Table 2. Participating Faculty Members
(Alphabetically By Faculty Member)

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
BAUM, LINDA G., MD, PhD	PROFESSOR	PATHOLOGY DEPARTMENT ADMINISTRATION (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	**Speciality**: Hematopathology, Hematology Technical Research Interest: Many biologic and disease processes are governed by carbohydrate-protein mediated cell-cell interactions. We examine these processes in the immune system, investigating the interaction of lymphoid cells with stromal cells, antigen presenting cells and tumor cells. Our goal is to understand mechanisms controlling cellular glycosylation and the roles of cellular glycans in lymphocyte development, defense against microbes and tumor cells, and cellular transformation. We focus on a family of lectins, the galectins, that participate in all these cellular processes. The outcome of galectin binding to lymphocytes depends on expression of specific glycan ligands on specific cell surface glycoproteins and the organization of the glycoproteins into discreet domains or lattices on the cell surface. The components of the lattice, the spacing of glycoproteins in the lattice and the separation of different glycoproteins into distinct lattices on the cell membrane all contribute to the outcome of galectin binding. We collaborate with CNSI members to use novel tools to examine the architecture of the lectin-glycoprotein lattices, by manipulating cellular glycosylation, examining binding to artificial ligands, and creating synthetic galectins that vary in ligand specificity and binding domain spacing and flexibility, to understand structural features of galectins that deliver specific cellular signals. **Scientific Interest(s):** Dr. Linda Baum is interested in the role of cell surface carbohydrates and endogenous lectins in the maturation and function of cells of the immune system. T-cells mature in the thymus and then migrate to organs such as spleen and lymph nodes, where they participate in the immune response to foreign invaders. Baum and her colleagues have found that a carbohydrate binding protein termed galectin-1 is expressed in human and murine thymus, lymph nodes and spleen. This endogenous lectin participates in the trafficking of T-lymphocytes from the circulation into these tissues and also mediates adhesion of T-cells to stromal cells within the organs. In addition, galectin-1 induces programmed cell death of

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				specific populations of T-cells at unique points in development, identifying a role for galectin-1 in modulating the immune response. Baum's lab has recently found novel immune system functions for other members of the galectin family, including galectins-3 and -9, such as regulating B-cell survival and dendritic cell function. Baum's current work focuses on identifying the cell surface counter-receptors which bind various galectins and participate in galectin-mediated cell adhesion, activation and apoptosis; and dissecting the structural features of these molecules essential to these distinct functions. She and her associates use a combination of cellular and biochemical assays to understand the mechanism of galectin functions.
BENSINGER, STEVEN J. , VMD, PhD	ASSISTANT PROFESSOR	PATHOLOGY DEPARTMENT ADMINISTRATION (MOLECULAR & MEDICAL PHARMACOLOGY)	MENTOR	***Linking lupus, cardiovascular disease and lipid metabolism*** It's still unclear why people with lupus have a more than 50-fold increased risk for cardiovascular problems such as accelerated atherosclerosis With LRI funding, Dr. Bensinger will pursue the novel concept that a protein called the "Liver X Receptor" (LXR)-already a well-known player in promoting atherosclerosis and inflammation-may also contribute to the accelerated atherosclerosis of lupus. Dr. Bensinger already has reported that a deficiency of LXR in mice leads to the development of lupus-like disease, providing the first evidence that a single transcription factor may regulate the cause and development of both atherosclerosis and autoimmunity. In further delving into these tantalizing links between lipid metabolism and inflammation, Dr. Bensinger seeks to uncover a role for LXR as a novel drug target for preventing and treating lupus atherosclerosis.
