Jerome Lejeune
FOUNDATION USA
Research Care Advocacy

JLF USA NEWSLETTER

Winter 2016

Committed to those with Down Syndrome and other genetic intellectual disabilities

Dear Friends,

We are sending our Winter 2016 Newsletter out to you just as the calendar is turning from December 2015 to another January, a new year filled with hope and promise for children and adults living with Down syndrome and other genetic intellectual disabilities.

First, I want to introduce you to our new Board Chairperson, Deb O'Hara Rusckowski. Deb has incredible energy, a diverse background in professional areas that are at the heart of what we do, and she is passionate about our mission. She was the perfect choice by our board to lead us into year 4, and beyond of our existence here in the U.S. I'm sure you will enjoy (and be amazed) by her bio.

I thought it might be interesting to focus this newsletter on hearing from a couple of the researchers we are currently funding. **For us, research is an important advocacy tool because like Jerome Lejeune, we believe it will soon provide real hope that the future for the community of persons we serve will be better than the past.** We can't thank these, and all the researchers working to improve lives, enough for dedicating themselves each day to finding solutions to the various problems that impede the flourishing of people with genetic intellectual disabilities. We are honored to be associated with them, and it is a privilege - with your help - to support their important work.

We are also introducing you to our new clinic in Dubai that just opened in October through an interview with Dr. Andre Magarbane, the clinic director.

As we come to the end of 2015, we especially want to thank all those generous persons who have supported our work. Putting your trust (and money) behind a new nonprofit takes vision and courage. We are mindful of that each day, and are so grateful for your trust.

For those of us who are privileged to carry on the legacy of Jerome Lejeune, our mission of research, care, and advocacy is seen as a means to an end, and not an end in itself. The true "end" is the PERSON with intellectual disability, and that drives us to do all we can each day to make their lives better. **Our hope is that all will come to love and respect them for who they are as human persons, and that the support we provide through our mission will allow them to flourish more fully in society** – not that they will be able to DO more, but so they can do whatever they choose with better health, more opportunity, and greater acceptance in society.

Wishing you peace, joy, safety and happiness in 2016, and extending our gratitude to you again for your support of the Jerome Lejeune Foundation.

Mark Bradford
President

2015b USA Research Funding

Research is at the heart of the mission of the Jerome Lejeune Foundation. Thanks to the generosity of our benefactors, we are able to offer two opportunities each year for researchers to apply for funding from the Foundation to support their research.

For the second cycle of 2015 our Scientific Advisory Board recommended three new grants to researchers working to improve the lives of people living with genetic intellectual disabilities. Two of these projects are investigating fragile X syndrome and the other is a project to improve reading comprehension in children with Down syndrome.

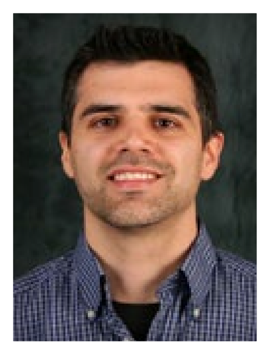
Nancy Raitano Lee, PhD
Drexel University, Philadelphia
Psychology Department

Elucidating the Cognitive Underpinnings of Reading Comprehension Difficulties in Children with Down syndrome

Current estimates suggest that individuals with Down syndrome, on average, read at an early elementary school level. Dr. Lee believes that children with Down syndrome have a syndrome-specific reading profile, that if better understood can be used to develop more effective reading interventions.

In this clinical study, Dr. Lee will identify predictive models of reading difficulties in people living with Down syndrome by contrasting their development with two other groups. Specifically, she will develop specific reading profiles for three groups of children: 1.) Those with Down syndrome, 2.) Those whose intellectual disability is due to mixed causes, and 3.) Typically developing youth. She will be searching for syndrome-specific weaknesses that may be strongly predictive of reading in Down syndrome compared to the other groups.

Anticipated benefit: The development of better strategies to teach reading comprehension for individuals living with Down syndrome.



Roberto Galvez, PhD
University of Illinois at Urbana-Champaign
Dept. of Psychology

The role of VEGF-A in Fragile X Syndrome abnormalities during development; implications for therapeutic interventions

Fragile X syndrome is the most common form of inherited mental retardation. Studies in a mouse model of fragile X have shown that they possess an increased level of a protein called vascular endothelial growth factor A (VEGF-A) that can cause an increase in the growth of axons and neurites, the long thread-like parts or projections of nerve cells that carry impulses from cell to cell, and also increase cell survival. This increase results in abnormalities of neuronal structures observed in people with fragile X.

