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

I have been directing a research group studying the immunology of HIV and retroviruses for most of my career. My research is 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. A particular long-term area of interest has been characterizing the antigenic properties of the gp120 variable domains (V1/V2, V3), and on optimizing the immunogenicity of targets in these region for use in vaccines. Key accomplishments in this area include the first identification of the V1/V2 domain as an important target for viral neutralization and a key determinant of extremely potent antibodies directed against quaternary epitopes, the first characterization of extremely sensitive quaternary neutralization epitopes expressed on trimeric HIV-1 Env complexes which include key determinants in the V1/V2 and V3 domains, and the first identification, the first characterization of potent glycan-dependent neutralization targets in the V2 domain that included conserved glycans as critical components of the epitopes; these studies set the groundwork for the subsequent characterization of broadly conserved neutralization epitopes localized to these regions. We also developed the initial scaffolded V1/V2 structures, the gp70-V1/V2 fusion proteins, that expressed the highly antigenic correctly folded forms of this region that were used to demonstrate that antibodies to sites in the V1/V2 domain correlated with protection in the RV144 vaccine trial, and these antigens have proven to be important reagents for analyzing the humoral response against the V1/V2 domain in subsequent vaccine trials.

More recently, my laboratory has applied enhanced methods of stabilizing memory B cells of infected humans and applied this to the cloning of novel monoclonal antibodies (mAbs) against HIV and TB. Although these approaches have previously 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 lipoarabinomannan (LAM), a major surface glycolipid of *Mycobacterium tuberculosis*, and have used these mAbs to characterize the antigenic diversity of LAM and the complexity of the antibody response against this antigen (Choudhary et al., 2018, J. Immunology, In press, mss submitted for publication). These include antibodies with high affinities and novel epitope specificities that are proving to be useful as enhanced immunodiagnostics. Collaborative studies with scientists at FIND and several other academic and industrial groups have demonstrated that these antibodies can significantly increase the sensitivity of assays that detect the presence of LAM in the human and serum of actively infected TB patients. We are continuing to probe the human antibody repertoire for antibodies against

LAM and additional TB antigens that may possess enhanced utility for immunodiagnostic and immunotherapeutic applications.

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, In press.

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. Submitted for publication.

D. Patel, A. Choudhary, W.J. Honnen, Z. Lai, R.S. Prattipati, T.L. Lowary and A. Pinter. Molecular characterization of structural requirements on novel human monoclonal antibodies against *M.tb* glycolipids formed in response to infection- role of isotype in reactivity. Submitted for publication.

Patent applied: A. Pinter, A.Choudhary and D.D. Patel. Novel Anti-LAM Mnooclonsl antibodies for diagnosis and treatment of Myvobacterium tuberculosis infections..

Additional manuscripts are being prepared by collaborators describing the enhanced sensitivity of immunodetection assays based on our novel human mAbs

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", Principal Investigator: Abraham Pinter, Ph.D. Agency: Bill and Malinda Gates Foundation. Period: 7/1/16-12/31/18.
The goals of this project are to isolate a large panel of human monoclonal antibodies specific for lipoarabinomannan of M.tb and to develop a sensitive and broadly applicable POC immunodiagnostic assays for TB infection.

Completed Projects

"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.

"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.