ISNV

International Society for NeuroVirology

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Editor-in-Chief: Dianne Langford, Ph.D.

A Message from the new ISNV President, Lynn Pulliam

It is a great honor and pleasure to serve as the next ISNV President, following Peter Kennedy's successful six years in office. The study of viruses and other infectious pathogens that infect and affect the brain continues to be a hot topic in medicine as well as in society in general. With Avi Nath as Vice President, we have come up with some new initiatives for our Society for the next three years that we'd like to share with you.

Our goals are to increase awareness of the ISNV and it's subspecialties, to support collaborations nationally and internationally, and to educate and mentor our junior scientists. Toward this end, we plan to help sponsor both satellite and international meetings. With our members' assistance, we also plan to increase global participation by more aggressively seeking industry and pharma support for speakers to include members from resource-poor

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Peter Kennedy completes his second term as ISNV President

Brian Wigdahl, Philadelphia PA

At the end of December 2009, Dr. Peter Kennedy of the United Kingdom will complete his second three-year term as President of the International Society for NeuroVirology and will hand the reigns over to Dr. Lynn Pulliam of the United States. Dr. Kennedy succeeded the Founding President of the ISNV, Dr. Brian Wigdahl, in 2004. With the support of Dr. Kennedy, the Society's membership has grown progressively and during the past year, surpassed 300. Over the past six years, the Society's financial stability has increased with the establishment of a reserve account that has been used on a consistent basis to fund additional trainee travel awards for our symposia. The Society was also formally audited by an independent accounting firm and was provided with a satisfactory report in conjunction with the change in treasurers in 2007. The Society now has its first administrative employee, Ms. Sandy

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Science News

Monoclonal antibody treatments and the emergence of Multifocal Leukoencephalopathy

Pasquale Ferrante
Department of Public Health – Microbiology – Virology, University of Milan

Monoclonal antibodies (MAbs) are considered effective therapies for autoimmune and lymphoproliferative disorders. Among the MAbs approved by the FDA, Natalizumab, Efalizumab and Rituximab have been thought to be promising for the treatment of Multiple Sclerosis (MS), psoriasis and lymphoma, respectively, because of their potential for patients failing other immunomodulatory treatments.

The three drugs act by recognizing different antigens: Natalizumab blocks lymphocyte extravasation, by interacting with the VLA4 receptor, and thus inhibiting the invasion of autoreactive cells into the Central Nervous System (CNS); Efalizumab targets LFA1, blocking the migration of T lymphocytes through the endothelium during inflammation; Rituximab binds to CD20 on human B lymphocytes, killing B-cells via different mechanisms such as complement and antibody-dependent citotoxicity.

As the effects are not selective, these drugs could reduce immunosurveillance within the CNS, leading to increased susceptibility to infections. In fact, during the post-market surveillance of the three MAbs, sides effects have been described. In particular, special attention has been addressed to the development of Progressive Multifocal Leukoencephalopathy (PML), a fatal demyelinating disease of the CNS, caused by the infection of Polyomavirus JC (JCV). Since the marketing approval by the FDA, 23 PML cases have been reported among the worldwide MS patients treated with Natalizumab, 3 among the patients treated with Efalizumab and 58 among the patients treated with Rituximab. Thus, enhanced pharmacovigilance for PML and additional measures necessary to ensure the safe use of Natalizumab and Rituximab were introduced, and due to the unfavourable balance between risks and benefits, Efalizumab was withdrawn from the market by the manufacturer.

Immunohistochemical evidence of JCV infection of a large number (panel A) and rare (panel B) oligodendroglial cells in brain of HIV positive subjects with OND and PML. In panel C immunohistochemical analysis of an autopsy sample of brain with cerebrovascular diesase used as negative control of immunohistochemistry is shown: no cells were stained. Immunoperoxidase, with light hematoxilyn counterstaining, original magnification 400x (Delbue S, Branchetti E, Boldorini R, Vago L, Zerbi P, Veggiani C, Tremolada S, Ferrante P. Presence and expression of JCV early gene large T Antigen in the brains of immunocompromised and immunocompetent individuals. J Med Virol. 80(12):2147-52, 2008).

