Spinal Muscular Atrophy Clinical Research Center

FALL 2010

COLUMBIA UNIVERSITY SMA CLINICAL RESEACH CENTER

INTERDISCIPLINARY RESEARCH TEAM

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From the Desk of the Director:

Darryl De Vivo, MD

It is again time to update you on our progress at the Columbia University SMA Clinical Research Center. We have added more staff and positioned ourselves for some exciting treatment opportunities on the horizon.

We welcomed Nicole Holuba in May of 2010 as our new Pediatric Nurse Practitioner to replace Vanessa Battista who resigned last November. Parenthetically, Vanessa is thriving in her new work environment in Boston and we enjoyed seeing her at the June 2010 Families of SMA Meeting in Santa Clara, CA. Nicole is picking up where Vanessa left off and is off to a great start. She is strengthening our multi-disciplinary team effort to ensure that we provide patients with the best clinical management consistent with the 2007 Standard of Care statement. She also is working closely with our collaborators in genetics and orthopedics. I hope you have had a chance to meet Nicole at one of your recent visits to the Center.

We also have welcomed Dr. Claudia Chiriboga to our attending staff joining Drs. Kulikova, Sproule, Constantinescu and myself as the Center physicians. Dr. Chiriboga has worn several hats over the years at Columbia including Director of Pediatric Neurology at Harlem Hospital and current Interim Director of Pediatric Neurology at the Columbia University Medical Center. She has had considerable experience in patient care and clinical research and has expertise in study design, biostatistics and clinical trials. These are valuable tools, indeed, as we position ourselves for more clinical trials in the near-term.

We are planning some small clinical trials to evaluate the role of exercise as a treatment in SMA, and the possible benefit of a recently FDA-approved drug, 4-Aminopyridine, as another possible treatment. 4-Amminopyridine (4-AP) has been approved by the FDA as treatment for patients with multiple sclerosis (MS). MS is certainly a very different disease than SMA, but patients with both diseases experience disabling fatigue. We hope that these two small clinical trials, one focusing on exercise and the other focusing on 4-AP, will provide us with proof of principle that these interventions hold some promise.

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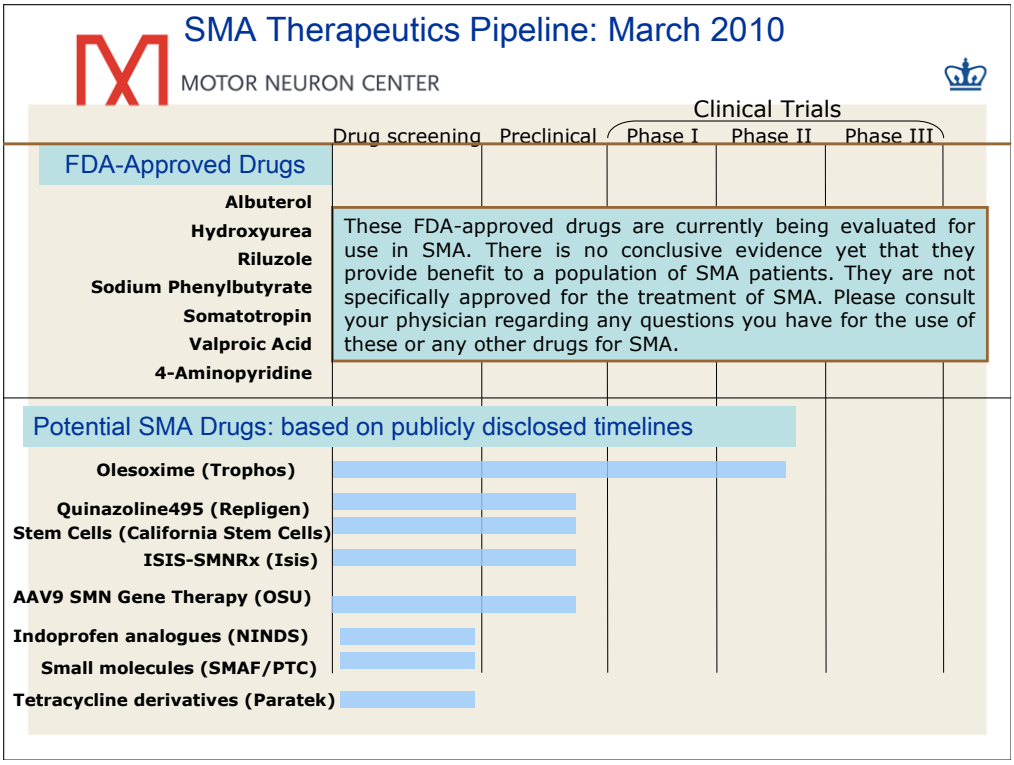
There are many other promising opportunities on the horizon which are summarized in the accompanying table. Some of these drugs are FDA approved for other diseases, and there is not much evidence at the moment that these drugs will help in SMA. Also, there is always the worry that such drugs could do harm. Please beware of this potential outcome and resist the temptation to try a drug that has no effective track record in SMA. Careful clinical trials are necessary to evaluate possible risk and possible benefit.