BERK, ARNOLD J., MD, PhD.	PROFESSOR	MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	**Transcription and Cell Cycle Control in Human Cells** We study molecular interactions that regulate transcription in mammalian cells, focusing particular attention on transcription factors encoded by oncogenes and tumor suppressors and the regulation of cell replication. Since the decision to initiate transcription is the key control point regulating expression of most genes, transcriptional regulation determines the properties of both normal and abnormal cells. Many of our projects involve proteins expressed early during infection by DNA viruses because these proteins have evolved to interact with key host cell regulatory proteins in order to maximize the yield of progeny virions. Consequently, they have directed us to critical cellular regulatory proteins with which they interact, such as p53, the Retinoblastoma protein family, the mediator of transcription complex, and chromatin modifying complexes. In recent years we discovered that the adenovirus large E1A protein activates

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				transcription from viral promoters by making a high affinity interaction with a specific subunit of the mediator of transcription complex, MED23. We found that activator-mediator interactions stimulate pre-initiation complex assembly on promoter DNA, and that these interactions also stimulate a post-recruitment step in transcription initiation responsible for the "paused polymerases" recently observed at most mammalian promoters. We also study inactivation of the p53 tumor suppressor by adenovirus E1B. Recently we discovered that repression involves sequestration of p53 in subnuclear domains called PML-nuclear bodies. This results from transient covalent attachment of SUMO1 proteins to monomers in a large molecular lattice of E1B and p53. Our recent work can explain the fascinating enigma of how all p53 molecules are inactivated when only ~1% are modified by SUMO1. Recently, we applied "ChIP on chip" methodology to discover how the adenovirus small e1a protein forces contact-inhibited human cells to proliferate: small e1a directly re-localizes major chromatin-modifying complexes on a global genomic scale. Finally, we also work in the area of gene therapy: we have engineered an adenovirus-Epstein-Barr virus hybrid vector that introduces stable episomes into infected cells in tissues of intact animals.
BRAUN, JONATHAN, MD, PhD	PROFESSOR	PATHOLOGY DEPARTMENT ADMINISTRATION (ACCESS PROGRAM, MOLECULAR & MEDICAL PHARMACOLOGY, MOLECULAR BIOLOGY)	TRAINING COMMITTEE, MENTOR	**Research Activities** The Cellular and Molecular Pathology Graduate Program The Medical Scientist Training Program (MSTP) UCLA STAR Postdoctoral Training California NanoSystems Institute (CNSI) Institute for Molecular Medicine (IMED) Broad Stem Cell Research Center Jonsson Comprehensive Cancer Center
CHENG, GENHONG / Ph.D.	PROFESSOR	MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	Our research is aimed at the process of innate and adaptive immune responses in host defense against bacterial and viral infections as well as tumor challenges. Upon recognizing pathogen infections, host cellular receptors such as Toll-like and Nod family receptors can trigger a series of signal transduction and gene expression networks (gene programs) to initiate innate immune responses. These innate immune responses can directly control the replication or spread of bacteria and viruses through induction of phagocytosis or antimicrobial products. In addition, innate immune response can also instruct the activation of adaptive immune response through induction of antigen presentation and co-stimulatory molecules. Defects in any steps in the process of innate and adaptive immune responses can increase susceptible of hosts to pathogen infections, whereas over-reactive immune responses can also lead to many inflammatory diseases and metabolic syndromes. We hope to understand the similarity and difference in host immune responses to

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				different types of bacterial and viral infections, the balance between immune and inflammatory responses, the crosstalk between host immune and metabolic systems. Our goal is to develop novel strategies to enhance our immune system against pathogen infections and tumor challenges while to prevent or inhibit inflammatory and metabolic diseases
CHRISTOFK, HEATHER, PhD	ASSISTANT PROFESSOR	MOL & MEDL PHARMACO//INST FOR MOL MED; ACCESS PROGRAM	MENTOR	Our research focuses on the interconnection of growth factor signaling and cell metabolism. In particular, we are interested in how signaling pathways control metabolic fluxes and the impact this may have on diseases such as cancer. It has long been appreciated that cancer cells exhibit an altered metabolism compared to their normal cell counterparts. We have discovered one mechanism by which cancer cells achieve this altered metabolism - by expressing the embryonic isoform of pyruvate kinase called PKM2 - and our findings support the idea that this altered metabolism is required to support cell growth. We are now exploring additional mechanisms of metabolic regulation with the goals of identifying novel drug targets for cancer and other proliferative disorders and better defining the role of metabolism in cell growth.