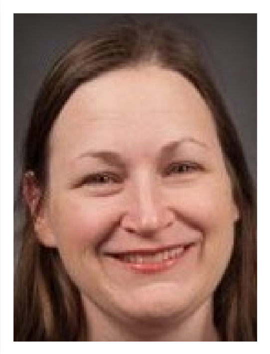
Continued on page 2

2015b USA Research Funding Cont.

Dr. Galvez and his team have shown that a drug called Avastin, an FDA approved medication used for metastatic cancer therapy, improves novel object recognition in adult mice with fragile X. Avastin acts in cancer patients by slowing the growth of new blood vessels and in mouse models of fragile X, it reduces a marker for this increased axonal growth to normal levels.

This improvement in memory suggests to them that neuronal abnormalities in fragile X are at least partially due to excess brain VEGF-A and also that many abnormalities in fragile X may be alleviated by blocking VEGF-A. Funding from the Jerome Lejeune Foundation will allow Dr. Galvez and his team to expand these findings by exploring the effectiveness of Avastin on alleviating fragile X abnormalities during development.

Anticipated Benefit: Further investigation of a potential therapy to improve developmental outcomes for individuals living with fragile X syndrome.



Wendy Machalicek, PhD BCBA-D
University of Oregon, Eugene

Project i-HELP Internet based behavioral consultation for families of children with Fragile x syndrome who engage in challenging behavior

Abstract of the research project:
Challenging behaviors such as self-injurious behaviors often appear during early childhood in males with full mutation fragile X syndrome. To date, behavioral intervention research with individuals with fragile X has been limited, in part due to the low incidence of the population in any particular geographical area negating experimental group design research. Dr. Machalicek believes, however, that the use of video teleconferencing technology offers a novel way to deliver time intensive parent coaching and feedback.

Funding from the Jerome Lejeune Foundation will allow Dr. Machalicek to evaluate the effects of distance parent education and coaching delivered via "real time" desktop videoconferencing on mother's use of an evidence based behavioral intervention to decrease challenging behavior of their young boy (ages 24 to 50 months) with fragile X. In addition, the sustained effects of this intervention will be evaluated for 18 months following conclusion of the intervention.

Anticipated benefit: The development of a novel methods of assisting parents of children with fragile X in addressing challenging behaviors to better incorporate them into families and communities.

Interview with
Dr. Alper Bozkurt

Dr. Alper Bozkurt, Assistant Professor in the Department of Electrical and Computer Engineering at North Carolina State University has received funding from the Jerome Lejeune Foundation USA to develop a small device to improve the assessment of obstructive sleep apnea in young children. We asked Dr. Bozkurt to share a bit about his work with us, and here are his responses. His responses provide insight into the importance of screening for OSA for both the short and long term well-being of children with Down syndrome.

1. At what age do you believe OSA is a factor for children with Down syndrome?

It is thought that about 60% of children with Down syndrome have had an abnormal sleep study by the time they are 4 years old. We believe that 30% of infants with Down syndrome display moderate to severe sleep apnea after they were screened based upon parental concerns. However, these reports are limited in their reliability because of the current difficulty in truly assessing OSA in young children.

2. How effective are current methods for diagnosing and treating OSA in young children?

Currently, most screening of young children follows upon parents reporting symptoms. Current testing with polysomnography is burdensome and not reliable. That is the reason we are developing this device, to make testing less burdensome and more reliable. In fact, our device will also provide a benefit to adults with Down syndrome by making a sleep study less intimidating. Treatment is another story. Traditional methods of treatment such as removing tonsils and adenoids, or continuous positive airway pressure using a CPAP device are still the standard of care, but there are others investigating new treatments, including phrenic nerve stimulation.