The table also lists several other opportunities that are emerging from pre-clinical trials, and some are already entering the clinical arena as phase I and phase II trials. Gene therapy and gene manipulation with antisense oligonucleotides are very promising in pre-clinical studies. Both approaches restore SMN gene function in cell models and animals models.

The Columbia SMA Clinical Research Center and the PNCR Network are positioned to play an active role when it is time to conduct trials. I hope you are also ready and prepared to join us as Reseach Participants. Together we will eventually make it happen and find a cure for SMA.

Thanks for your support,

Darryl C De Vivo, MD

Director, SMA Clinical Research Center

Hello from Dr. Chiriboga

By Claudia Chiriboga, MD

As the newest member of the SMA Clinical Research Center I wish to take this opportunity to introduce myself and share my background with the SMA newsletter readers. Although I am new to the Center, I am not new to Columbia, as I have been a member of the Division of Pediatric Neurology here for over 20 years, and since 2007, I've been the interim director of the Division, but wait, let me not get ahead of myself.

As a matter of background, I was born in Peru and educated in Argentina, where I graduated with Honors from the Faculty of Medicine at the National University of Buenos Aires in 1982. After obtaining my medical degree I came to New York City where I have worked ever since. In 1985, I completed pediatric training at St. Luke's-Roosevelt Hospital and was hired by Dr. De Vivo, then director of the division of pediatric neurology, to begin train-

(**Dr. Chiriboga...***continued from page 2)*

ing in child neurology. In 1988, after I completed training, I joined the Division of Pediatric Neurology at Columbia Presbyterian Medical Center under the leadership of Dr. De Vivo.

From early on, I have been interested in research, perhaps influenced by my father who was a scientist and liked to share his work with my sister and me (my first pet as a child was a white lab rat.) During my child neurology training I was drawn to clinical research. To this end, I completed a Neuroepidemiology fellowship at Sergievsky Center of Columbia University and received a Master in Public Health from the Mailman School of Public Health at Columbia University in 1991. Subsequently, I was awarded a Clinical Investigator Award and later obtained independent NIH funding. Since that time, I have been engaged in clinical research that has focused on motor function in children in a variety of disorders (prematurity, infections and perinatal exposures) that result mostly in increased tone. In addition to my research I practice general child neurology and, having trained with Dr. De Vivo, I have ample experience in the diagnosis and treatment of children with neuromuscular disorders. Every year I lecture on neuromuscular disorders to the physical therapy and occupational therapy students from Columbia University.

I am truly delighted to join the SMA clinical research center and contribute as a member of the team. For someone with my training in clinical methods and clinical trials experience this is an exciting time to engage in translational research. Nowhere is this excitement more palpable than in the area of SMA, where the scientific advances that have taken place in the last decade in the understanding of its molecular biology and neuropathogenesis, and an ever increasing understanding of how to manipulate SMN gene expression, make it feasible to envision therapeutic options in the not so distant future. I am honored and humbled to be a part of that research effort and to work with such a dedicated group of physicians and therapists and families. Further, I wish to thank the SMA Foundation for its generous support that has made this entire venture possible. I look forward to meeting all of the SMA families during your visit to the neuromuscular clinic.

Early Introduction of Power Wheelchairs in Children with SMA

By Sally Dunaway, PT, DPT

Weakness brought on by SMA can result in severe limitations in functional mobility. Here at the SMA clinic we are assessing the feasibility of independent mobility in children at an earlier age than previously considered. Introduction of power mobility early has the potential to enhance development by simulating normal skill acquisition.

There are few reports to date on early power mobility in SMA, and many children are not prescribed one until school age. Our study looks at introducing power mobility at an early age (16-36 months); could measurable results be observed that would enhance development and simulate normal skill acquisition that these children otherwise wouldn't be exposed to? Beginning this process earlier could have significant benefit, including promoting motor learning, visuospatial system development, self-exploration, cognition, and social development.

To date, six children under the age of 3 have been evaluated for power mobility. They were able to trial a demo power wheelchair at a seating evaluation done in our clinic. A successful trial requires demonstration of a few skills on The Power Mobility Skills Checklist. A custom power wheelchair is then prescribed to fit each individual child and is submitted to insurance. This process can be long and taxing, however, we find it is well worth the effort.

