BIOGRAPHICAL SKETCH

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NAME: Abraham Pinter, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): APINTER

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Brooklyn College, Brooklyn, New York	B.S.	1969	Chemistry
Columbia University, New York, N.Y.	Ph.D.	1973	Chemistry
Rockefeller University, New York, N.Y.	Post-Doc.	1974-5	Animal Virology
Memorial Sloan-Kettering Cancer Center, NY, NY	Post-Doc	1975-6	Viral Oncology

A. Personal Statement

A particular long-term area of interest of my research has been studying the immunology of HIV and retroviruses. These studies were centered on characterizing the structural and immunological properties of HIV Env proteins and studying mechanisms for the resistance of HIV against the natural humoral immune response against this virus. This work has entailed the development of enhanced methods for stabilizing memory B cells of infected patients and cloning of novel monoclonal antibodies (mAbs) against HIV-1 Env which possess potent and broadly neutralizing activities. Although these approaches have been applied to great benefit in the HIV field, there has been little effort to date to explore the human antibody response towards bacterial pathogens. Such antibodies can serve as important reagents for improved diagnostics, and potentially can provide alternative approaches for regulating infection and pathogenesis. With funding from the Gates Foundation we have been recently used these methods to isolate a number of human mAbs directed against novel epitopes in *Mycobacterium tuberculosis* (*M.tb*). A particular focus of this work has been the isolation and characterization of mAbs specific for lipoarabinomannan (LAM), a major surface glycolipid of *M.tb* that is an important diagnostic target. We have used these mAbs to characterize the antigenic diversity of LAM and the complexity of the antibody response against this antigen. These include antibodies with high affinities and novel epitope specificities (1), that possess enhanced properties as immunodiagnostics (2-4). Collaborative studies have demonstrated that these antibodies can significantly increase the sensitivity of assays that detect the presence of LAM in the urine (2) and serum (3,4) of actively infected TB patients. We have also initiated studies with a major diagnostic company to apply these antibodies to an enhanced lateral flow assay, and have shown the enhanced sensitivity of these reagents for the immunodetection of LAM-derived antigens in the urine of HIV-coinfected TB patients over the current commercially available kit (Alere Determine^{TM} TB LAM Ag). Despite this significant improvement in sensitivity, there remains a need for further enhancment of the affinities and specificities of the capture and detection reagents, in order to develop this as a highly sensitive and accurate POC assay for TB infection, which is the focus of our efforts in the present application.

1) A. Choudhary, D. Patel, W. Honnen, Z. Lai, R.S. Prattipati, R.B. Zheng, Y-C Hsueh, M.L. Gennaro, A. Lardizabal, B.I. Restrepo,M. Garcia-Viveros, M. Joe, Y. Bai, K. Shen, K. Sahloul, J.S. Spencer, D.Chatterjee, T. Broger, T.L. Lowary, and **A. Pinter**. 2018. Characterization of the antigenic heterogeneity of lipoarabinomannan, the major surface glycolipid of Mycobacterium tuberculosis, and complexity of antibody specificities toward this antigen. J. Immunology. May 1;200(9):3053-3066. PMID:29610143.

2) A.G. Amin, P. De, J. Spencer, P.J. Brennan, J. Daum, B.G. Andre, M. Joe, Y. Bai, L. Laurentius, M. Porter, T. Lowary, W.J. Honnen, A. Choudhary, **A. Pinter** and D. Chatterjee. 2018. Detection of LAM in Urine and Serum of HIV-positive and HIV-negative TB Suspects using an improved Capture-Enzyme Linked Immuno-Absorbent Assay and Gas Chromatography/Mass Spectrometry. Tuberculosis 111, 178–187. PMID:30029905

3) G. B. Sigal, **A. Pinter**, T. L. Lowary, M. Kawasaki, A. Li, A. Mathew, M. Tsionsky, T. Plissova, K. Katsuragi, W. Honnen, A. Choudhary, P. Nahid, C. M. Denkinger, M. D. Perkins, T. Broger. 2018. A novel sensitive immunoassay targeting the MTX-Lipoarabinomannan epitope meets the WHO's performance target for Tuberculosis diagnosis. Journal of Clinical Microbiology, In press.