CLARK, AMANDER THERESE, Ph.D.	ASSISTANT PROFESSOR	MOLECULAR, CELL & DEVELOPMENTAL BIOLOGY (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	Infertility affects approximately 6.1 million women and their partners in the United States* (*National Survey of Family Growth, CDC 1995). This corresponds to about 10% of the reproductive-age population. Although there are many causes of infertility, normal differentiation of the germ cell lineage is essential to reproductive fitness, and therefore, abnormalities in germ cell development frequently result in infertility. Our lab uses human and mouse embryonic stem cells (ESCs) together with mouse genetics to examine fundamental mechanisms involved in; Formation and function of the mammalian germ line with an emphasis on humans Mechanisms that inhibit cell fate decisions.
COLICELLI, JOHN J., PhD	PROFESSOR	BIOLOGICAL CHEMISTRY (ACCESS PROGRAM, MOLECULAR BIOLOGY, NEUROSCIENCE)	MENTOR	Dr. John Colicelli studies how cells detect stimulatory signals, transmit this information to subcellular compartments and respond appropriately. Of particular interest are signal transduction mechanisms mediated by RAS, the most common mutation-activated gene in human tumors. A better understanding of RAS function in cell proliferation and tumorigenesis should facilitate the development of effective cancer therapeutics. To this end, Colicelli studies the pathways regulated by RIN1, a downstream effector. The RIN1 protein stimulates ABL tyrosine kinases, which can be oncogenic in hematopoietic tumors. Ongoing projects in this area include studies of how RIN1 promotes leukemogenesis, and whether this connection can be exploited in the development of novel therapeutics. In epithelial cell-derived tumors, RIN1 may play a very different role. Preliminary data suggest that RIN1 may function as a tumor suppressor in

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				breast cancer. Researchers are continuing to examine this connection and its implications for diagnosis, prognosis and treatment of breast cancer. Pancreatic ductal cancers, which almost universally carry activating mutations in the KRAS gene, are a more recent area of focus. Colicelli and his colleagues are part of a multi-lab effort to define signal transduction changes in pancreatic cancer and identify targets for therapeutic intervention. Finally, a portion of the lab is studying the role of RIN1 in neuronal plasticity. RAS (upstream of RIN1) and ABL (downstream of RIN1) are known regulators of learning and memory. Their experiments with a Rin1-/- disruption mouse strain confirm a role for this pathway in learning, but the mechanism remains unclear
CROOKS, GAY, M.B., B.S	PROFESSOR	Path & Lab Med	MENTOR	**Human Hematopoietic Stem Cells, Lymphopoiesis and Transplantation** The Research Program in the Crooks Laboratory is focused on the identification and functional definition of human hematopoietic stem and progenitor cells and how they can be isolated and manipulated to improve the results of transplantation. Two specific areas of investigation related to tumor biology that have evolved from this central focus: 1. the elucidation of AKT signaling pathways activated in response to dimerization of intracellular c-Mpl, and 2. Study of the downstream mechanisms of VEGF-mediated angiogenesis.
DAWSON, DAVID, MD, PhD	ASSISTANT PROFESSOR	PATH & LAB MED	MENTOR	Pancreatic cancer is a highly aggressive and lethal cancer due to its typically advanced stage at initial diagnosis, poor response to chemotherapy and propensity to recur and metastasize. My research addresses the role of epigenetic modifications, including DNA methylation and histone modifications, in mediating pancreatic cancer progression. In addition, we are exploring the importance of specific growth signaling pathways such as Wnt in pancreatic cancer. We are particularly interested in understanding the intersecting roles of epigenetics and growth signaling pathways in the evolution and maintenance of pancreatic cancer stem cells, as accumulating data support the concept that cancer stem cells may be critical determinants of chemoresistance, metastasis and disease recurrence in pancreatic cancer.