3. How does your device differ or improve upon current ways of diagnosing OSA in children?

Traditionally, polysomnography is done in a sleep lab and is actually quite invasive. As I have said previously, most screening is done by interviewing parents regarding symptoms. Our device is a miniaturized wireless system that can simultaneously record electrophysiological signals (electroencephalography (EEG), electrooculography (EOG)), cerebral hemodynamic changes (Near Infrared Spectroscopy (NIRS)) and head movement (inertial measurements) to study and predict abnormal sleep performance in children (age 2 – 5 years) with Down syndrome. This device is currently in use with adults at risk for obstructive sleep apnea syndrome, but with modifications could be well-suited for pediatric populations.

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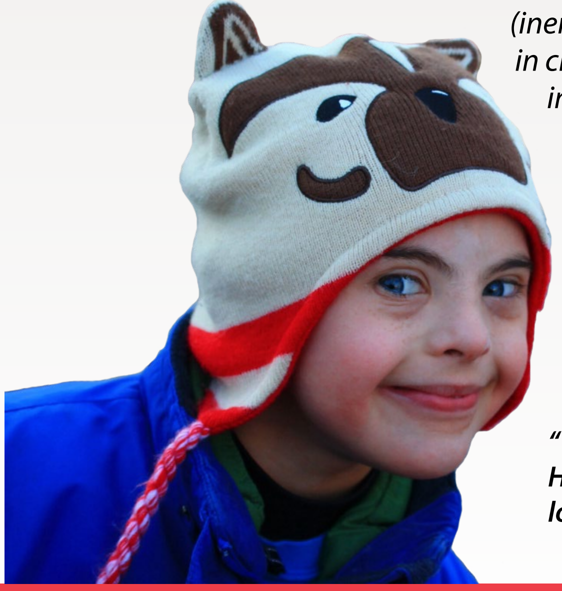


"We are so grateful for John Paul. He teaches us the real meaning of love and acceptance."

Interview Cont.

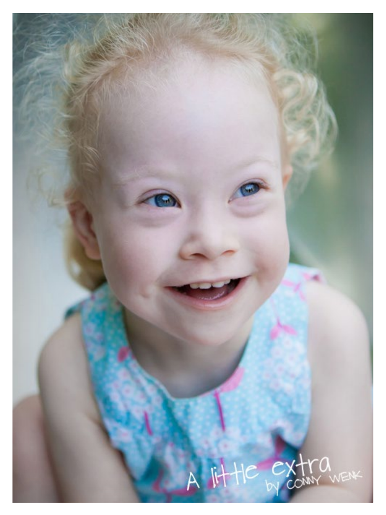
Dr. Alper Bozkurt

4. With an earlier diagnosis are there effective ways of treating OSA in young children?

Absolutely. We can apply current research to known cases of OSA in young children and measure the success more effectively.

5. What do you believe will be the long-term benefits of earlier diagnosis and treatment?

Researchers know that OSA can be the cause of some degree of intellectual impairment. The brain, as well as the heart and other organs, need oxygen. OSA can cause behavioral problems, growth delays, high blood pressure, heart problems and others. Parents often think of lethargy as a symptom, but hyperactivity can also be a symptom of OSA in children with Down syndrome.



6. When would you expect your device to be available for use in the clinic?

Our initial prototype was designed for adult subjects and we will use our Jerome Lejeune Foundation grant to miniaturize the system to pediatric level. We are expecting to start feasibility studies by the end of Spring of 2016. Then we will have a larger clinical study to assess the efficacy of the system. We are hoping that our system will be available for general use in clinic within 2-3 years.

NOW AVAILABLE

Jerome Lejeune to the Least of These My Brothers and Sisters (DVD)

To celebrate the 20th anniversary of the death of Dr. Jerome Lejeune, **filmmaker Francois Lespes conducted extensive interviews with those who knew Jerome Lejeune, or have been affected by him in some way.** He combined these interviews, conducted in both France and the U.S., into a beautiful documentary on his life: Jerome Lejeune to the Least of These My Brothers and Sisters.

Mr. Lespes probes Lejeune's character through his interviews and his presentation is enriching and informative. **It also causes one to challenge the depth of their commitments when confronted with this man who sacrificed honor and prestige, and even funding for his research program** to hold fast to what he knew to be true: that every human being is worthy of respect and that a doctor's obligation is to defend his patients from those who might want to do them harm at any cost.

This DVD presents the documentary with English voices dubbed over the French. Also included is the original French version and another version with Spanish subtitles. As a special bonus, there are additional recollections by friends, family, and former colleagues who reflect on his genius, his faith, and ultimately his profound humanity.