Certainly, the immunosuppression induced by the drugs provides suitable conditions for increased JCV replication and spread to the CNS, where the virus selectively destroys the oligodentrocytes, but to date the model of viral dissemination/reactivation and of PML development remains undefined.

Thus, long term surveillance is required to quantify the incidence of PML and high index of suspicion is needed, especially in patients developing neurological symptoms during the treatment. As biologic agents aimed at immune system manipulation are currently widely used in therapy, the risk of life-threatening infections will continue to be problematic.

Moreover, as JCV is widely diffused in the healthy population and there is no cure for PML, understanding the pathogenesis of this devastating neurological disorder is an urgent need. In particular, defining the risk factors that allow a normally non-pathogenic virus to produce lesions in the brain and to reactivate in treated patients will be a big and exciting challenge for neuro- virologists around the world.

NIH News

A Note from NIDA

Diane Lawrence, Bethesda MD

Studying HIV/AIDS in substance users is complex, with variability in drug use patterns as well as added issues of coinfections, comorbidities, and both disease-related and treatment-related complications. However, use of licit and illicit substances is a reality in a large proportion of HIV-infected and at-risk individuals, and must be considered for successful outcomes in treatment and prevention. Over the last few years, the National Institute on Drug Abuse (NIDA) has put significantly greater emphasis on supporting basic and clinical biomedical HIV/AIDS research. NIDA's

HIV/AIDS Etiology and Pathogenesis research funding, of which 50% supports HIV neuropathogenesis projects, increased 25% from FY2008 to FY2009. Several initiatives have stimulated exciting new research directions, including past RFAs on HIV neuropathogenesis, viral and host genetics, proteomics, pharmacodynamics of drug interactions, and epigenomics. NIDA created the Avant-Garde Award, modeled after the NIH Pioneer Award, to attract high-impact transformative research that is likely to open new avenues of research for the prevention and treatment of HIV/AIDS in drug abusers. NIDA also has a strong interest in building HIV/AIDS training through NRSA fellowship and training grant support, support of AIDS International Training Programs, and a strong mentored K program (including AIDS K99/R00 awardees). To facilitate the entry of newly independent and early career investigators into research on the intersection of drug abuse and HIV/AIDS, NIDA developed the AIDS-Science Track Award for Research Transition (A-START) mechanism (PAR-10-021). More information on NIDA's AIDS Research Program can be found at http://www.drugabuse.gov/AIDS, or by contacting Diane Lawrence, who has been involved with ISNV for several years and has encouraged NIDA to become more involved. Dr. Lawrence will be happy to discuss potential ideas for research or symposia.

Summary of Third Meeting on HIV Infection and the Central Nervous System, Stressa, Lago Maggiore, Italy, Oct. 22-24, 2009

Jeymohan Joseph and Avi Nath

The first day was an "Assessment of Resources & Opportunities for NeuroAIDS Research in Eastern Europe & Central Asia with respective representatives. Wide variations in HIV incidence were reported among countries: Bulgaria, Turkey, and Lithuania with the lowest levels; whereas, Russia and Ukraine were among the highest. High incidences of tuberculosis meningitis among HIV patients were reported from Georgia, Ukraine and Romania. The Romanian NIMH-funded studies are among the first globally are aimed at understanding the impact of clade F on HIV neuropathogenesis. The Global Initiative on Psychiatry supported by the Ministry of Foreign Affairs in the Netherlands is implementing a project "Mental Health and HIV/AIDS in Central Asia, Caucasus and South East Europe" to foster a better understanding of mental health issues in HIV-infected individuals in the region.

The second day of the meeting focused on "Biology of CNS infection and injury: Past, present and future" encompassing a wide range of topics including clade-specific differences in neurocognitive dysfunction and data showing increased clade D-specific neurocognitive dysfunction compared to clade A. Several talks were presented on the dynamics of antiretrovirals in CSF and in HIV-infected macrophages, with the newer entry inhibitors showing excellent CNS penetration. Discussion revolved around the need for IC50 versus IC90 as a relevant endpoint for measuring CSF antiretroviral levels and the need for determining CNS toxicity and brain levels of these drugs. Interestingly, data from an international cohort showed that withdrawal of antiretroviral therapy resulted in improved cognitive function. Discussion followed on the possible underlying mechanisms to explain this counterintuitive observation.

