Appendix E

Specific Examples of Contributions of AIDS/HIV Research to Other Fields

Number of responses	Specific examples (listed by area and field)
179	**BASIC SCIENCES**
21	**Biochemistry**
2	Biochemistry of polymerase protease, transcriptional activation and regression, all applicable to different biological systems
1	Glycoprotein and gene product characterization
1	Identification of regulatory genes, their function, and role in latency
1	Mechanism of ribonucleic acid (RNA) synthesis control
1	Control of transcription and translation
1	Protein processing
1	Gene organization
2	Protein structure/enzyme of human immunodeficiency virus (HIV) (e.g., reverse transcriptase)
2	Crystal structure of proteins; design of substrate inhibitor
1	Studies of aspartic protease and thein inhibition
1	Novel understanding of protein-deoxyribonucleic acid (DNA) or RNA interactions
1	Structure/function studies of inhibitors of reverse transcriptase and viral protease
1	Binding of protein to DNA
1	Interaction of envelope proteins with cellular CD-4 receptors
1	Viral coded enzymes and their expression
1	Identified functional domains and mechanism of DNA polymerase
1	Progress in the “anti-sense” approach to treatment of viral disease and cancer
1	Isolation of regulatory c-effecter and viral proteins

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
22	**Cell Biology**
1	**Regulatory Genes**
3	**Cell transport, protein processing interaction by cytokines, autocrin pathways, cell activation**
2	**Cell receptor interactions leading to normal function, abnormal function and cell death**
1	**Identification of cell lines allowing replication**
1	**Role of cytokines as growth factors**
1	**Compartmentalization of pathologic products**
1	**Cell fusion mechanism, transection**
2	**Viral effects and cell function**
1	**New understanding of RNA splicing and regulation of nuclear-cytoplasmic transport, new understanding of regulation of transcription**
2	**Understanding of CD-4 receptor function**
1	**Mechanism of receptor/ligand endocytosis and transport to and release from lysosomes**
2	**Understanding of basic growth and development process**
1	**Mechanism of latency-- many contributions to cell biology**
1	**Viral replication, budding, and morphology**
1	**Enhanced understanding of intra and intercellular communication, (e.g., activation signals, secondary messengers)**
1	**Major impact on signal transduction, mechanism of c-effecter activation/differentiation**

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
16	**Genetics**
2	**Genetic organization and control of all retroviruses including HIV, human T-cell lymphotropic virus, (HTLV), other tumor and immunodeficiency viruses**
3	**Regulation of gene expression**
1	**Mutation rates**
2	**Relatedness of HIV and simian immunodeficiency virus**
1	**Retroviruses as vectors for gene transfer**
1	**Studies of mutation in in vivo**
1	**Mechanism of integration into host genome**
1	**Mechanism and fidelity of viral RNA reverse transcription and proviral integration**
1	**Recombination**
1	**Research on genetic factors that influence susceptibility to infection and patterns of immune dysfunction**
1	**Identification of regulatory genes and their function**
1	**Transcriptional regulation**
34	**Immunology**
1	**Understanding of retroviruses**
1	**Understanding basic pathogenesis**
1	**Stimulated research on effect of alcohol on immunological system (cellular and humoral immune responses and neurohormonal immunodulation)**
1	**Cell and antibody mediated immune recognition of antigen and prevention of infection**

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Cell mediated immune response controls susceptibility to some protozoal (Pneumocystis), fungal (Cryptococcus), and bacterial (p.multocida) infections
2	Elucidation of lymphocyte biology, subsets, networks interactions, profound insight into CD-4 lymphocyte biology and function
6	T-cell function, immunoregulation, cellular immunology in general
1	Mechanism of virus targeting and immunoresponse suppression
1	Mechanism of immune control of viruses
1	Pivotal role of CD-8 bearing T-cells in the immune process
1	Role of immune disregulation
2	Better understanding of roles of T and R lymphocytes in the immune process
1	Careful characterization of lymphokine and monokine regulation and CD-4 and adhesion molecule function
2	Enhanced understanding of interactions of cellular components and lymphokines
3	Deeper understanding of immune system and of multiplicity of diagnostic probes
1	Immunoregulation, cytokine action, immunodeficiency, animal models
1	Understanding of resistance of viruses
1	Importance of microphage as a viral reservoir
1	AIDS has essentially had a confirmatory role on aspects of cell-mediated immunity
1	Knowledge of antibodies to surface antigens operate
1	Elucidation of peptide sequences that specifically signal T-lymphocytes
1	Elucidation of immune epitopes