DENNY, CHRISTOPHER , MD	PROFESSOR	PEDIATRICS-ADMINISTRATION, PEDIATRICS-HEMATOLOGY/ONCOLOGY (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	**Molecular Mechansisms of Oncogenesis** Genomic mutation is a primary force in the genesis of human malignancy. Molecular isolation of genes involved in tumor-specific rearrangements has identified mechanisms of tumorigenesis and has formed a basis for studying transformation pathways of human cancers. My lab has focused on the 11;22 translocation that occurs in Ewing's sarcoma and PNET, two lethal and poorly understood pediatric cancers of presumed neural crest

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				origin. This rearrangement fuses a previously unknown gene, termed EWS, to FLI-1, a member of the ETS family of transcription factors. We have isolated this chimeric molecule both as genomic and cDNA clones, and have shown that EWS/FLI can transform rodent fibroblast lines. This is consistent with the notion that it plays an active role in Ewing's sarcoma oncogenesis. Mutation analyses, DNA-binding studies and subcellular localization experiments have lead us to hypothesize that EWS/FLI is acting as an aberrant transcription factor that is qualitatively different from normal FLI-1. A novel method for identifying differentially expressed genes has been developed to isolate potential target genes that are modulated by EWS/FLI. This cohort of EWS/FLI regulated genes is now being analyzed with a long term goal of defining important genetic pathways that are activated during cellular transformation.
DORIGO, OLIVER, MD. PhD	ASSISTANT PROFESSOR	OB & GYN	MENTOR	Our work focuses primarily on investigating molecular therapies that can reverse the platinum resistant phenotype in ovarian cancer. We are particularly interested in targeting the oncogenic PI3kinase/Akt/mTOR in human ovarian cancer which has been associated with platinum resistance. We have recently demonstrated that the dual PI3kinase and mTOR inhibitor NVP-BEZ235 (Novartis Pharmaceuticals) decreases ovarian cancer cell proliferation to a significantly greater degree than mTOR inhibition alone. More importantly, we found NVP-BEZ235 to be effective in cisplatin resistant cells, and sensitize ovarian cancer cells to the effects to cisplatin. In addition, treatment of mice with established tumor disease using the above described transgenic mouse model resulted in significantly prolonged survival compared to control animals. To elucidate novel mechanisms of platinum resistance, we have generated several novel, syngeneic pairs of human ovarian cancer cell lines that differ greatly in their sensitivity to cisplatin. These cell lines have been extensively characterized using protein analysis and gene expressions studies. We have identified a number of differentially expressed genes and proteins in cisplatin resistant cells that are related to PI3Kinase/Akt/mTOR and Insulin Growth Factor Receptor (IGFR) signaling. We are particularly intrigued by our observation that the expression of IGFR protein is significantly down-regulated in cisplatin resistant cells. Using retroviral gene transfer and siRNA technocology, we are currently investigating whether modulation of IGFR expression impacts on the sensitivity of human ovarian cancer cells to cisplatin in cell culture and xenograft models.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
ECONOMOU, JAMES S., MD, PhD	V Chancellor for Research/Prof of Surgery	SURGERY- CHAIRMAN (MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC, MOLECULAR & MEDICAL PHARMACOLOGY)	ADVISOR, TUMOR GENE THERAPY	**CLINICAL INTEREST** Cryotherapy, Limb Perfusion, Liver, Melanoma James Economou, M.D., Ph.D., received his doctorate in Immunology at the Johns Hopkins University in Baltimore. He is the chief of the Division of Surgical Oncology at UCLA. As deputy director of UCLA's Jonsson Comprehensive Cancer Center (JCCC), Economou ensures collaborations between departments, oversees two Specialized Programs of Research Excellence (SPORE) in prostate and lung cancers, supervises seed grants, and helps coordinate National Institutes of Health training programs. A coordinator (with Dr. William McBride) of the Human Gene Medicine Program, he works with the cancer center senior leadership to identify program goals, provide funding and space support and give academic oversight. Economou performs about 400 surgeries a year, specializing in melanoma, primary and metastatic liver cancer and sarcomas. Along with Drs. John Glaspy and Antoni Ribas, he leads a laboratory that is developing gene therapy treatments for melanoma and liver cancer. In addition to his administrative duties in the cancer center, surgical oncology and the Human Gene Medicine Program, Economou also sits on two National Cancer Institute (NCI) study sections boards composed of senior investigators who review grant applications. His NCI responsibilities give him valuable insight into the peer review process, information he passes along to young cancer center scientists who must rely on grant funding to support their research.
