XIth International Symposium on Amyloidosis

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THE XI\textsuperscript{th} INTERNATIONAL SYMPOSIUM ON AMYLOIDOSIS

Hosted by the Amyloid Treatment and Research Program at Boston University School of Medicine

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WOODS HOLE, MASSACHUSETTS
Preface

The Xth International Symposium on Amyloidosis was held at the Marine Biological Laboratory campus in Woods Hole, Massachusetts, USA on November 5-9, 2006. There were 275 attendees at the Symposium and 198 papers were presented. The focus of the meeting was new basic science and translational research in the systemic amyloidoses. The scientific program included presentations on the mechanisms of disease and cellular toxicity, AA amyloidosis, familial amyloidosis, AL amyloidosis, clinical trials, and emerging translational approaches. We thank the International Organizing Committee for choosing speakers, reviewing abstracts, and supporting the meeting in so many ways.

The Symposium opened with a tribute to Dr. Alan S. Cohen for his outstanding contributions to amyloid research. In 1967, Dr. Cohen presented his discovery of the fibrillar nature of amyloid at the First International Symposium on Amyloidosis in Groningen, the Netherlands, setting the pace for future work on amyloid protein identification and interaction with the microenvironment of tissues. Dr. Cohen is the Founding Editor and Editor-in-Chief of Amyloid. The Journal of Protein Folding Disorders.

The Keynote Address of the Symposium was given by Dr. Stanley Prusiner, Nobel laureate for his discovery of “prions,” the class of infectious agents that replicate without nucleic acid and contain a protein which polymerizes into amyloid. Dr. Prusiner’s research has led to significant progress in understanding neurodegenerative diseases and diseases of the central nervous system.

We enjoyed a tour and dinner at the Kennedy Museum and Library in Boston on the eve of Election Day in the US. The festive occasion included a welcome by Dr. Karen Amman, Dean of Boston University School of Medicine, and an eloquent after dinner talk by a patient who described her painful experience with AL amyloidosis in 1996 just after her marriage. She is in remission now and has 2 beautiful adopted children. A standing ovation was a tribute to her stirring speech that reminded us what our work is all about.

The International Society of Amyloidosis formally thanked Dr. Robert Kyle for his work as first President of the Society. Dr. Kyle established the Society as an official group with bylaws indicating our purpose to promote research, education, clinical studies, and symposia worldwide.
Dr. Gianpaolo Merlì assumed the Presidency of the Society until the next Symposium, proposed for Italy in 2010.

We are very grateful to an anonymous donor for generously supporting the meeting and for suggesting the Marine Biological Laboratory site. We also thank the National Institutes of Health (R13 DK077562) for their support of keynote speaker travel expenses and awards to young investigators and students. The large number of young scientists at this meeting promises a healthy future for research on amyloidosis.

Martha M. Skinner, M.D.
John L. Berk, M.D.
Lawrence H. Connors, Ph.D.
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Outstanding Achievement Award

presented to

ALAN S. COHEN, M.D.

The Organizing Committee was pleased to present an award for outstanding achievement in the field of amyloidosis to Dr. Alan S. Cohen in recognition for his career as researcher, clinician, Program founder, editor, and colleague.

Dr. Cohen was the Founding Editor and is Editor-in-Chief of *Amyloid: The Journal of Protein Folding Disorders*. He is a Distinguished Professor of Medicine in Rheumatology at Boston University School of Medicine. He is the author or editor of 12 books and more than 700 research publications. He has served in many leadership positions at Boston University School of Medicine including Director of the Arthritis Center, Chief of the Division of Medicine at Boston City Hospital, Director of the Thrombolyse Memorial Laboratory, Founder and Director of the Amyloid Treatment and Research Program, and he was the President of the American College of Rheumatology. He is a member of many prestigious organizations including the American Society of Clinical Investigation and the Association of American Physicians. He has been the recipient of numerous distinguished awards among which are the Outstanding Alumnus Award from Boston University School of Medicine, the Jan Van Breemen Gold Medal from the Dutch Rheumatism Society, and the Gold Medal Award from the American College of Rheumatology.