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Development of SCID mouse model that can be used to evaluate “human-like” immune response to a number of pathogens
1	Model for research on other immune deficiency disorders; insight into normal and immune function and regulation
20	Microbiology
1	Viral genetics
2	Elucidation of genetic complexity and biology of human and primate retroviruses
4	Insight into HIV related opportunistic infections
2	Co-pathogenesis relations to other retroviruses and to fungi
2	Served as a paradigm for the study of viral pathogenesis
1	Microbial pathogenesis
1	Mechanism of viral latency and transactivation
1	Virus growth and assay techniques
1	Methods to allow the search for potential retroviral disease causing agents
1	Better understanding of all opportunistic infectious agents
1	Applications of polymerase chain reaction (PCR) techniques to diagnosis of cancer
1	Studies of viral evolution and monitoring of viral spread through Africa and world populations
1	Field of human retrovirology has been opened
1	Expression of active enzymes in E.coli

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
15	**Molecular Biology**
3	Control of genes, reverse transcriptase mediated alteration of genomes, insertion of control elements
2	Broadly applicable principlein transcriptional activation, transcriptional and translational control mechanism, RNA processing, advances in genetic engineering
1	Regulator circuits
1	Encoding and sequence similarities
1	Excellent virus for the study of cis and trans regulation factors
1	Genetic variation, processing signals
1	Gene structure and regulation
1	Application of novel strategies (e.g., PCR)
1	Stimulated use of PCR
1	Studies of how accessory genes affect viral latency and transcription
2	Identification of HIV genes and their function and components of HIV lifecycle have implications for all other viruses
15	**Pathology**
2	Pathogenesis of viral induced immune suppression
1	New insights into AIDS dementia, other retroviral nervous system disease such as Tropical Spastic Paraparism caused by HTLV-1
5	Better understanding of the pathologies of Kaposi's sarcoma (KS) and opportunistic infections
1	New organ system relationships

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Growth of human cells (organs) in immunodeficient animals (mice) -unique experimental model
1	Improved concepts of pathological consequences of infectious agents
1	Understanding effect of virus
1	Neuropathology of central nervous system (CNS) complications
1	Microglial or microphage involvement in AIDS encephalopathy
1	Development of new techniques to isolate and culture microbes in pathology specimens
13	Pharmacology
5	Development of antiviral, antifungal and anticancer therapies/agents
3	Better understanding of antiviral drug action
1	Development of CD-4 blocking strategy
1	Protease inhibitors
1	New treatment methods, such as synthetic peptides
1	New drug design and modeling
1	Targeted drug development established for AIDS provides a model and kind of knowledge for development and testing compounds against other viruses; drugs developed against HIV may have other applications; development of animal models for chemoprevention of retroviral transmission; Development of tests for toxicity
22	Virology
1	Viral Genetics
7	Profound insight into new classes of retroviruses--human and primate, immunodeficiency

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
4	Mechanism of retrovirus replication, integration and control of RNA synthesis
2	Mechanism of persistent infection and latency
1	Detailed analysis of virus replication
2	Co-pathogenisis with other related and coexisting viruses
1	Regulation of retroviral genes by host factors (e.g., 50 kd cellular protein binds to LTR (long term repeat) of HIV-1 and regulates transcription)
1	Life cycle of RNA viruses
1	Identification of receptors, varying protein coats
1	Latency and integration of retroviruses
1	Pathophysiology of retroviruses
1	Other
1	Psychobiology- relation of specific pathology caused by HIV infection in brain to behavioral changes in victims- results will eventually have importance for other dementias (e.g., Alzheimers)
168	MEDICAL DISCIPLINES
4	Cardiology
4	Understanding mechanism of AIDS-related cardiomyopathies
8	Dentistry
1	Drastically changed dental research. Dental research has turned significantly to basic research (virology, microbiology, molecular biology, immunology) in understanding oral soft tissue and salivary gland disease; has begun to use biostatistics and epidemiology in more areas and has begun to explore behavioral and attitude studies;
4	Emphasized need for and improved infection control

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Understanding oral complications of immunosuppression
1	Study of the mechanism of thrush
1	Possible role of salivary components as antiviral agents
11	Dermatology
2	New dermatopathic illness (and descriptions of them) secondary to HIV
6	Broader understanding of nature/treatment of skin pathology in immunodeficient subjects, including KS
1	Dermal functions of immunologic system surveillance
1	Methods for in situ and PCR hybridization
1	Viral causes of skin deficiencies
6	Endocrinology
2	Helped in the development of tools to study autocron events and growth factor regulation
1	Better understanding of circulating cytokines
1	Insights into adrenal failure and AIDS-associated endocrinopathies
1	Autoimmune system
1	Understanding of neuro-endocrine pathways
5	Family Practice
1	Psycho-social-medical care of complex illness affecting mind, body and family
1	importance and methods of obtaining accurate sexual history
2	Management of AIDS in community setting
1	New focus on epidemiology within family practice research