4) N. A. Owens, **A. Pinter**, and M.D. Porter. 2018. Surface-enhanced Resonance Raman Scattering for the Sensitive Detection of a Tuberculosis Biomarker in Human Serum. Journal of Raman Spectroscopy, In press.

B. Positions and Honors.

Positions and Employment

1976-1978 Research Associate, Laboratory of Viral Oncology, Memorial Sloan-Kettering Cancer Center
1978-1982 Adjunct Assistant Professor, Department of Chemistry, York College of the CUNY
1979-1982 Associate, Laboratory of Viral Oncology, Memorial Sloan-Kettering Cancer Center
1980-1985 Assistant Professor, Department of Genetics and Molecular Biology, Sloan-Kettering Division, Cornell University Graduate School of Medical Sciences.
1982-1985 Assistant Member, Laboratory of Viral Oncology, Memorial Sloan-Kettering Cancer Center
1985- Associate Member, Head, Laboratory of Retroviral Biology, Public Health Research Institute
1985- Research Associate Professor, Department of Microbiology, NYU School of Medicine
1991- Member, The Public Health Research Institute
Research Professor, Department of Microbiology, NYU School of Medicine
2002- Member, Strategic Planning Committee, Public Health Research Institute
2004- Professor, Department of Medicine, New Jersey Medical School, UMNDJ
2009- Associate Director, Viral Research Unit, Public Health Research Institute, NJMS, UMDNJ
2013- Professor, Rutgers University

Other Experience and Professional Memberships

Phi Beta Kappa (1969); Sigma Xi (1972); NIH Postdoctoral Fellow (1974-76); Member, American Society of Microbiology (1974 -); Charter Member, American Society of Virology (1982); Special Fellow, Leukemia Society of America (1979-81), Member, International Association for Comparative Research on Leukemia and Related Diseases (1985-); Member, International AIDS Society (1989-); Ad Hoc Member, Experimental Virology Study Section, NIH, 6/86; Member, Special Review Committee, NCVDG for the Treatment of AIDS, NIAID, 5/87; Member, NIAID AIDS Review Committee (1987-1991); NIH Reviewers Reserve (1991-1995); Ad hoc Member, HIV Vaccine Study Section (2000-3); Member Editorial Board, Journal of Virology (1992-2001); Ad hoc Reviewer, Journal of Virology, Virology, Retrovirology, Vaccine, other journals (ongoing); Ad hoc Member, NIH Study Sections (2003-current).

C. Contributions to Science

List of Publications are available at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/abraham.pinter.1/bibliography/45519212/public/?sort=date&direction=descending

Five most significant contributions to science

I. Harnessing the human antibody response against TB antigens for improved diagnostic and therapeutic reagents.

Using techniques developed and used to great benefit in the HIV field, we have been exploring the human humoral immune response to infection by TB and have isolated a series of novel human monoclonal antibodies (mAbs) against antigens that are useful diagnostic or therapeutic targets. These include a panel of mAbs isolated that recognize various epitopes in lipoarabinomannan (LAM), the major surface glycolipid and an important diagnostic target for active TB infection. Our new mAbs possess higher affinities and novel epitope

specificities than the previously described mAbs. In studies with scientists at FIND and other collaboratorsl we have shown that these new reagents can significantly extend the sensitivity of the current assays for urinary LAM and broaden the utility of these assays for a greater fraction of patients. We are also exploring the therapeutic utility of these antibodies and developing means of optimizing their functional activities for various components of the innate immune response..

A. Choudhary, D. Patel, W. Honnen, Z. Lai, RS.. Prattipati, R.B. Zheng, Y.-C. Hsueh, M.L. Gennaro, A. Lardizabal, M. Joe, Y. Bai, K. Shen, K. Sahloul, J. Spencer, D. Chatterjee, T. Broger, T. L.Lowary and A. Pinter. 2018. Characterization of the antigenic heterogeneity of lipoarabinomannan (LAM), the major surface glycolipid of *Mycobacterium tuberculosis,* and complexity of antibody specificities towards this antigen. Journal of Immunology, 2018 May 1;200(9):3053-3066. doi: 10.4049/jimmunol.1701673.