Once their power wheelchair is approved and delivered, participating families are contacted to document hours practiced and time to achievement of independence with each skill. Four children have attained independence in all items on

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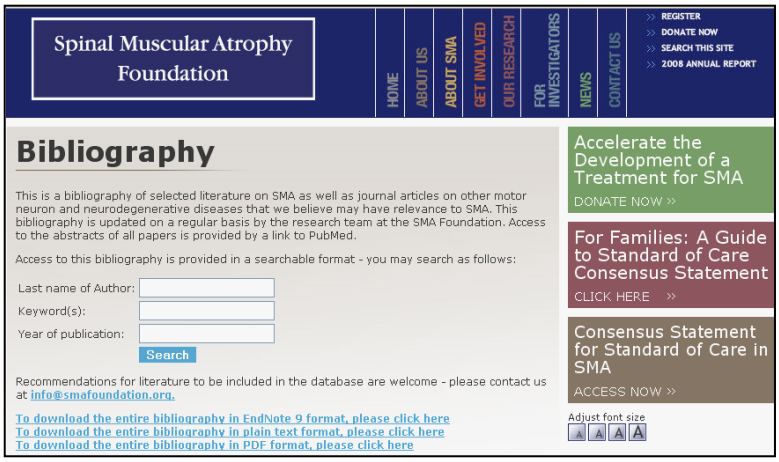
The SMA Foundation Website: A Tool for Understanding Progress in SMA Treatment Development

By Mackensie Yore, Research Associate, SMA Foundation



We at the SMA Foundation send our thanks to the SMA Clinic for this opportunity to re-introduce our website to local families. We hope that families and drug developers alike will find the information at www.smafoundation.org useful in understanding the development of SMA treatments, and we encourage you to explore the site at your leisure.

Basic information about SMA is provided in our 'Frequently Asked Questions' page on the site. If you are familiar with pages from other SMA organizations, this may look somewhat familiar. However, we have recently added links to certain powerpoint presentations used in meetings with industry and government representatives to introduce them to SMA, which may be of interest to you as well. For folks who want to dive deeper into specific subjects, more presentations will be added in coming months.

Each week, we scour scientific and medical literature to find published articles related to SMA and its potential treatments; over the years we have amassed an extensive collection of SMA citations in our SMA Bibliography. You can use the bibliography's search engine (see screen shot above) to browse our library and find publications covering the many aspects of SMA and SMA therapeutics development. The citations found there can be accessed through Pub Med or at your local library. The SMA bibliography can be found at http://www.smafoundation.org/bibliography, or from our homepage using the 'About SMA' tab on the menu.

One important question we address daily is, "how close is SMA to a treatment or cure?" To provide families with the most up-to-date snapshot of SMA treatments progress, we are working to create an annotated SMA therapeutics pipeline diagram that will list many of the potential SMA treatments and show the progress each has made in the drug development process. We anticipate adding this feature within the next month.

Finally, you can use the SMA Foundation website to help win Federal support for SMA clinical trials through the SMA Treatment Acceleration Act. This legislation asks Congress to help us obtain much-needed funds for clinically evaluating any of the potential treatments for SMA. You can help get this legislation approved by writing a letter to your congressional representative and urging them to support the SMA Treatment Acceleration Act. More information about the provisions of the Act and sample letters to congressional representatives can be found by scrolling over the 'Get Involved' tab at the top of the homepage and selecting 'Legislative Action'.

We are optimistic about the potential treatments for SMA currently being explored by biotech and pharmaceutical companies, and we hope you'll make frequent use of our website (www.smafoundation.org) to keep track of exciting, and hopefully life-changing, developments in this field.

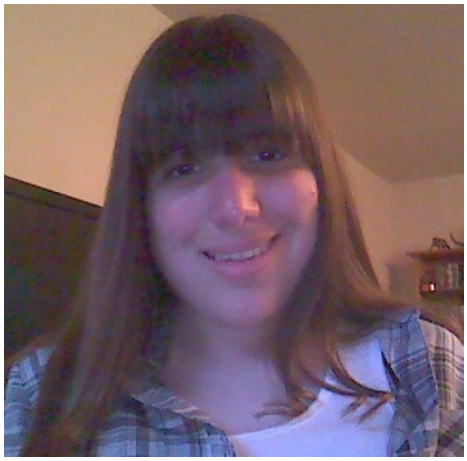
The mission of the SMA Foundation is *to accelerate the development of a treatment for Spinal Muscular Atrophy*. Our team contributes to the development of SMA treatments by:

- Fostering alliances among academia, government, and pharmaceutical and biotechnology companies working on SMA
- Increasing support and funding for SMA from the federal government
- Educating government leaders, members of the pharmaceutical and biotechnology industries, and the public at large about SMA.