It was also pointed out that nearly 40% of patients in the post-ART era with neurocognitive abnormalities have no evidence of encephalitis at autopsy, suggesting a need to revisit neuropathology in this patient population. A variety of neuroimaging techniques that had been used to detect abnormalities in HIV-infected individuals were presented as well. Techniques, such as diffusion weighted imaging, functional MRI and spectroscopy may be sensitive approaches for identifying asymptomatic dysfunction.

Elevations in CSF levels of neurofilament and neopterin soon after a primary infection suggest that viral neuroinvasion occurs fairly quickly after infection. The presence of pleocytosis in the CSF was associated with a more rapid decay of viral load. The variability in the env region from brain-derived sequences was reported to be low compared to the periphery, with unique mutations in the V1/V2 region that enhance macrophage tropism. Additionally, a metabalomics screen of SIV-infected macaques with encephalitis found increases in phospholipase A in both CSF and brain.

Basic and clinical aspects of JC virus and PML were the focus of the third day of the meeting. Clinical presentations and diagnostic neuroimaging tools including magnetic transfer imaging were discussed. Risk factors for PML and challenges in diagnosis and management of emerging complications, such as IRIS, were addressed. Predictors of outcome in PML patients included reports of associations of increased T-cell responses to JCV with better outcome, and higher CSF viral loads with poor outcome. Virus-host interactions with emphasis on serotonin receptor and sialic acid moieties in mediating JC virus entry, viral mutations important for viral release from peripheral reservoirs and regulatory region rearrangements were discussed. Results from ongoing clinical trials for mefloquine used in PML patients was considered as well.

ISNV Highlight - Pankaj Seth, Ph.D.

Dianne Langford, Philadelphia PA

When it comes to HIV neurovirulence, studies from Dr. Pankaj Seth's group at the National Brain Research Centre in Manesar, Haryana, India are on track with answers to why infection by some clades of HIV-1 may result in higher incidences of HIV-associated dementia than other clades. Recent findings from his lab published in Annals of Neurology describe the significance of the dicysteine C30C31 motif in the HIV-1 Tat protein sequence (Annals of Neurol. 2008, 63(3): 366-76). The neurotoxic potential of isogenic variants of Tat corresponding to HIV-1B (C30C31) and -C (C30S31) was assessed in human fetal CNS progenitor cell-derived astrocytes and neurons. Results suggested clade-specific functional differences in Tat-induced apoptosis in primary human neurons, demonstrating that HIV-1C Tat is relatively less neurotoxic than Tat from clade B. Recently, Dr. Seth's laboratory has made yet another interesting observation describing a previously undefined role of HIV-1 Tat. Studies from his group have found that Tat affects the proliferation and differentiation capabilities, particularly neurogenesis, of human neural precursor cells (unpublished data).

Dr. Seth was first introduced to the field of Neurovirology in the summer of 1996 while working in Pathology at the Uniformed Services University in Bethesda, MD. In 2002, Dr. Seth joined the laboratory of Dr. Eugene Major at the National Institute of Neurological Disorders and Stroke (NINDS). Dr. Seth accepted a faculty position at the National Brain Research Centre in 2003 where he established his own laboratory to study NeuroAIDS. With over 30 peer-reviewed research publications, Dr. Seth and collaborators at Johns Hopkins and NIH, continue to investigate potential clade-specific characteristics in HIV-1-associated CNS disease.

Peter Kennedy completes his second term as ISNV President continued

Weiss, who has greatly contributed to the efficient running of the ISNV.

Dr. Kennedy's support was instrumental in the formation of seven ISNV committees covering fundraising, membership, publications, women in neurovirology, investigators in training, meetings, and international interests. The committees are headed by chairs and have greatly contributed to, and facilitated, the smooth running and diversification of interests of the Society. The formation of the Women in Neurovirology Committee as a distinct entity in 2004 has also led to several new ISNV activities including a number of special mentorship workshops at the past several symposia.

During his presidency, Dr. Kennedy has guided four international symposia in Europe and the USA, all of which were sponsored in part by the ISNV. The symposia have continually improved in quality and have provided opportunities for a spectrum of speakers to present their latest experimental results to the neurovirology community. The past several symposia have seen the development of the Paradigm Builder Lecture, Women in NeuroVirology Lecture, Bill Narayan Lecture, and Neurological Infections Lecture. Dr. Kennedy has taken great pride with regard to the development of trainees, with increased funding for more travel awards and the award of plaques for best presentations named in honour of past ISNV Pioneers in Neurovirology.