A.G. Amin, P. De, J. Spencer, P.J. Brennan, J. Daum, B.G. Andre, M. Joe, Y. Bai, L. Laurentius, M. Porter, T. Lowary, W.J. Honnen, A. Choudhary, A. Pinter and D. Chatterjee. 2018. Detection of Lipoarabinomannan in Urine and Serum of HIV-positive and HIV-negative TB Suspects using an improved Capture-Enzyme Linked Immuno-Absorbent Assay and Gas Chromatography/Mass Spectrometry. Tuberculosis, 111, 178–187.

G. B. Sigal, A. Pinter, T. L. Lowary, M. Kawasaki, A. Li, A. Mathew, M. Tsionsky, T. Plissova, K. Katsuragi, W. Honnen, A. Choudhary, P. Nahid, C. M. Denkinger, M. D. Perkins, T. Broger. 2018. Lipoarabinomannan (LAM) is detectable in the urine of HIV positive and HIV negative tuberculosis (TB) patients. Journal of Clinical Microbiology, 2018, In press.

T. Broger, B. Sossen, E. du Toi, A.D. Kerkhoff, C. Schutz, E. Ivanova, A. Ward, D.A. Barr, A. Macé, R. Burton, S. Ongarello, A. Pinter, C. Boehme, M.P. Nicol, G. Meintjes, C.M. Denkinger. Novel point-of-care lipoarabinomannan (LAM) assay with superior sensitivity, for the detection of tuberculosis in people living with HIV. Submitted for publication.

II. Identifying multiple mechanisms for the unusual neutralization resistance of HIV-1

These studies demonstrated a multiplicity of mechanisms used by HIV to mask sensitive neutralization epitopes from commonly produced antibodies. These include the masking by the V1/V2 domain of conserved immunogenic epitopes that is a critical factor in the resistance of the majority of HIV-1 isolates, a V3-mediated masking activity present in subtype C isolates that enhance the stability of closed conformations that occlude sensitive epitopes, and novel positions in the C3 and C5 domains that regulate the closed conformation and account for the unusual phenotype of the MW965 clinical isolate. These studies provide important insight for HIV-1 immunogen design and vaccine development.

Qualls, Z.M., A. Choudhary, W. Honnen, R. Prattipati, J.E. Robinson, and A. Pinter. 2017. Identification of novel structural determinants in MW965 Env that regulate the neutralization phenotype and conformational masking potential of primary HIV-1 isolates. Journal of Virology, In press.

Salomon, A., W. J. Honnen, Z. Lai, X. Bu, M.K. Gorny, S. Zolla-Pazner and C. P. Krachmarov. A. Pinter. 2014. Specific V3 sequences common in subtype C isolates induce a neutralization-resistant phenotype that is independent of V1/V2-dependent masking. Virology, 448:363-74.

Krachmarov, C.P, W. J. Honnen, S.C. Kayman, M.K. Gorny, S. Zolla-Pazner and A. Pinter. 2006. Relative effects of epitope masking and V3 sequence variation on the neutralizing activities of human monoclonal antibodies specific for the V3 region of human immunodeficiency virus type 1. J. Virol, 80:7127-35.

Pinter, A., W. J. Honnen, Y. He and S C. Kayman. 2004. The V1/V2 domain of gp120 is a global regulator of sensitivity of primary human immunodeficiency virus type 1 isolates to antibody-mediated neutralization. J. Virology, 78:5205-5215.

III. Characterization of quaternary V2- and V3-dependent epitopes as highly sensitive targets for neutralization of HIV

These papers were the first to show the importance of quaternary structure in HIV neutralization. We identified and characterized the determinants of a highly potent V1/V2-dependent antibody that was highly dependent on quaternary structure. The Honnen and Krachmarov papers identified the 160 and 167 positions as critical determinants for these epitopes and defined other key determinants in both the V2 and V3 domain. This information was influential in the rapid characterization of the broadly neutralizing V1/V2-dependent family of mAbs isolated more recently.

Pinter, W. J. Honnen, P. D'Agostino, M. K. Gorny, S. Zolla-Pazner and S. C. Kayman. 2005. The C108g epitope in the V2 domain of gp120 functions as a potent neutralization target when introduced into Envelope proteins derived from human immunodeficiency virus type 1 primary isolates. J. Virology, 79:6909-6917.