The DVD is available from the Jerome Lejeune Foundation for $16 plus $4 shipping (each copy). Order online at www.LejeuneUSA.org/DVD.

Interview with Dr. Andre Magarbane

about the new Lejeune clinic in Dubai

Dr. Andre Magarbane, a former student of Dr. Jerome Lejeune, lives in Beirut, Lebanon where he is on the medical faculty of a university there, but he also spends part of each month in Paris working with the Jerome Lejeune Institute. Dr. Magarbane has just opened a new clinic in Dubai for the Jerome Lejeune Foundation and here we ask him about this new project and its intended purpose in serving the Down syndrome community there.

1. Dr. Magarbane, you live in Beirut where you work as a geneticist and you are also the director of research at the Jerome Lejeune Institute in Paris where you collect, process, and curate some 4,000 specimens in the Institute's biobank. You are also an active researcher and now you have opened a new clinic in Dubai, the Centre Medico-Psycho-Pedagogique for the Jerome Lejeune Institute. You are a busy man. What inspired the Jerome Lejeune Foundation and Institute to open this new clinic in Dubai, and how is it responding to an unfulfilled need in the UAE?

The idea started when we noticed that very few things were done for intellectually disabled persons. So we decided to initiate some activities like lectures, workshop and this collaboration with the Jerome Lejeune Foundation. For the moment it is not a clinic, but a paraclinic where speech therapists, physical therapist, and psychologists will be present to help children presenting different problems from intellectual disability to isolated dyslexia.

2. Working as a physician in both Europe and the Middle East (Lebanon and Dubai), is it possible to compare the needs of individuals in both places and how children and adults with Down syndrome are accepted in their families and society in each place?

People with intellectual disabilities are much more accepted in Europe than in Arab countries where it is still a big thing to have a child with these kinds of genetic problems. It is assumed in that culture that the parents did something wrong. We have to change this.

3. The clinic in Dubai has both a medical and pedagogical purpose. What do you see as the greatest need of those living with Down syndrome in Dubai? How many patients do you anticipate serving there and do you anticipate that you will be serving both the Emirati population as well as those living and working in Dubai from other countries?

We will offer excellent follow-up for all children brought to us. We aren't certain how many patients will use the Center yet, but we will welcome all who come to us. Whether they are from poor or rich families, they will all be welcomed and treated by the same staff.

Continued on page 6

"Mia is sunshine and light and everything good in the world. She's compassionate, a peacemaker and a nurturer. She's incredibly loyal and loving."

Interview with Dr. Andre Magarbane Cont.

4. You have done some fascinating research on transcriptomes. Can you briefly describe what you have learned and if there are any therapeutic implications gathered from your research.

Yes. To be very simplistic, transcriptomes are readouts of how genes in a cell are expressed. We established a transcriptome of DS patients with so-called "high" and "low" IQs and found that two genes on chromosome 6 called HLA-DQA1 and HLA-DRB1 may be a factor in distinguishing between the two populations. Larger multi-center studies are needed to determine in a valid way the presence of such markers. The ability to determine valid markers could have major consequences for identifying targets for treatment. For example, the genetic association with HLA suggests the involvement of the immune system in intellectual disability and offers new targets for drug development. Continued and increasing investments in research on the genetic and molecular basis of T21 promise to transform the lives of these individuals and the communities in which they live.

5. You have been involved in working with the Jerome Lejeune Institute for several years. Can you provide a brief summary of how the mission has evolved in light of new research developments and/or changing needs of those living with Down syndrome and other genetic intellectual disabilities.

The Jerome Lejeune Foundation, and the Jerome Lejeune Institute remain on the cutting-edge of scientific research into the cause and treatment of genetic intellectual disability. The last few years have been a particularly exciting time in Down syndrome research, and I am proud to say that we have been at the forefront of supporting and conducting this research globally. The Foundation's current involvements in drug development and in conducting and funding clinical trials both at the Jerome Lejeune Institute, and elsewhere, ensure that the future for children and adults living with Down syndrome, in particular, is full of hope.

Meet Our New Chairperson, Deb O'Hara Rusckowski

The Board of Directors of the Jerome Lejeune Foundation USA elected Deb O'Hara Rusckowski as our new chairperson in New York on November 20th and they could not have made a better choice. Deb is deeply committed to the nonprofit sector, and especially to the Jerome Lejeune Foundation where she is able to combine her three passions of nursing, business, and bioethics.

