Steven Krilis – SHORT CURRICULUM VITAE – November 2017

RESEARCH SUMMARY AND SIGNIFICANCE

Professor Krilis has made seminal discoveries and transformed the way both basic scientists and clinicians understand the complex and potentially fatal antiphospholipid syndrome (APS). The APS is the commonest acquired disorder of thrombosis and in women manifests as recurrent miscarriage. His laboratory was the first to identify and purify the major autoantigen in this disorder. This was a major paradigm shift. The major autoantigen β_2-glycoprotein I (β_2GPI) is involved in the critical regulatory pathways for the development and regulation of thrombosis in APS. He has also made ground breaking discoveries in the area of mast cell biology and in particular the role of serine proteases in a number of human inflammatory disorders.

The discovery that β_2GPI is the major autoantigen in the APS has been paradigm shifting and initially quite controversial. However, this has not only reshaped the scientific and clinical perspectives on the autoantigen and pathogenic mechanisms in this disorder, it has led to a new diagnostic test and potentially new treatments based on the identification of the true autoantigen for this disorder. Professor Krilis's discoveries in this field have provided critical experimental evidence and have been responsible for development of therapeutic targets and diagnostic ELISA assays by a number of diagnostic and pharmaceutical companies.

Seminal discoveries in Professor Krilis's laboratory include; the discovery of the major autoantigen that the pathogenic autoantibodies from patients with the APS recognise; demonstration that autoantibodies detected in the cardiolipin ELISA assay are distinguished from those that have infection and are not associated with APS; identification of a specific region of β_2GPI that is critical for phospholipid binding and the ability of patient autoantibodies to bind β_2GPI; identification of GpIbα as a major platelet receptor for β_2GPI; epitope mapping of the major autoantibody binding site on β_2GPI; patenting of an anti-β_2GPI ELISA that is currently being used worldwide in every major hospital to diagnose and monitor the treatment of APS patients; generation of β_2GPI null mice using a gene targeting approach; recent discovery that β_2GPI becomes post-translationally modified in-vivo via an oxidative mechanism and this significantly alters the biological and immunological activity of β_2GPI; based on this latter finding Professor Krilis's laboratory has developed a novel ELISA that identifies the oxidative posttranslational forms of β_2GPI in human plasma and showed in a large international study that the level of the oxidised form of β_2GPI is associated with development of APS; association of posttranslational modification of complement factor H (CFH) (which has the same complement control proteins modules as β_2GPI) and age-related macular degeneration (AMD).

Based on international criteria (Google Scholar citations Publish or Perish 4) the Krilis laboratory is now recognised at the leading edge in the field with a total citation of over 14,850 and a Hirsch index of 52. He has been CIA on many grants with continuing NH&MRC project grant funding as CIA for 32 years. He has been awarded a number of awards and as a reflection of his international standing was awarded Honoris Causa Doctorate, University of Athens, Greece in 2011. He has had numerous invitations as symposium and plenary speaker at leading international conferences in the field of autoimmunity, thrombosis and inflammation.

Professor Krilis is on a number of leading thrombosis and immunology journals and his opinion is actively sought after by leading journals and leading international and national funding agencies.

Professor Krilis's research is at the cutting edge of the field and is internationally recognised as evidenced by the citations, H factor and invitations to speak as plenary and symposium speaker at major international meetings and to contribute to the international peer review process and as a consultant to the pharmaceutical industry.

PROFESSIONAL CAREER

Professor Krilis is an advocate of medical research with a major emphasis on translational research. He was responsible for establishing the department of immunology and infectious disease, and establishing a vibrant research programme when there was no research infrastructure or research being performed at St. George Hospital, Sydney. Professor Krilis has been the driving force in directing the growth of the research programme at St. George Hospital. His major goal is to deliver research outcomes of national and international significance.

He has demonstrated leadership in basic research, clinical medicine and in the academic sphere at a national and international level through directorship of hospital and an academic department; contribution to clinical and academic boards; membership of numerous hospital and university committees, and participation on prestigious international boards for medical research and committees associated with government funding of medical research. Professor Krilis currently holds the Chair in Immunology, Infectious Diseases at St. George Hospital, University of New South Wales and is the Director of the Department of Infectious Disease, Immunology and Sexual Health, Faculty of Medicine St. George Hospital Clinic School and actively contributes to hospital and university policy and on grant review panels for NH&MRC project grant funding.

He has the responsibility of a very busy clinical department and running of a hospital-wide infectious disease and immunology inpatient, outpatient and consultative service for the St. George Hospital campus and affiliated hospitals. He is responsible for directing and managing teams associated with NH&MRC and other funding programs. He has had continuous NH&MRC project grant funding as CIA for 32 years. He currently holds 2 NH&MRC project grants. He supervises Masters and PhD students associated with these grants. He makes a significant contribution to teaching medical students, basic physician trainees, interns and nurses through clinical tutorials, formal lectures, case discussions. He is a member of the Scientific Advisory Committee for the St. George Hospital Medical Research Foundation and advises on research policy for the institution. Professor Krilis has an international profile in the medical and biomedical research community where he has leadership roles through participation on international committees and boards. He contributes to peer review for a variety of international granting bodies from the USA, UK, Holland, Israel and other countries.