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
9	Gastroenterology
1	New gastrointestinal (GI) illness associated with HIV
2	Better understanding of development of leukepenia, KS, and opportunistic infections of the GI tract
1	Improved understanding of Cryptosporidium
1	Mechanism of inflammatory bowel disease
1	Interaction of intestinal infections and malabsorption syndromes, nutritional deficiencies
1	How other viruses lead to intestinal pathology
2	Insights into the diagnosis and treatment of GI infections; treatment of chronic diarrheal disease
10	Hematology
1	Understanding of blood transfer in disease
1	Identification of cellular subpopulations and the function and development stages for each subtype
1	New spectrum of immunodeficiency associated cancers
1	Lymphocyte, microphage biology
1	Major stimulus to the cloning and study of colony stimulating factors
1	Role and use of colony stimulating factors
1	Improved understanding of regulation of bone marrow and mechanism of ITP
1	Stem cell renewal
1	Improved protection of the nation's blood supply

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Insight into role of wide range of blood components and related dysfunction/disease
18	Infectious Disease
1	Understanding the impact of loss of lymphocyte function and therapeutic strategies for dealing with infections in an immunocompromised host
3	New spectrum of immunodeficiency-associated infection
3	Better understanding of spectrum of opportunistic viral illness
6	Treatment of opportunistic infections, including new antiviral and antifungal
1	New understanding of multiple infectious agents, including AIDS and several opportunistic pathogens
1	New concept in the management of infectious diseases, their epidemiology, and their prevention
2	Detailed understanding of a virus
1	Understanding transmission of sexually related disease
2	Nephrology
2	New concepts in glomerulopathies
15	Neurology
1	Understanding AIDS encephalopathy
1	Better understanding of subcortical dementia
3	New spectrum of associated neurological illness, dementia, and peripheral neuropathy
1	AIDS dementia reveals alternative mechanisms of cognitive decline, indirect chemical bases, with absence of direct pathology

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
3	Better understanding of role of viruses in CNS disorders, improved recognition of viral causes of subtle disorders of mental function
1	New understanding of viral encephalopathy at mechanistic and clinical level
3	Insight into mechanisms of dementia and degenerative CNS disease, HTLV, and multiple sclerosis
1	Relevance of microphage-derived cells and possibly soluble protein factors on the function of the nervous system
1	Blood-brain-barrier affects CNS microphage and other cells' roles in infection
7	Obstetrics/gynecology
4	Improved recognition of maternal-fetal viral transmission
1	Avoidance of internal fetal monitoring and use of scalp electrodes
1	New studies of cervical neoplasias associated with immunosuppression, viral transmission during pregnancy
1	Studies of exogenous virus transplacental transmission and transmission during breastfeeding
21	Oncology
4	New understanding of Kaposi's Sarcoma (KS)
1	Understanding of viral-induced changes in cell function
1	Importance of drugs influencing, DNA structure and function
3	New spectrum of immunodeficiency-associated cancers and further information about these rare cancers
3	Mechanism of oncogenesis
2	New insight into viral etiology of neoplasm

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Knowledge of unrestrained epithelial growth that seem to underlie KS and its relationship to oncogenesis and growth factors
2	Gene control, cell proliferation, and cell regulation as they relate to the formation of malignant cells
2	Regulatory gene (tat) transected into mice, cancer symptoms of Kaposi's sarcoma tat has a direct effect on development of tumors
1	Mechanism of cell transformation
1	Defining genomes of leukemia
7	Ophthalmology
7	*New* understanding of cytomegalvirus (CMV)-retinitis (therapy with gancyclovir) will have broader applications
5	Pathology
1	Importance of viral-cell interactions in the induction of disease of all systems
2	Development of more efficient and accurate techniques for measuring presence of virus in tissues and developing diagnostic technology, (i.e., T/B lymphocytes and ratios)
1	Use of in situ hybridization to detectHIV
1	Methods for RNA detection in situ
9	Pediatrics
2	Better understanding of maternal-fetal interrelationships, cell transfer, passive immunity, and genetic basis of disease
1	New approach to medical and social care
1	Effects on understanding of pediatric immunodeficiencies (e.g., primary as well as maternal/fetal transmission of viruses)
2	Pediatric immunodeficiency and congenital viral infection