FOX, C F., PhD.	PROFESSOR	MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC (BIOINFORMATICS, BIOMEDICAL ENGINEERING, MOLECULAR BIOLOGY, MOLECULAR BIOLOGY)	PI EMERITUS	Present P:I (Yr 35) of the UCLA Tumor Cell Biology Training Program
GOMPERTS, BRIDGITTE, MD	PROFESSOR, MD.	JONSSON COMPREHENSIVE CANCER CENTER, SPECIALTY PEDIATRIC HEMATOLOGY-ONCOLOGY	MENTOR	Dr. Brigitte Gomperts studies the role of adult stem cells in repair and regeneration of the lungs. Through her lab's work in non-small cell lung cancer they have identified a putative tumor-initiating stem/progenitor cell population that is usually transiently involved in repair, but is associated with a poor prognosis if it persists and is found in NSCLC tumors. This stem/progenitor cell population is involved in aberrant repair after injury and persistence of this cell leads to indefinite self-renewal. This property of indefinite self-renewal is then thought to allow the acquisition of genetic and epigenetic changes that lead to malignancy. The Gomperts lab

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				studies these stem cell populations during the stepwise progression to lung cancer. The overall goal is to understand the genetic and epigenetic mechanisms of lung carcinogenesis from stem/progenitor cells in the airway epithelium and ultimately develop therapies that prevent the development of lung cancer.
Name/Degree(s)	**Rank**	**Primary (& Secondary) Appointment(s)**	**Role in Program**	**Research Interest**
GRAEBER, THOMAS G, PhD	ASSISTANT PROFESSOR	MOLECULAR & MEDICAL PHARMACOLOGY (ACCESS PROGRAM, BIOINFORMATICS, BIOMEDICAL ENGINEERING)	MENTOR	His work in cancer biology started with the discovery that hypoxia, a common feature of solid tumors, induces p53 protein levels, and that p53 deficient cells are less prone to undergo apoptosis in low oxygen conditions, conferring a survival advantage. These findings led to a model of hypoxia as a physiological selective force against apoptosis-competent cells in developing tumors, thus explaining the previously unaccounted for high frequency of p53 mutations in cancer. In computational biology, he developed an algorithm to identify potential autocrine signaling loops in cancer using gene expression microarray data. The algorithm integrates biological data (in this case, cognate ligand-receptor partners) into the analysis of raw gene expression data, and a number of leads from this method have been verified to play critical roles in cell signaling. Recently, his lab has developed a mass-spectrometry based protocol for identifying tyrosine-phosphorylated proteins from cancer cell lysates. They are using this proteome-wide 'phosphorylation profiling' assay to identify the signaling pathways activated by various oncogenic initiating events (e.g. kinase mutations), and to elucidate the interconnectedness of classical signaling pathways into a more comprehensive signaling network. His lab is also analyzing large gene expression and proteomics datasets on human prostate cancer and mouse models of prostate cancer, and developing bioinformatic algorithms to identify conserved/critical oncogenic mechanisms through cross-species comparisons. In modeling cancer signaling, one of the lab’s goals is to identify minimal sets of informative components that best reflect the state of the cell and serve as molecular targets for nanodevice-based diagnostics, PET imaging, and patient-tailored treatment.
HANKINSON, OLIVER,. PhD	PROFESSOR	PATHOLOGY DEPARTMENT ADMINISTRATION (ACCESS PROGRAM, ENVIRONMENTAL HEALTH SCIENCES, MOLECULAR BIOLOGY, MOLECULAR TOXICOLOGY)	TRAINING COMMITTEE, MENTOR	Dr. Oliver Hankinson's research focuses on the mechanism of carcinogenesis by environmental chemicals and the response of cells to reduced oxygen. Specifically, Hankinson studies polycyclic aromatic hydrocarbons (found in cigarette smoke and smog), dioxin (a widespread pollutant) and related compounds. Carcinogenesis by these compounds depends upon their

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				binding to the aryl hydrocarbon receptor (AHR) and the subsequent dimerization of AHR with the ARNT protein. He is studying the molecular mechanism of activation of gene transcription by the liganded AHR/ARNT dimer (including the role of coactivator proteins in this process) and is analyzing a number of novel dioxin-inducible genes his group has discovered. In addition, he studies the roles of AHR and ARNT in animal models of carcinogenesis. ARNT also dimerizes with HIF-1a to form HIF-1 (Hypoxia Inducible Factor), which is the master regulator of the hypoxic response. Hankinson is studying the molecular mechanism of gene activation by HIF-1 and the role of HIF-1 in tumor angiogenesis and growth. Current research projects include analyzing the mechanism of transcriptional activation by the AHR/ARNT and HIF-1a/ARNT dimers, particularly the potential roles of coactivator proteins in these processes; analyzing novel genes that are transcriptionally activated by chemical carcinogens and hypoxia that may therefore be involved in carcinogenesis and/or the growth of tumors; isolating and analyzing genes transcriptionally activated by hypoxia; and determining the role of ARNT in development, response to hypoxia and response to chemical carcinogens, via analysis of ARNT conditional knockout mice.
