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W2W -2011: Some reasons for hope, many more reasons for action!

Returning from Working2Walk 2011, if you are currently sitting in your wheelchair and ''waiting'' for the cure, you could be disappointed by the absence of a fantastic scientific breakthrough. Even though some interesting and encouraging results were presented, the long awaited cure is not there yet…

Coming back from Maryland, you might as well become pessimistic as you got to better understand the huge scientific complexity behind spinal cord injury. You might have become even more frustrated when you realized that the problem is by far not just scientific but also systemic! As it is, discussions at W2W made it again very clear that the system/framework in place is not geared towards a cure, let alone a fast one! It does not allow a swift translation of promising therapies but rather leads to working in silos with publications as a main target and with competition sometimes getting unsound as resources get scarcer. Many researchers will disagree with the latter statement but we do have to conclude, again and again that cross-collaboration could and should be improved further. Not to mention the fact that our researchers rarely have control of what happens beyond their laboratory and that the translation of their work is largely subject to the goodwill (understand financial interest) of biotechs /pharmaceutical companies owning the relevant patent. A good example of this is Chondroitinase, an enzyme that was tested on rats by Dr Jerry Silver with some degree of success, but the human application of which depends on decision by the Acorda company and a Japanese patent owner, besides remaining scientific challenges. When referring to a misaligned ''system'', we also refer to an FDA regulation which is rightfully striving to guarantee optimal safety but does not seem to be geared for a swift translation of promising therapies, and even less for their necessary combination. Yet another reason for frustration by the attending sci patient community was the fact that most work is currently done on acute spinal cord injury. The latter choice might seem illogical as the number of chronic cases is obviously far higher (10 to 20 times bigger market) and therapy efficacy measurements would be far more robust when dealing with chronic sci, since spontaneous recoveries can be mostly excluded. Also the focus on acute SCI does not seem optimum, if you consider the inherent logistic difficulties with regard to recruiting acute candidates for clinical trials (illustrated, for example, by the Geron phase 1 trials, for which only 4 patients have yet been recruited, within almost 2 years after the trial kickoff, and for which go to market of the stem-cells alone can only be expected, in the very best case scenario, within 8 years from now!).

However, there is another view of W2W- 2011: that of the exponential progress accomplished over the past few decades by dedicated researchers and that of the fantastic potential for action by the sci community, should they manage to mobilize and collaborate with all stakeholders of the chain. The attending SCI representatives, coming from all over the

world, have indeed not only shown their commitment to a cure, but also their deep and integral knowledge of the subject, ranging from scientific aspects to financial and systemic challenges. Opinions will differ as to how far we still are from a cure or even from significant functional returns, but one fact is not questioned at all: we have never been so close! In other words, it is time to act, time to join forces, think out of the box and apply new ways and strategies towards functional returns. All in all, a more cohesive and aggressive target-driven approach (sometimes referred to as ''moon shot approach'') seems to be of essence. Settling for a cure as the medium term target and deriving strategies from there would naturally lead to a more integral (from bench to bed) , collaborative and innovative approach, and to more timely and effective outcomes. Simple? Of course, not. Yet time for hope alone is over. It is now time for action.

Going more into the individual presentations made during W2W-2011, here is a rough overview and links to more detailed information through video:

- ***R. Douglas Fields, PhD, Chief, Nervous System & Plasticity Development Section, National Institutes of Health, NICHD*** **"The other brain/ glia and their role in spinal cord injury''**

  In his presentation R. Douglas Fields highlighted that the glia/glial scar is both the problem and the answer to the problem. Astrocytes, being the main components of the scar have indeed been shown to promote repair and release growth factors.

- ***I. Richard Garr, JD, CEO & Director, Neuralstem, Inc.*** **"Neuralstem's Approach to Spinal Cord Injury"**

  I Richard Garr showed latest outcome from the ongoing Neuralstem Inc's trials on 12 ALS patients with their fetal-derived neural stem cells. He stressed that the trophic effect of those cells might rescue some cells in acute sci's. Effect is expected to be lower in chronics. Trials on sci are on-hold as the FDA wants to see safety data from the ALS trial first (total 18 patients)

- ***Joseph Gold, PhD, Senior Director, Neurobiology and Cell Therapies Research, Geron Corporation*** **"Update on a Phase I Safety Trial of Human Embryonic Stem-Cell Derived Oligodendrocyte Progenitor Cells (GRNOPC1) in Subjects with Neurologically Complete, Subacute Spinal Cord Injuries"**

  Joseph Gold explained the targeted impact of the Geron' embryonic stem cells currently tried on human acute sci. Those cells do not regenerate neurons but do induce remyelination. As to safety, 900 rats have been transplanted with the cells and none of them developed an teratomas (tumor).So far 4 patients have been transplanted. Time to market is expected to be 8 years in total, if all goes according to plan. At this stage, combination therapies are still theoretical.