Responding to her election as Board chairperson, Deb said "Jerome Lejeune's family has done an amazing job of continuing his incredible legacy in France. I am excited and honored to have been entrusted to lead the Jerome Lejeune Foundation USA into a new phase. We are exploring meaningful partnership with other organizations, and continue to search for more and more ways to expand the profound love, that was the hallmark of Jerome Lejeune's life, to the community of the intellectually disabled in the U.S."

Deb has been a Critical Care nurse for over 30 years. She earned both her BSN and an MBA from Northeastern University in Boston and held several marketing positions at Hewlett Packard, Agilent and Marquette Electronics. Deb graduated from Boston College in 2014 with yet another degree, a Masters in Theology with a concentration in bioethics.

Continued on page 7

Meet
Deb O'Hara Rusckowski Cont.

Deb's past philanthropic engagements include four years on the Board of the American Heart Association, and five years on the Board of Directors for Boston's Healthcare for the Homeless Program. She is a member of the Federal Disaster Medical Team and was deployed to New York City on September 11, 2001 after the terrorist attack on the World Trade Center. She has been on missions to Bosnia twice and the Dominican Republic several times.

In 2007, Deb initiated a nursing educational program at CRUDEM's Hôpital Sacré Coeur in Milot, Haiti, and continues to serve on the board while working to improve nursing education. With a deep commitment to the people of Haiti, she spent several weeks working there after the devastating 2010 earthquake, both on the ground and on the USNS Comfort ship for Project HOPE.

Deb currently works for the United Nations on the Committee to Stop Trafficking in Persons (CSTIP). She is coordinator of an educational exhibit called a GIFT Box that has been exhibited in Boston/New England and Haiti to raise awareness and empower people in the fight against human trafficking. She is also involved with several other philanthropic Boards in addition to the Jerome Lejeune Foundation, including RAD-AID, and the World Youth Alliance (WYA). Deb is a member of the American Association Order of Malta and serves on its Board of Councilors, and she participates in the Order's annual pilgrimage to Lourdes as a member of the medical team. She is also leading a media project for Cardinal Dolan, the Archbishop of New York, placing radio ads with Catholic messages on secular radio. In addition, she is on a Steering Committee for the Sisters of Life.

Deb served for seven years as Coordinator/Director of the Respect Life Office for the Archdiocese of Boston, and implemented a new chastity curriculum for schools and parishes. She also initiated a young adult program called Pure in Heart in Boston, Haiti, Ireland, UK and Kenya, and brought Theology of the Body training and a Natural Family Planning program to Haiti.

Born in Milwaukee, Wisconsin, she grew up mostly in Boston but now resides in New York City with her husband Steve.

Interview with Dr. Hilde van Esch

Dr. Hilde van Esch published an article recently with her colleagues on research that was funded by the Jerome Lejeune Foundation. Dr. van Esch is studying a rare x-linked chromosomal disorder called MECP2 duplication syndrome that only affect boys. Dr. van Esch has shared some of her findings with us here and points to the possibility of one day providing targeted therapeutic interventions to improve the lives of those boys born with this genetic condition.

If we are not mistaken, you were the first to describe MECP2 duplication syndrome. How did you make this discovery and do you know the incidence of this syndrome in the population?

In the Center for Human Genetics at the University of Leuven, we have a long tradition in genetic research of intellectual disability syndromes that are linked to the X chromosome.

Continued on page 8

Interview Cont.

Dr. Hilde van Esch

Back in 2005, we developed a specific micro-array chip, to look for genomic aberrations on the X chromosome in the many unsolved X-linked families. In four different families we detected an extra copy of a small region on the long arm of the X chromosome (duplication) in all severely affected male individuals. Within this duplicated region, the MECP2 gene is present, and given the important role of this gene during brain development and functioning, we hypothesized that increased protein dosage would be responsible for this syndrome. Our initial hypothesis has been confirmed with the many novel cases reported and diagnosed today.

It is however difficult to know the exact incidence, but we know that the MECP2 duplication is one of the most frequent aberrations on the X chromosome found in male individuals with severe developmental delay.