Dr. Kennedy also played an active role in forging an official alliance with the Society of Italian Virologists so that there was a reciprocal arrangement for reduced membership fees for members of one society joining the other. Having shown significant and sustained leadership of the Society, Dr. Kennedy leaves it in excellent shape for his successor to take over. The ISNV thanks Dr. Kennedy for his exceptional efforts over the past six years.

ISNV Highlight - Monique Lafon, Ph.D.

Dianne Langford, Philadelphia PA

Dr. Lafon joined the Pasteur Institute in Paris, France in 1983 with the charge of developing an immunological research program in the Rabies Unit. After receiving a PhD in microbiology/biochemistry from the University Paris VII, Monique joined the faculty at Pasteur as Assistant Professor and served as Co-director of the WHO International Reference Center for Rabies. Currently, Dr. Monique Lafon serves as the Chef de Laboratoire and as Head of the Unit of Viral NeuroImmunology formed in 2001 at the Institut Pasteur.

Dr. Lafon describes the main theme of her group as "studying how some neurotropic viruses favor neuronal survival and identifying the virus encoded entities which control them." Dr. Lafon explains the challenges for her group "to attribute death or survival functions to specific domains of the rabies virus G, interactions with discriminator cell proteins and to analyze the role of innate immune response in rabies virus neuroinvasiveness." Among the extensive work conducted by Lafon and colleagues is a study showing that human cerebellar cortical neurons express Toll-like receptor 3 during neuroviral diseases such as rabies viral encephalitis, herpes encephalitis and in neuropathological diseases including Alzheimer's and stroke (Jackson et al. 2006). These studies suggest that neurons may contribute to the inflammatory reaction in a variety of neurological diseases. A more recent study by Lafon and colleagues describes the exploitation of the host immuno-inhibitory protein, B7-H1 by the neurotrophic rabies virus to promote successful host invasion (Lafon et al., 2008). In the murine model of rabies infection, significantly increased B7-H1 expression was induced in infected neurons. Likewise, B7-H1 knockout mice showed markedly less severe clinical rabies than wild type mice.

With over 100 publications and three patents, Dr. Monique Lafon's group continues to contribute to our understanding of how neurotrophic viruses utilize the host cell's machinery to promote successful infection. In addition to serving on numerous scientific advisory committees and journal review boards, Dr. Lafon is also dedicated to teaching students at all levels in their education.

A Message from the new ISNV President, Lynn Pulliam continued

regions. We will publish an expanded quarterly Newsletter to our members that will feature several new columns including: 1) junior and senior PI profiles, 2) national and international meeting announcements, 3) NIH news, 4) updates from our ISNV subcommittee Chairs, 5) biotech/pharma news, and 6) scientific classified ads and topics of interest. Dianne Langford is Editor of the ISNV Newsletter and Shilpa Buch is Chair of the Publications/Communications Committee. Both Dianne and Shipa have made communication with our members a top priority.

We plan to expand the ISNV website to include a members only link. This will include ISNV Board of Directors and subcommittee minutes to keep our members involved plus membership contact information. Other ideas are welcome.

Finally and in addition to all of the above, I remind you that there are tangible advantages to being a member of ISNV. Our Society fosters networking and collaborations and I will work to bring in new members. We promote students and junior faculty through mentoring, awards and opportunities to present at international meetings. I look forward to working with our members and creating an interdisciplinary approach to this most exciting subspecialty.