- *W. Dalton Dietrich III, PhD, Scientific Director, The Miami Project* - **"Current Studies Targeting Therapeutic Hypothermia and Schwann Cell Transplantation"**

  View video - 31 minutes

  At first, W. Dalton Dietrich described the hypothermia clinical trial project. Hypothermia was tried on worst case scenario patients (cervical Asia A). 33% of those patients reversed to Asia C. A clinical trial protocol has been worked out. The trial would involve 212 patients and take 5 years to complete. Miami Project is currently waiting for a grant (total cost of the trial amounts USD 10-12m).

  Secondly, the Miami Project has submitted (Sept 2011) an IND to the FDA to start a clinical trial using Schwann cells. Those Schwann cells, according to W. Dalton Dietrich, have been shown to promote regeneration, to produce growth factors and to remyelinate. In a second stage, they will be combined with Rolipram and with the Invivo scaffold. Another possible combination involved the F05 Peptide.

- *Jonathan Slotkin, MD, Medical Director - InVivo Therapeutics*
  "Biomaterials in the Treatment of Spinal Cord Injury"
  View video: soon to be seen on http://www.unite2fightparalysis.org/2011_w2w_videos

  The Invivo scaffold is now being tested on monkeys in the Caribbean. Jonathan Slotkin also indicates that Invivo now has an injectable scaffold that is including MP, ''retaining the positive effects of MP without the negative effects''. The scaffold is mainly seen as an instrument to deliver some drug or cell to the spinal cord. Implantation of the scaffold will be made after a laminectomy, for both the solid and the injectable version. All work is currently done on acute SCI, even though Jonathan Slotkin confirmed Invivo's great interest in chronic sci market, being their second stage.

- *Anthony Caggiano, MD, PhD, Vice President, Preclinical Development, Acorda Therapeutics* - **"The Challenges of Chondroitinase Development for Spinal Cord Injury"**

  View video - 28 minutes

  Anthony Caggiano showed the positive outcome of Chondroitinase studies made on rats and cats, but stressed that major challenges remain, when it comes to delivery of this enzyme into a human spinal cord. Its distribution has indeed been shown to be limited (area covered). Next steps are to check the effect on pigs (ie on a bigger spinal cord) and to check the feasibility of a direct injection of the enzyme. Anthony Caggiano estimates that the total cost incurred to go to a phase 3 clinical trial would be around USD 300-400M!

- *Jerry Silver, PhD, Professor, Department of Neurosciences, Case Western Reserve University* - **"Robust Functional Regeneration Beyond the Glial Scar"**
  View video - 34 minutes

  Jerry Silver highlighted the effect of chondroitinase on rats with a chronic cervical injury. He showed clear improvement in terms of breathing and bladder control, ie both functions targeted by his trial. Next stages, eg translating those trials to human sci, however, are depending on Acorda's decision (the enzyme is currently not produced anymore) and on whether a solution is found to safely and effectively deliver the Chondroitinase to a human spinal cord.

- *Stephen Davies (in breakout session only)*

- *Wise Young (in breakout session only)*

- *Keith Tansey, MD, PhD, Director, Spinal Cord Injury Research & Restorative Neurology Programs, Crawford Research Institute, The Shepherd Center* **"Combining Robotic and Electrophysiological Methods to Measure and Augment Locomotor Recovery after Spinal Cord Injury"**
  View video: soon to be seen on http://www.unite2fightparalysis.org/2011_w2w_videos

- *John McDonald, MD, PhD, Director, International Center for Spinal Cord Injury at Kennedy Krieger Institute* **"Functional Electrical Stimulation (FES) Helps Replenish Progenitor Cells in the Injured Spinal Cord of Adult Rats"**
  View video: soon to be seen on http://www.unite2fightparalysis.org/2011_w2w_videos

- *Heidi Marchand, PharmD, Asst. Commissioner for Special Health Issues, FDA* – **FDA approval procedures**

  Heidi Marchand explained the FDA procedures and the various steps taking place between lab experiments and a go to market of a drug or a therapy in the USA.

  View video: soon to be seen on http://www.unite2fightparalysis.org/2011_w2w_videos

- *Naba Bora, PhD, Director, CDMRP, Department of Defense* - **"Congressionally Directed Medical Research Programs for Spinal Cord Injury"**

- ***Advocate panel and discussion with the audience, led by Martin Codyre, Havey Sihota and Dennis Tesolat-.*** **"Voice of the International Spinal Cord Injury Community"**
  View video - 40 minutes

  See a summary in Marilyn's/U2fP blog here:
  http://unite2fightparalysis.wordpress.com/2011/10/30/enough-with-the-rats/

  Additional information and details over all W2W 2011 sessions are also available in the following live blog: http://sci.rutgers.edu/forum/showthread.php?t=167114