W.J. Honnen, C. Krachmarov, S.C. Kayman, M.K. Gorny, S. Zolla-Pazner and A. Pinter. 2007. Typespecific epitopes targeted by monoclonal antibodies with exceptionally potent neutralizing activities for selected strains of human immunodeficiency virus type 1 map to a common region of the V2 domain of gp120 and differ only at single positions from the clade B consensus sequence. J. Virology, 81:1424-32.

C.P. Krachmarov, Z. Lai, W.J. Honnen, A. Salomon, M.K. Gorny, S. Zolla-Pazner, J. Robinson, A. Pinter. Characterization of structural features and diversity of variable region determinants of related quaternary epitopes recognized by human and rhesus macaque MAbs possessing unusually potent neutralizing activities. J Virol., 2011, 85:10730-10740. PMCID: 3187505

Moore, P. L., E. S. Gray, D. Sheward, M. Madiga, N. Ranchobe, Z. Lai, W. J. Honnen, M. Nonyane, N. Tumba, T. Hermanus, S. Sibeko, K. Mlisana, S. S. Abdool Karim, C. Williamson, A. Pinter, and L. Morris. 2011. Potent and broad neutralization of HIV-1 subtype C viruses by plasma antibodies targeting a quaternary epitope including residues in the V2 loop. J Virol., 2011, 85:3128-41, PMC3067856

IV. Identification of glycan-dependent neutralization epitopes in the V1/V2 domain as important targets for neutralization of HIV

These papers identified key determinants of a novel V1/V2-specific mAb that possessed potently neutralizing activity with limited breadth. This epitope was shown to be dependent on the glycan at position 160 and a Gly at 167, two positions that subsequently were found to be critical for a large class of broadly neutralizing quaternary-dependent mAbs.

Patent. A. Pinter. HIV-1 gp120 V1/V2 domain epitopes capable of generating neutralizing antibodies. Patent awarded June 29, 2004, issued Nov. 9, 2004, US Pat. 6,815,201.

Wu, Z., S.C. Kayman, W.J. Honnen, K. Revesz, H. Chen, S. Vijh-Warrier, S.A. Tilley, J. McKeating, C. Shotton and A. Pinter. 1995. Characterization of neutralization epitopes in the V2 region of human immunodeficiency virus type 1 gp120: role of glycosylation in the correct folding of the V1/V2 domain. J. Virol., 69, 2271-2278.

Honnen, W.J., Z. Wu, S.C. Kayman and A. Pinter. 1996. Potent neutralization of a macrophage-tropic HIV- 1 isolate by antibodies against the V1/V2 domain of gp120. Vaccines 1996: Molecular Approaches to the Control of Infectious Diseases. pp. 289-297.

Pinter, W.J. Honnen, S.C. Kayman, O. Troshev and Z. Wu. 1998. Potent neutralization of primary HIV-1 isolates by antibodies directed against epitopes present in the V1/V2 domain of HIV-1 gp120. Vaccine, 16, 1803-1811.

V. Discovery of critical role of epitopes in the V1/V2 domain in vaccine protection against HIV

These studies utilized our gp70-V1/V2 fusion protein system to identify and define sites in the V2 domain that were the critical determinants for protection in the RV144 vaccine trial, the first and only large-scale human trial to show protection. This information is critical in understanding mechanisms of vaccine-induced protection against HIV and has strongly influences the design and evaluation of future vaccine studies.

B. F. Haynes. P. B. Gilbert, J. McElrath, et al. Immune Correlates Analysis of the ALVAC-AIDSVAX HIV-1 Vaccine Efficacy Trial. N Engl J Med 2012;366:1275-86. PMCID: 3371689

H.-X. Liao, M. Bonsignori, S. M. Alam, et al., HIV-1 Envelope Antibodies Induced by ALVAC-AIDSVAX B/E gp120 Target a Site of Vaccine Immune Pressure and Region Recognized by V2V3 Broad Neutralizing Antibodies. Immunity. 2013 Jan 24;38(1):176-86. doi: 10.1016/j.immuni.2012.11.011. Epub 2013 Jan 11. PMID: 23313589.

S. Zolla-Pazner, A. C. deCamp, T. Cardozo, et al., Analysis of V2 Antibody Responses Induced in Vaccines in the ALVAC/AIDSVAX HIV-1 Vaccine Efficacy Trial. 2013. PLoS One. 2013;8(1):e53629. doi: 10.1371/journal.pone.0053629. Epub 2013 Jan 17.