2010 Upcoming Conferences

February

The International Neuroinfectious Disease Conference: February 27-28, 2010 in Addis Ababa, Ethiopia (For more information go to www.ISNV.org)

March

14 TH International Congress on Infectious Diseases: March 9-12 in Miami, FL
(For more information go to www.isid.org/14th_icid/)

April

4th European Congress of Virology: April 7-10 in Cernobbio-Lake Como, Italy American
(For more information go to www.clinical-virology.org/pages/cvn/cvn_08/cvn_meetings.html)

Academy of Neurology: April 10-17 in Toronto, Canada
(For more information go to www.aan.com/go/am10)

Society on NeuroImmune Pharmacology: April 14-17 in Manhattan Beach (Los Angeles),CA
(For more information go to www.s-nip.org)

May

American Society for Microbiology: May 23-27 in San Diego, CA
(For more information http://gm.asm.org/)

June

17th Annual Meeting of the Psychoneuroimmunology Research Society: June 2-5 in Dublin, Ireland
(For more information go to www.pnirs.org/meetings/index.cfm)

July

29 th Annual American Society for Virology Scientific Meeting: July 17-21 in Bozeman, Montana
(For more information go to www.asv.org/)

International AIDS Society: July 18-23 in Vienna, Austria
(For more information go to www.aids2010.org/)

August

14th International Congress of Immunology: August 22-27 in Kobe, Japan
(For more information www.ici2010.org/)

The printing of this newsletter was sponsored by The Institute for Molecular Medicine & Infectious Disease

Committee Reports

Fundraising Committee Update

Igor Koralnik, Boston MA

As we prepare for our 10th Symposium next year in Milan, our committee has been diligently focused on obtaining support from some of the big pharmas such as GSK, Abbot, Tibotec, Pfizer, Gilead, Merck, BMS, Alnylam, Teva and Biogen Idec. In addition, we are utilizing our own contacts with various industries, including local vendors and within our own institutions.

Some of our key strategies include speaking directly with decision makers in the organizations, providing a detailed outline that includes various levels of conference sponsorship/advertising opportunities and enlisting the assistance of the ISNV membership in identifying sponsors and/or promoting their own programs to our captive audience.

We welcome your assistance in our efforts to raise funds and will gladly provide the necessary tools for marketing the ISNV to the outside community. For additional information or any questions, please contact the ISNV Office at mail@isnv.org.

"Communication is the Key": Update from the Publications/Communications Committee

Shilpa Buch, Kansas City KS

As the new Chair of the Publications/Communications committee, we have come up with refreshing new ideas that are guaranteed to stimulate our readers with exciting information in the field of Neurovirology. First and foremost the newsletter will become a quarterly publication with both paper and electronic circulation and a mission to keep our members informed of the "hot topics" in the area of Neurovirology. In addition to our star attraction of highlighting a junior and a senior stellar scientist, we will now be showcasing updates on sensational news and publication(s) in Neurovirology/CNS infections from the national and international arenas. Additionally, you as members will be given regular updates on the progress made by all the sub-committees of ISNV as they continue their efforts to keep up the mission of the society. We will also highlight pertinent news from the Research as well as the Biotech/Pharma Industry to bridge the bench to bedside paradigm. Since scientific meetings are a breeding ground for most active collaborations and networking, we will be keeping you abreast of relevant national and international meetings that would be of interest to our membership. And last, but certainly not least; we will be bringing to you the voice of NIH and it's Institutes through our columns that will disseminate the roadmap and the current funding areas of interest. Effective communication is our mantra!

Publications/Communications Committee

Shilpa Buch (Chair)
Kamel Khalili
Bruce Brew
Janice Clements
Pasquale Ferrante
Dianne Langford
Fred Krebs

Fundraising Committee

Igor Koralnik (Chair)
Krzysztof Reiss
Scott Letendre
Brian Wigdahl
Avindra Nath

Classifieds

Summer NeuroAIDS Fellowship

The Mount Sinai Institute for NeuroAIDS Disparities (MSINAD) in New York City is seeking applicants for the 2010 class. This 6-week NIMH funded opportunity offers intensive didactic and experiential training in the science and behavioral aspects of neuroAIDS disorders as they pertain to minority populations. All expenses for the summer are paid, and a generous pilot grant is awarded to all scholars. Applications are due Feb 1, 2010 for Summer 2010. For details and application visit http://www.msinad.org/ or email: desiree.byrd@mssm.edu. Minority candidates are strongly encouraged to apply