Dr. Cohen began his research in amyloidosis while a fellow in Rheumatology at the Massachusetts General Hospital at the urging of Dr. Evan Calkins. He isolated amyloid as a specific and unique fibrous protein, achieved its high resolution characterization for the first time with the electron microscope, and reported it at the First International Symposium on Amyloidosis.
held in Groningen, the Netherlands in September, 1967. He conducted biochemical studies on the relationship of the amyloid fibril to other proteins, carbohydrates, GAGs, and lipids, as well as immunological and protein sequence studies that led to the definition of amyloid disease types. Reports from Dr. Cohen and his colleagues have been presented at every subsequent International Symposium on Amyloidosis.
We were pleased to have Dr. Stanley Prusiner give the keynote address at the XIth International Symposium on Amyloidosis. Dr. Prusiner is the Director of the Institute for Neurodegenerative Diseases and Professor of Neurology and Biochemistry at the University of California, San Francisco. He is the editor of 12 books and author of over 330 research articles. Dr. Prusiner is a member of many prestigious societies and the recipient of numerous prizes, including the Potamkin Prize for Alzheimer's Disease Research from the American Academy of Neurology (1991); the Richard Lounsberry Award for Extraordinary Scientific Research in Biology and Medicine from the National Academy of Sciences (1993); the Gardner Foundation International Award (1993); the Albert Lasker Award for Basic Medical Research (1994); the Paul Ehrlich Prize from the Federal Republic of Germany (1995); the Wolf Prize in Medicine from the State of Israel (1996); the Keio International Award for Medical Science (1996); the Louisa Gross Horwitz Prize from Columbia University (1997); and the Nobel Prize in Physiology and Medicine (1997).
Dr. Prusiner discovered an entirely new class of pathogens that replicate without nucleic acid. Through this work, he created a new field of research that has resulted in significant progress in understanding degenerative diseases of the central nervous system (CNS). In 1982, Prusiner proposed that scrapie was caused by an infectious protein that he called a “prion.” Over the next decade, Prusiner and others accumulated a wealth of data demonstrating how an infectious pathogen devoid of nucleic acid can multiply and cause CNS degeneration. After purifying prions from the brain, Prusiner discovered that they were composed of a single protein, which he called “prion protein” or PrP. Prusiner found that a fragment of the protein polymerized into amyloid; subsequently, he and his colleagues demonstrated that amyloid plaques in the brains of animals and humans dying of prion diseases were composed of PrP. This was the first time that cerebral amyloid was shown to be the cause of a CNS disease.
Report of the Nomenclature Committee

Nomenclature committee report


The nomenclature of amyloidosis is based on the biochemical nature of the major amyloid fibril proteins and has achieved general acceptance among researchers. Thus, instead of primary and secondary amyloidosis AL- and AA-amyloidosis are almost always used. There are still some problems to be resolved and some aberrant and questionable designations are often used. Among these is the by the neuroscience community almost universally utilized designation APP for the protein precursor of the Aβ-protein. APP means ‘amyloid precursor protein’, which sounds like there is a single known amyloid fibril protein. The correct nomenclature is AβPP which is also recommended by the Nomenclature Committee and Amyloid: The Journal of Protein Folding Disorders.

DEFINITION OF AMYLOID

A recurrent question, also discussed at this meeting, is the definition of amyloid. Presently we agree that amyloid is an in vivo produced protein substance, characterized by a fibrillar electron microscopic appearance and specific properties with some dyes, particularly affinity for Congo red with a resulting green birefringence. At this meeting it was accepted that extracellular deposition should no longer be included in the definition since there is no good reason to differentiate between intra- and extracellular deposits when they may have the same nature, biophysical appearance and properties. It now appears that some typical amyloidoses may start with intracellular fibril formation but continue with amyloid fibril propagation outside cells. This means also that neurofibrillary tangles, containing hyperphosphorylated tau protein should be regarded as a localized form of amyloid. The congophilic and green birefringence of these structures is well-known and they have been shown to have the same X-ray diffraction pattern as other amyloid fibrils. On the other hand, inclusions lacking (i.e. in Parkinson’s disease), as well as synthetically formed fibrils exhibiting, typical amyloid properties are not included according to the current definition.

SYSTEMIC VERSUS LOCALIZED AMYLOID

Another question, which was discussed at this meeting, is the definition of systemic amyloidosis, a question which at a first glance may seem simple. The term is usually used when there is involvement of several organs. However, there are amyloid forms that may affect one kind of structures in several organs. One example is AMed-amyloid, derived from the precursor lactadherin. This type of amyloid affects the aortic media, particularly the thoracic part, but may also occur in other large arteries in different parts of the body, albeit to a lesser extent. In spite of the multiple sites of deposition, AMed amyloidosis has been classified as localized. Mild ATTR-amyloidosis, when derived from wild-type TTR, may also be characterized by small deposits in arteries in different organs, although there are usually some deposits also in the myocardium. This form is called Senile Systemic Amyloidosis (SSA). The principal difference between these two forms of amyloidosis seems to depend on where the fibril protein precursor is expressed.
Lactadherin is synthesized close to the AMed deposits while in SSA, the fibrils are derived from circulating TTR, mainly produced by the liver. We therefore suggest, on the basis of observations to date, that the fibril protein in a systemic amyloidosis should originate from the plasma while localized amyloid protein is synthesized at the site of deposition. We will see whether such a definition holds.

**TABLE OF HUMAN AMYLOID PROTEINS**

There is since earlier an accepted list of amyloid fibril proteins and this was updated with two novel proteins at the meeting. These are AαA (see above) and ASemI, derived from semenogelin I. ASemI is the fibril protein in localized seminal vesicle amyloid. In addition, the protein which we provisionally called Aβn (A to be named) (1) has been given the designation A0αp since the precursor is now identified as odontogenic ameloblast-associated protein (NCBI accession # EF113908). There are presently 27 known human amyloid fibril proteins of which 13 are found associated with systemic disease. The number of proteins giving systemic amyloidosis is not expected to increase much but there are still several localized amyloid forms that have not been characterized as yet.

An updated table will soon be published in Amyloid: The Journal of Protein Folding Disorders.

**REFERENCES**