Patient Spotlight: Laura Nellen

By Rachel Jerome

At nineteen years old, Laura Nellen is entering her second year at the University of San Diego. Laura was diagnosed with SMA Type III when she was two and half years old. At the time of her diagnosis, her mother was told that she might never be able to walk, the first of many projections that Laura would prove otherwise. Laura was walking by three years old, and did so without the use of assistive devices.



Time and again Laura has continued to be a source of inspiration for others through her perseverance and varied accomplishments. One of her earliest and proudest achievements was at seven years of age when she participated in a swim-a-thon fundraiser for SMA and surpassed everyone's expectations. "People never expected that I would be able to do 25 laps without stopping," says Laura. Of course, she did, and successfully raised money to contribute to Families of SMA. She has continued her fundraising efforts for Families of SMA throughout her childhood and clearly finds her fundraising work gratifying.

Laura is currently majoring in Biochemistry and minoring in Visual Arts at the University of San Diego and plans on continuing to medical school after graduation. Her favorite aspect of school is the opportunity it provides to learn and make new friends. In addition to being the first student in a wheelchair to graduate from her high school, Laura lists her decision to enroll at UC San Diego as one of her many accomplishments. Not only did she move nearly three thousand miles away from her family, she is also completely independent in her activities and travel to and from school.

Laura had spinal fusion surgery in 2003 and underwent almost 6 months of rehabilitation. She is proud of her ability to overcome obstacles like this with a fierce determination and credits her mother's support and encouragement as her main source of inspiration. "She has always been there for me…pushing me to my limits to do the best I can in everything I do," says Laura of her mother. Laura's outlook is best summed up by her personal motto, "Never say I can't, because if there's a will, there's a way".

All of our patients are awesome and inspiring; we know you think so, too! If you would like to suggest a patient who's accomplishments should be featured in future SMA Newsletters, please let us know: send an e-mail to jm598@columbia.edu. We look forward to hearing from you.

Columbia MDA Clinic Hosts Sibshops Training

By Nicole Holuba

The Muscular Dystrophy Association and Columbia University Pediatric Neuromuscular Center hosted a very successful Sibshops program developed specifically for the brothers and sisters of our patients on September 25th, 2010. Siblings of children with disabilities have their own unique needs and experiences. Sibshops helps siblings of children with special health and developmental needs obtain peer support and education. The program acknowledges that being a brother or sister of a person with special needs can be as rewarding as it is challenging and emphasizes that brothers and sisters have much to offer one another if they are given a chance.

The next Sibshops will be held in the early spring of 2011. For questions please contact: Rachel Mirkin, Columbia University Child Life Volunteer at Rachel.l.mirkin@gmail.com or Nicole Holuba, Pediatric Nurse Practitioner at nh2282@columbia.edu.

SMA Clinical Research Center seeks participants for new study

The Columbia University SMA Clinical Research Center is currently recruiting SMA Type 3 subjects to participate in a randomized trial of the effects of cardiovascular and strengthening exercising on people with SMA. Individuals who qualify for this study must be between the ages of 8 and 50, have genetically confirmed SMA, and be able to walk independently for at least 25 meters.

The study will last for 18 months, and will require that subjects come for visits at the Columbia SMA Clinical Research Center every 3 months. Each visit will consist of a series of tests that include motor function measures, a physical exam, questionnaires, an exercise capacity test which involves riding a stationary bicycle, and a test where the subject is asked to walk as far as they can in six minutes.

During the study subjects will be asked to closely follow a specific training regimen at some points and at other points they may be asked to exercise in the same manner they do normally. The exercises they will be asked to perform include biking on a stationary cycle and lifting hand weights. The main goal of the study is to see if individuals who participate in the exercise protocol have increases in their strength and/or function.

If you are interested in participating, please contact Megan Montgomery, Research Coordinator, at 212-305-1336 or mm3296@columbia.edu for more information.

(***Early Mobility...****continued from page 3)*

the checklist in an average of 7.9 months. On average, these 4 children used their power wheelchair 1.9 hours per day. One child has attained independence in 63% of items and another has attained independence in 38% of items in three months. Because of these success stories, we believe early power mobility is feasible in young children with SMA.

We've learned that on average, children under 3 years of age can be independent power wheelchair drivers within 7.9 months of delivery. There is more to learn such as motor learning principles and the effects of practice and feedback. We believe that by evaluating the quality and time spent in meaningful practice as wheelchair skills are mastered we can improve and enhance training for early power mobility. The SMA Clinic is determined and dedicated to helping any family interested in undergoing power wheelchair evaluations and encourage this process to begin as early as 16 months old.

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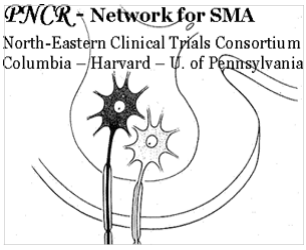

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