Research Associate/Post Doctoral Fellow

The department of Pharmacology and Experimental Neuroscience at the University of Nebraska Medical Center wishes to employ a dynamic and driven PhD for a Research Associate/Post Doctoral position to support a newly federally funded project studying the mechanism of how drugs of abuse synergize with HIV proteins to exacerbate CNS pathology. The chosen candidate must be familiar with molecular biology techniques, and should have neuroscience experience. An understanding of estimation of neurotransmitters and familiarity with electrophysiology and voltage clamp electrophysiology in human and rat brain tissue slices for exploration of LTP and LTD will be an asset. Candidate should be familiar with handling rodents. Proficiency in behavioral test analyses in rodent models will be an asset. Candidate must be driven, have a passion for science, and should be hardworking with strong interpersonal skills. Individuals from diverse backgrounds are encouraged to apply. Please email Dr. Shilpa Buch for more details at: sbuch@unmc.edu

Post-Doctoral Fellow

The Department of Neuroscience at Temple University School of Medicine has an opening for a post-doctoral fellow to study HIV-associated CNS dysregulation. The successful candidate must have extensive experience in molecular biology and a strong background in neuroscience. Primary cell culture, small animal handling experience a plus. Excellent written and spoken communication skills are necessary. Capacity to work in a large group setting is critical. The successful candidate will be highly self-motivated, passionate about science and determined. Contact: Dianne Langford at: tdl@temple.edu

Research Position in fMRI in NeuroHIV

A position is currently available in the Departments of Neurology and Radiology at Washington University in St. Louis. Research focuses on the application of functional MRI methods in their application to neuroHIV. Anticipated activities entail task design creation, image reconstruction, and image data processing and analysis. Opportunities will be provided for pursuing own research interests in multi-modality image analytical techniques. Individuals with a background in electrical engineering, biomedical engineering, physics, or computer science will be considered. Resources utilized in these studies will include 1.5 and 3.0T MRI scanners, experimental presentation software (e-Prime), and MATLAB and UNIX based analyses. Proficiency in C/C++ programming for data analysis algorithm development and linear algebra, and familiarity with IDL, Unix, Linux, or Matlab. Skills in Freesurfer, Perl, ANALYZE, statistics packages such as R, SAS, a plus. A Ph.D. in computer science, physics, biomedical or electrical engineering, or related fields will be considered. Interested candidates please send a letter of research interests and CV to Dr. Beau Ances via at bances@wustl.edu).

Post-Doctoral Fellow

The CNS Infections Research Group of the Department of Neurology (Drs. Beckham, Clarke, Tyler) at the University Colorado, Denver seeks a post-doctoral fellow. The successful candidate will use primary neuronal cultures, organotypic mouse brain cultures, and well-described mouse models of viral encephalitis to examine mechanisms of cell death and survival within the CNS following viral infection. Requirements: PhD in microbiology, neuroscience or related discipline. Experience with small animal models, gene expression analysis, fluorescence microscopy, brain slice cultures, neuronal cell culture, molecular cloning and transgenics. The candidate will be expected to communicate and interact with large groups.
Contact: Penny Clarke, PhD. Penny.Clarke@ucdenver.edu

Faculty Position

Neuropathogenesis of Infectious Diseases
University of Texas Medical Branch, Galveston
The Center for Biodefense and Emerging Infectious Diseases, University of Texas Medical Branch (UTMB) is seeking applications for an Assistant or Associate Professor with a desire to pursue a career in the neuropathogenesis of infectious diseases, particularly acute viral or bacterial infections that affect the central nervous system. The ideal candidate will have a background in neuroscience, and it is expected that future research will include high biocontainment infectious agents. Outstanding collaborative opportunities are available at UTMB on a wide variety of these neuropathogenic agents.
The successfully appointed candidate will develop an independent program of externally funded research. Particularly attractive opportunities to build collaborative projects in vaccine development, endothelial cell pathobiology, and/or animal models of infectious diseases exist at our institution.
Interested individuals should send a letter of interest, statement of current and future research objectives, and CV to Dr. Scott Weaver, Search Committee Chair. Electronic applications (Word file or PDF) are preferred and should be sent to: kischuen@utmb.edu

The University of Texas Medical Branch at Galveston is an equal opportunity, affirmative action institution which proudly values diversity. Candidates of all backgrounds are encouraged to apply.

Contact the ISNV Administrative office at:

Tel: (215) 707-9788 **Fax: (215) 707-9838**

Email: mail@isnv.org **www.isnv.org**

IMM&ID Institute for Molecular Medicine & Infectious Disease

Center For Scientific Communication & Outreach

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Drexel University College of Medicine

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