Li SS, Gilbert PB, Tomaras GD, Kijak G, et al., FCGR2C polymorphisms associate with HIV-1 vaccine protection in RV144 trial. J Clin Invest. 2014 Sep;124(9):3879-90. PMID: 25105367.

N. Yates, A. deCamp, B. Korber, H.-X. Liao, A. Pinter, J. Peacock, L. Harris, S. Sawant, P. Hraber, X. Shen, S. Rerks-Ngarm, P. Pitisuttithum, S. Nitayapan, P. Berman, M. Robb, G. Pantaleo, S. Zolla-Pazner, B. Haynes, S.

Munir Alam, D. Montefiori, and G. Tomaras. HIV-1 Envelope Glycoproteins from Diverse Clades Differentiate Vaccine Elicited Antibody Responses and Antibody Durability. JVI, in press.

D. Additional Information: Research Support and/or Scholastic Performance

Current Support

"Exploring the human humoral response for ultrasensitive antibodies to lipoarabinomannan (LAM) of M.tb", Bill and Melinda Gates Foundation. Principal Investigator: Abraham Pinter, Ph.D. Period: 7/1/16-12/31/18.
This grant provided initial support for our studies to isolate panels of human monoclonal antibodies specific for lipoarabinomannan of M.tb and to characterize the immunogical properties of this antigen, that provide the basis of the current proposal.

"Validation of urine/serum LAM in HIV/nonHIV TB suspects and POC Test Development".
NIH R01 AI132680-01. Period: 07/01/2018-06/30/2022.
P.I., Delphi Chatterjee (Colorado State University). A. Pinter, Co-Investigator.
The goals of this grant are to develop pre-treatment protocols for enhancing the utility of existing monoclonal antibodies against LAM in detecting TB infection in well-characterized adult cohorts with suspected TB in high TB burden countries which have both high and low levels of HIV infection.

"Testing the utility of a novel chemical capture technology for the immunodetection of LAM antigens present in the urine of actively infected TB patients". Bill and Melinda Gates Foundation grant. Period: 07/01/2018-03/28/2019. P.I.- Lance Liotta (George Mason University), A. Pinter- Co-investigator.
The purpose of this grant is to demonstrate the utility of a combination of chemically modified hydrogel nanocages and high affinity monoclonal antibodies for the efficient detection of LAM in the urine of TB patients.

Completed Projects

"Strategies for Eliciting Broadly Neutralizing Abs against Conserved HIV-1 Quaternary Epitopes" Principal Investigator: Abraham Pinter, Ph.D. Agency: NAIAD, Type: P01-AI088610-01, Period: 3/01/2010 – 2/28/2016.
The goals of this HIVRAD Program Project are to characterize novel quaternary neutralization epitopes, to insert them into pathogenic SHIVs and to develop vaccination strategies that are capable of inducing similar antibodies.

"Optimizing protective vaccine targets in the V1/V2 domain of HIV-1 gp120". Principal Investigator: Abraham Pinter, Ph.D. Agency: NAIAD, Type- R01 AI102718-01 Period: 07/01/2012-06/30-2016.
The goals of this proposal are to characterize the structure and immunological properties of alternative conformational forms of the V1/V2 domain and isolate and characterize monoclonal antibodies directed against novel epitopes in the V1/V2 domain that contribute to protection.

"Conformational Stabilization of the HIV-1 Env Trimer". Principal Investigator, Chris Marshall, Ph.D. Agency: NIAID. R44-AI091507. Period: 09/01/2013 – 08/31/2016.
The goals of this project are to utilize novel methods for crosslinking protein oligomers to stabilize the native HIV-1 trimer and improve its immunogenicity.

"Ultrasensitive immunoassay for TB utilizing engineered human mAbs. Principal Investigator: Abraham Pinter, Ph.D. Agency: New Jersey Health Foundation Innovation grant, #PC 20-15. Period: 1/1/15-12/31/15.
The goals of this project are to enhance the affinities and anti-proliferative activities of mAbs directed against the major surface glycolipids of Mycobacterium tuberculosis by engineering the structures of the constant domains.