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
2	Provided insight into development of immune system in children
1	Insight into neurological development and immune function
10	Psychiatry
1	Stimulated research on HIV-related psychopathology (e.g., AIDS-related dementia)
2	Improved understanding of AIDS-related dementia (will relate to other dementias)
1	Improved understanding of intravenous (IV) drug users interaction and environment
1	Behavior modification and studies of high-risk behavior
2	Reaction to terminal illness of patients and families
1	Crisis intervention therapy
1	Studies of sexual behavior
1	New approach to substance abuse
17	Pulmonary medicine
5	New spectrum of illnesses
3	New pulmonary diagnostics for viral respiratory illness
1	Outpatient management of severe viral disease (i.e., aerosolized antiviral agents for pneumocystis)
3	Detailed understanding and improved management of Pneumocystis carinii pneumonia
2	Improved bronchoscopic techniques
3	Improved treatment of lung infections (e.g., pneumonias)

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
4	**Rheumatology**
2	**Autoimmune diseases**
1	**Immune cell function**
1	**Better understanding of rheumatoid arthritis, lupus, etc.**
54	**APPLIED MEDICAL SCIENCES**
21	**Diagnostics**
2	**Development of PCR**
1	**Virus culture**
1	**Identification of pathogen, stage of infection, types of immune response, and cellular populations**
4	**Stimulating use/development of newer diagnostic tests such as those employing PCR and RIA**
1	**Antibody, reverse transcriptase and other assays**
1	**Protection of the blood supply**
1	**Better clinical screening for PCP, KS, CMV retinitis**
2	**Development of new diagnostics**
2	**Improvement of old diagnostic techniques**
1	**Imaging advances-- GI tract, nodes, and mesentery**
1	**Rapid diagnostic serologic tests for screening**
1	**Improved techniques for measuring T and B lymphocytes**
1	**Improved anatomic pathology for diagnosis of tissue infection with viruses**
1	**Use of PCR as means of detecting extremely low levels of virus in blood**

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Improved diagnostics for HIV associated disease
17	Drug development
1	Drugs that will influence gene expression and prevent viral induced changes in human genome
1	Aerosolizes pentamidine for pneumocyctis
1	Drugs to inhibit viral replication
10	New antiviral, antiparasitic, antibiotic behavior therapy
1	Expedited approval use of medication
1	Initiation of search for protease inhibitors and inhibitors of reverse transcriptase
2	Technique of targeted drug development
3	Other therapeutics
1	CD-4 mimicking recombinant products
1	Synthetic peptides
1	Improved microbial treatments
12	Vaccine development
3	Many advances in understanding of vaccines in general via HIV work
1	New concepts in vaccine development (e.g., anti-idiotgsic vaccines)
1	Application of genetic engineering techniques, work on animal models
2	Recombinant technologies applied
1	Learning to produce vaccines against agents that mutate rapidly
1	Development of simian AIDS vaccine

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	New vectors, adjuvants, assay systems
1	Progress toward developing viruses for complex viruses
1	Applications of insights into nature of immune response/immunogenecity; nature and function of adjuvants; Advances in techniques of molecular biology/ molecular genetics
1	Other
1	Safer blood banking
41	EPIDEMIOLOGY
7	Biostatistics
1	New methods for conduct of clinical trials and drug evaluation
1	Development of methods for clinical trials with high dropout rates
4	Advances of epidemic modeling techniques
1	Improved data collection techniques
19	Clinical trial development
3	Development of alternative tracks for drug testing
2	Expedited “real world” trials
2	Development of multiple sites and investigators in trials
3	Development of community-based trials
1	Ability to conduct successful clinical trials in non academic setting
4	Negative effect: sanctioning uncontrolled or unsophisticated trials for drug efficacy
2	Stimulated development of cohort studies of surrogate endpoints

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
2	AIDS research has helped overcome special study design problems posed by unique population and risk groups.
11	Disease surveillance
3	Improved methods (e.g., those used by Centers for Disease Control (CDC)), beyond those used for sexually transmitted diseases; Will have major effects on other disease surveillance efforts
	Risk evaluation
	Improved methods of disease ascertainment
	Increased awareness of difficulties of surveillance for a stigmatized disease
	Improved reporting to the CDC
	Surveys by ASPN--more realistic than health department estimates
2	Greater sophistication in techniques of data collection and analysis
	Examination of issues concerning underreporting
4	Natural history of disease
	Large surveys of susceptible and high-risk individuals
	Understanding of behaviors (not groups) that put people at risk
	Better understanding of the behavior of virus in the CNS
	Broader application of role of cofactors, insights into the relationship of immune function and susceptibility of disease
0	Other