Can you describe the features of MECP2 duplication syndrome?

The first symptoms are already present at birth. Most children are hypotonic and sometimes have feeding problems. Their motor and cognitive development is severely delayed. Some children learn to walk independently and can use some single words. In half of the children, epilepsy occurs, starting during childhood. These epilepsies are often drug-resistant and can have an important impact on further development and functioning. We also notice an increased susceptibility to infections, mostly of the upper and lower airways. This might results in early demise, unfortunately.

Your research also points to a possible treatment for MECP2. I believe it is a drug also used to inhibit the growth of cancer cells. How does this drug appear to resolve the cellular defects in MECP2dup?

We know that MECP2 plays an important role in the control of other genes (switching them on or off). That is the reason that we used more than 35 different drugs that are known to have an effect on gene regulation. Only one of them was able to rescue the abnormal morphology and the abnormal electrophysiology that we observed in the disease neurons. Indeed, NCH51 has been shown in other experiments (in a dish) to have an effect on cancer growth. One can hypothesize that in the case of cancer, also the gene regulation is disturbed. However, we will need more in depth experiments to unravel the exact mechanism of this drug.

Does your research have any benefit for other genetic intellectual disabilities?

Although we focused on one particular neurodevelopmental disease, I am confident that everything we can learn about normal and abnormal neurodevelopment, will be of benefit for other syndromes. We now know that the common denominator of many intellectual disability syndromes is the dysfunction of the synapse (the billions of places where neurons communicate with each other). It is clear that we need drugs that not only target specific proteins, but rather have an effect on entire pathways, irrespective of the underlying genetic defect.

**This is only part of Dr. van Esch's interview. See the newsletter online to read the complete version.

Ways YOU Can Help

Become a Donor

Your gift supports our mission of research, care, and advocacy following the medical and ethical standards of Dr. Jerome Lejeune, the "father of modern genetics." Please make a tax-deductible contribution today.

Become a Volunteer

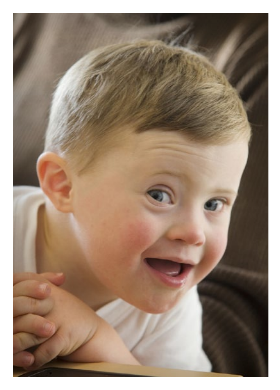
Contact us at contact@LejeuneUSA.org to join our network of volunteers and advocates.

Invite us to a Meeting

If you are a member of a local Down syndrome support group, we would love to learn more about your work and tell you about the work of the Foundation.

Spread the Word

Pass this newsletter on to families you know who might be interested in joining us in our exciting work.



Want to Learn More?

To learn more about the important research we fund, read stories about the care we provide and explore and join our network, visit our website at **www.LejeuneUSA.org**.

Giving to JLF USA

The Jerome Lejeune Foundation USA is a registered 501(c)(3) charitable organization. All contributions made to the Foundation in the U.S. are fully deductible from federal income tax.

YOU are the Jerome Lejeune Foundation. TOGETHER we can do amazing things!

Checks are welcomed at the address below, or you may go to the following link to contribute online: ***www.LejeuneUSA.org.***

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Pioneering Innovative Therapies *to improve the lives of those with genetic intellectual disabilities*

Created in 1996 in Paris and in 2012 in the United States, the Jerome Lejeune Foundation is registered with the Internal Revenue Service as a 501(c)(3) nonprofit corporation serving individuals with genetic intellectual disabilities and their families...

Research in order to identify targeted treatments for patients affected by genetic intellectual disabilities. The Jerome Lejeune Foundation is the world's largest private funder of research on trisomy 21 (Down syndrome) and other disabilities. The Foundation funds projects in basic science, and also early clinical trials on drugs that offer hope that commercially available products will one day be available to improve the lives of people affected by genetic intellectual disabilities.

Care to provide specialized medical treatment and follow-up throughout the patient's life. The U.S. Foundation is involved in improving medical education and developing guidelines for care of individuals modeled after the work of the Lejeune Institute in Paris, a medical clinic which provides care to over 6,000 patients.

Advocacy for the fundamental human rights of persons with genetic intellectual disabilities. The Jerome Lejeune Foundation is committed to the inherent human dignity of all persons and the protection of life from conception to natural death.

Are You Connected?

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