ACADEMIC HONOURS AWARDS AND FELLOWSHIPS

One of three Committee Members for the Scientific Review Panel for the HUJ-CREATE program, Singapore University 2015, international member Singapore Prime Ministers Review Panel Life Sciences Research 2016-2019.

Order of Phlebology Medal (OPM) for outstanding research on the antiphospholipid syndrome. Australasian College of Phlebology. (5/7/2016)

Emeritus Fellow. Australasian College of Phlebology. (5/7/2016)

Distinguished Scientist Visiting Fellowship, Awarded by the Japanese Society for Promotion of Science, University of Hokkaido, Sapporo, Japan. (20/6-21/7/2015)

Harvard Club of Australia Fellowship (2012 for 2013). One of only two awards for an Australian researcher to undertake research at Harvard University. Visiting Professor Department of Medicine, Harvard Medical School, USA. (3/13-9/13)
Honoris Causa Doctorate University of Athens, Greece. (2011)
Honorary Membership the Turkish Society of Research & Education in Rheumatology, Turkey. (2005)
Distinguished Alumni Award in Science and Engineering, University of New South Wales, Australia. (2004)
AAAAI Training Program Director's Retreat Award. Chicago, USA. (2003)
Israel Academy of Sciences, Batsheva de Rothschild Visiting Professor, Israel. (2002)
Visiting Professor of Medicine, Department of Medicine, Harvard Medical School, USA. (10/3-10/9.2001)
Recipient – Gold Cross of St. Andrews – Greek Orthodox Archdiocese of Australia, for his international contributions to clinical and basic research in medicine. (1999)
UICC Senior Fellowship, Visiting Professor Department of Rheumatology, Immunology, Harvard Medical School. (1993-1994)
Visiting Professor of Medicine, Department of Immunology, Rheumatology, Harvard Medical School, USA. (1/8/1993-1/2/1994)
Bob Pitney Award for studies into the molecular analysis of the Bsp-1 antigen. University of NSW Medical Faculty. (1991)
Honorary Fellow, Hellenic Society of Rheumatology. (1991)
Fogarty International Post-Doctoral Research Fellowship, National Institute of Health, USA. (1983)
Applied Health Science Fellowship from the National Health and Medical Research Council. (1981-1984)
Recipient, National Health and Medical Research Council Scholarship. (1978-1981)
Honours Graduate, University of New South Wales, Australia. (1973)
Gilbert Ashby Memorial Prize for General Proficiency in Medicine. (1972)
Keith Harrison Memorial Prize for Proficiency in Medicine. (1972)

SELECTED INTERNATIONAL TALKS 2015-2017

2017- Life Sciences Institute Immunology Program in the National University of Singapore, Singapore.
Stanford University, CA, USA.
Symposium Speaker, 2016- 9th APSTH Education Congress Taipei International Convention Center, Taiwan.
The 9th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis, Taipei International Convention Center, Taiwan.
University of Athens, Athens, Greece.
Keynote Speaker, 15th International Congress on Antiphospholipid Antibodies, Northern Cyprus, Turkey.
FASEB Science Research Conference on 'Functional Disulfide Bonds in Health and Disease, Steamboat Springs, Colorado, USA.
2015 - Sixth Annual APS ACTION Summit in San Francisco, California, USA.
Keynote Speaker, International Diabetes Summit Forum, Tianjin, China.
Visiting Professor and Invited Speaker. The role of β2GPI in the antiphospholipid syndrome. Organised

by Professor Ricardo Morishita, Kanazawa University, Kanazawa, Japan. 15.6.2015.
Symposium Speaker, Immunology Programme Life Sciences Institute. National University of Singapore – 2015

OVERVIEW

Professor Krilis's research has fundamentally transformed how clinicians and scientists understand the fundamental immune and cellular mechanisms that regulate autoantibody production in the antiphospholipid syndrome (APS) and the posttranslational modification of the major autoantigen $\beta_2$glycoprotien I (β_2GPI) in the APS and how this contributes to the pathogenesis of thrombosis and in human inflammatory disorders that are characterised by oxidative damage such as systemic lupus erythematosus (SLE) and age-related macular degeneration (AMD). These include seminal discoveries on the identification of the major autoantigen in the APS. This was a major paradigm shift and the finding has resulted in significant advances in the understanding, diagnosis and treatment of APS patients over the last 23 years. In addition Professor Krilis has made ground breaking discoveries on the role of β_2GPI and its oxidative posttranslational modification in the pathological thrombus formation and its role with complement factor H in AMD. This has led to utilising the true antigen β_2GPI rather than using cardiolipin a negative charged phospholipid which binds β_2GPI that has been previously used to assay for these autoantibodies. The ELISA patented by Professor Krilis's laboratory has been adapted for numerous assays in clinical and diagnostic research laboratories and this has revolutionised the diagnosis of APS and monitoring of these patients. Recent findings that β_2GPI is a substrate for the oxidoreductase enzymes and interacts with coagulation factors such as FXI, FXIa and thrombin has opened up a new area of investigation in haemostasis. His laboratory has recently discovered that CFH, a protein in the same superfamily as β_2GPI can be also posttranslationally modified and this modification is associated with an increased risk of AMD, the leading cause of blindness in the western world. These discoveries have been paradigm shifting and have had a major impact in the understanding of APS pathogenesis, pathological thrombus formation and the role of posttranslational modification on autoantibody generation in APS and the role of posttranslational modification of CFH in AMD pathogenesis.