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
68	**PUBLIC HEALTH AND HEALTH SERVICES RESEARCH**
14	**Health behavior change**
1	**Stimulated prevention research on relation between alcohol abuse and alcoholism and high risk behavior, particularly unsafe sexual behavior and IV drug use**
1	**Increased study of lifestyle changes that relate to disease prevention**
5	**Increased knowledge of disease leading to change in high risk sexual behavior among homosexual men**
1	**Generally, increased efforts in a traditionally poorly studied area**
1	**Safe sex practices**
1	**Ability of targeted health education to influence behavior of population groups (i.e., homosexuals)**
1	**Brought to forefront risk behaviors clearly related to infection**
2	**Prototype programs for altering behavior-- sexual practices, drug use or abuse**
1	**Studies of behavior change- relationship to knowledge and attitudes**
9	**Health care financing**
1	**Illustrates problems of catastrophic illness**
5	**Focused problems on broader deficiencies in health care financing**
1	**Focus on cost of drugs and drug development**
1	**Raised issues regarding reimbursement for experimental therapies**
1	**identification of gaps in Medicare and Medicaid funding**

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
10	Health care organization and delivery
1	Stimulated prevention, early intervention and treatment research on substance abuse, particularly IV drug use
3	Contributed to understanding long term care issues (not focused on elderly), hospice, nursing homes, particularly use of community supports (i.e., San Francisco model)
1	A better understanding of community-based models of care
2	Expedited knowledge and application of knowledge about out-of- hospital care previously thought necessary in hospitals
1	Demonstration of importance of home care, case management
1	Improved evaluation of treatment programs
1	Negative effect: principles for the control of communicable disease have been grossly compromised
12	Health education
1	Stimulated research on health education and education efforts in preventing high-risk behaviors facilitating HIV infection
2	General education about communicable disease, infection control
1	Education about sexually transmitted diseases (STDS)
3	Improved knowledge of how to design and conduct health education programs to change behavior
1	Has increased sexuality awareness in school systems and institutions
1	Has increased awareness of infection control in industry
1	Has demonstrated clear connection between lifestyle practices and disease infection

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
1	Has demonstrated the use of television and mail for health education campaign
1	Design of focused education and education delivery systems to targeted groups, (e.g., gay men, IV drug users, Blacks, Hispanics) and general population
9	Sexually transmitted disease
1	Routes and mechanisms of transmission
1	Closer attention to other STDs in prevalence studies
2	Refocused awareness on STD's
1	Knowledge about gay sex behavior
1	Knowledge of practices and attitudes of gay community
1	Called attention to lack of knowledge and data on sexual behavior and practices
1	Has shown the interrelationship among STDs
1	Almost all AIDS behavior change research and education strategies are applicable to control of other STDs
5	Sociology/anthropology
1	Better understanding of patterns of sexual behavior among homosexuals and drug-addicted people
1	Understanding of stigma, prejudice, gay behavior
1	Improved survey procedures with hard-to-reach populations
1	Has emphasized our lack of knowledge of sexual attitudes and customs
1	Further understanding of individuals' risk-taking behaviors, social organization, disorganization, ways to alter people's decisionmaking processes

SPECIFIC EXAMPLES-continued

Number of responses	Specific examples (listed by area and field)
9	**Substance abuse**
4	**Increased knowledge and awareness of substance abuse and its patterns**
1	**Had an overall stimulating effect on substance abuse research**
1	**Focused attention on an underfunded discipline--AIDS/HIV research will relate to the broader socio-economic and medical problems that drug abuse creates.**
1	**Demonstrated the connection of substance abuse to other disease**
2	**Increased information about factors leading to substance abuse, about the 'drug culture," about treatment programs**
0	**Other**
2	**OTHER**
1	**Radiology- brought about advances cross sectional imaging**
1	**Increased public awareness of issues in substance abuse and homosexuality**
4	**Additional comments**
1	**In 1979, no human or primate immunodeficiency-causing retrovirus were known. Now there are eight. There are surely many more. Need research to allow us to prevent such illness and disease, rather than respond to it.**
	Too soon to tell the results (spinoffs) of AIDS research. It takes a long time for advances to impact other fields.
	There have been many dividends from the AIDS/HIV research, in many scientific fields. The successful identification of the virus and clarification of its mode of transmission has helped to convince the American public of the quality of biomedical research.
	AIDS research has made little contribution to our overall understanding of basic biology. To the contrary, our understanding of basic biology has made possible all AIDS research.