HERSCHMAN, HARVEY R., PhD	PROFESSOR	BIOLOGICAL CHEMISTRY, INSTITUTE FOR MOLECULAR MEDICINE (ACCESS PROGRAM, MOLECULAR & MEDICAL PHARMACOLOGY, MOLECULAR BIOLOGY, NEUROSCIENCE)	EXECUTIVE COMMITTEE; MENTOR	**Research Interest:** We study how extracellular stimuli elicit changes in cell growth and differentiation, as a result of induced transcription of "primary response" genes. One gene we discovered encodes a second form of cyclooxygenase (COX-2), the rate limiting enzyme in prostaglandin production and the target of a new generation of anti-inflammatory, anti-pyretic and analgesic pharmaceutical agents. We also identified synaptotagmin 4 as a depolarization-induced neuronal gene; a candidate for a mediator of depolarization-induced synaptic plasticity. Lastly, we have merged principles of cell biology, molecular biology and molecular imaging technologies to develop procedures that repetitively, non-invasively and quantitatively image reporter gene expression in intact, living animals.
HORVATH, STEVE, PhD	PROFESSOR	HUMAN GENETICS (ACCESS PROGRAM, BIOINFORMATICS, BIOSTATISTICS, BIOSTATISTICS)	TRAINING COMMITTEE; MENTOR	I am heading the Array Data Analysis Group (ADAG) at UCLA, which specializes in the analysis of DNA and tissue microarray data and is comprised of faculty and students in the departments of Human Genetics, Biostatistics, and the Bioinformatics Program. ADAG has 3 missions: education, data analysis and research. Please see www.genetics.ucla.edu/labs/horvath/adag.htm **Family-based Allelic Association Tests for Finding Complex Disease**

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				Genes Family-based allelic association tests (FBAT) are used to determine whether genetic markers are associated with disease occurrence. Family-based tests are attractive because they are robust to population admixture effects. Many complex genetic diseases, e.g., Alzheimer's disease, have late age of onset so that it can be difficult to obtain the genetic information of the patient's parents. We developed the sibship disequilibrium test that uses discordant sibships and we collaborated Profs Laird and Xu to develop and implement the family based allelic association test (FBAT) method and software www.biostat.harvard.edu/~fbat/default.html). The FBAT method provides haplotype tests for family-based studies that are efficient and robust to population admixture, phenotype distribution specification, and ascertainment based on phenotypes. It can handle missing parental genotypes and/or missing phase in both offspring and parents. It yields either haplotype-specific (univariate) tests or multi-haplotype (global) tests. **Tissue Microarray Data: Random Forest Clustering** We have been excited about the potential of tissue microarray data for cancer genetics. Tissue microarrays are a new high-throughput tool for the study of protein expression patterns in tissues and are increasingly used to evaluate the diagnostic, prognostic importance of tumor biomarkers. Lack of appropriate statistical methodology have inspired us to develop and apply appropriate data analysis methods. Since it is standard practice in the tumor marker community to use cut-off values for tumor marker expression values, we realized the value of using tree- and forest- based prediction methods for these data. In particular, we have focused on the use of random forest dissimilarities for tumor class discovery and have studied the theoretical properties of a random forest dissimilarity www.genetics.ucla.edu/labs/horvath/RFclustering/RFclustering.htm. The random forest dissimilarity weighs the contribution of each covariate in a natural way: the more related the covariate is to other covariates the more it will affect the definition of the dissimilarity. Dependent markers may correspond to disease pathways, which drive the clinical outcomes of interest. **Systems biology: weighted gene co-expression networks** High-throughput approaches for analyzing the expressed genome provide an unprecedented opportunity to enhance our understanding of human disease. Identifying disease-associated genes that predict patient survival or that may be therapeutically targeted remains a significant challenge. A relatively new approach to analyzing complex microarray data involves application of graphical network models to identify topological relationships between genes. By elucidating the higher level

