke about the opportunities that exist to collaborate with clinicians and researchers in Thailand towards developing spinal cord injury therapies. This year he enlightened us with the facilities and core services that are present in Bangkok for large animal preclinical research. There are

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a large number of dogs that are injured, mostly due to road accidents, and facilities exist for their treatment and testing of novel therapeutics. The opportunity to work with the researchers in Thailand and take advantage of the facilities they have developed is an approach that StepAhead is actively pursuing. Our next speaker Dr. Jim Faed (University of Otago, New Zealand) outlined the experience his research group has had in gaining approval for a chronic spinal cord injury clinical trial in New Zealand. The regulatory issues that must be addressed are significant, however with the help of individuals such as Dr. Faed, learning from their experiences will certainly benefit StepAhead as it moves into supporting clinical testing of new therapies. Dr. Faed's trial is now approved and has begun. Our final lecture of the meeting came from Dr. Gustavo Moviglia (Director Cell Therapy Center at the Universidad Maimónides, Buenos Aires, Argentina). He has been pioneering the testing of novel therapeutic approaches for patients with chronic spinal cord injury using cellular and immunological approaches. Dr. Moviglia spoke at our meeting last year where he told us of a recent trial they had done at his Institute. This year he provided the basis for a combined cellular therapy and bio-matrix approach. StepAhead's relationship with Dr. Moviglia will be important not only for his clinical insight and keen eye for identifying promising approaches, but it will also provide us with a collaborative clinical team where new therapeutics can be tested in well-designed and controlled clinical trials.

Our co-founder and president Dr. George Owen brought the meeting to an end with a closing statement summarizing the current state of the art in chronic spinal cord injury. He highlighted the growing need and necessity to support research in this area and to move promising therapeutic interventions into the clinical testing phase as quickly as possible so each approach can be vetted and those that do not work can be dropped while those that show promise can be further developed.

In all, this was one of our strongest meetings ever. It has raised hope and promise that with continuing support from the Australian government, private foundations, community organizations and the people of Australia that we will win this battle to repair spinal cord injury.

Annual Scientific Conference 2011

This years' conference is to be held on Wednesday 30th November & Thursday 1st December at the Education Centre, St. Vincent's Hospital, Fitzroy. Further details will be provided over the coming months.