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				organizational pattern of gene coexpression networks that regulate cellular phenotype, this approach has the potential to identify key disease genes. We have worked on gene co-expression network methods that can be used to explore the system-level functionality of genes. The gene network construction is conceptually straightforward: nodes represent genes and nodes are connected if the corresponding genes are significantly co-expressed across appropriately chosen tissue samples. In reality, it is tricky to define the connections between the nodes in such networks. An important question is whether it is biologically meaningful to encode gene co-expression using binary information (connected=1, unconnected=0). We have introduced a general framework for `soft' thresholding that assigns a connection weight to each gene pair. A technical report and an R tutorial can be found here: http://www.genetics.ucla.edu/labs/horvath/CoexpressionNetwork/
IRUELA-ARISPE, LUISA M., Ph.D.	PROFESSOR	MOLECULAR, CELL & DEVELOPMENTAL BIOLOGY (ACCESS PROGRAM, MOLECULAR BIOLOGY, MOLECULAR, CELLULAR & INTEGRATIVE PHYSIOLOGY, ORTHOPEDIC SURGERY)	MENTOR	Our research focuses in understanding the molecular mechanisms that regulate angiogenesis during development and in pathological conditions. For this we have undertaken investigations to determine the contribution of three key signaling pathways, namely VEGF, Notch and integrins during vascular morphogenesis and tumor growth. Using constitutive and inducible endothelial- and smooth muscle-specific deletions by Cre-lox technology, we have found that these pathways participate at several stages to ensure that patterning, heterotypic cell interactions and responses to the environment are correctly performed. Disturbances in each of these pathways, either temporally or spatially, have been instructive in elucidating their contribution to vascular morphogenesis. Blood vessels are an essential component of the homeostasis of to every tissue and abnormalities in vascular function are associated with inflammatory disorders, tumor growth, ischemia, diabetes to cite only a few. Establishing parallels between tumor and developmental vascular growth can be instructive to derive novel therapeutic avenues guided towards suppression of neoangiogenesis in cancer or induction of vascular growth during ischemia and tissue repair.
KOHN, DONALD B., MD	PROFESSOR	MICROBIOLOGY, IMMUNOLOGY & MOLECULAR GENETICS/PEDIATRICS	MENTOR	The major focus of the research in the Kohn lab is the development and implementation of gene therapy using hematopoietic stem cells (HSC). Current projects include: a. New approaches to gene therapy for ADA-deficient SCID, including the use of lentiviral and foamy viral vectors for ex vivo gene transfer to HSC, direct in vivo ADA gene delivery and ADA gene correction using zinc finger nucleases to augment

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				homologous recombination. b. Immunotherapy for cancer and leukemia by modifying HSC to express T cell receptors and chimeric antigen receptors targeted against tumor-associated antigens. c. New approaches to gene therapy for sickle cell disease, including the use of lentiviral for ex vivo transfer of an “anti-sickling” beta-globin gene to HSC, and beta-globin gene correction using zinc finger nucleases to augment homologous recombination. d. Development of improved gene delivery vectors to achieve specific patterns of transgene expression. **Specialty:** Pediatric Hematopoietic Stem Cell Transplantation **Affiliation(s):** Professor, Department of Microbiology, Immunology, and Molecular Genetics, Department of Pediatrics Member, Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research Member, JCCC Tumor Immunology Program Area **Hospital Affiliation(s):** Ronald Reagan UCLA Medical Center Santa Monica-UCLA Medical Center and Orthopaedic Hospital
KORNBLUM, HARLEY I., MD, PhD	PROFESSOR-IN RESIDENCE	NEUROPSYCHIATRIC INSTITUTE (ACCESS PROGRAM, NEUROSCIENCE, NEUROSCIENCE INTERDEPARTMENTAL PROGRAM , PEDIATRICS-ADMINISTRATION)	MENTOR	**STEM CELLS, BRAIN TUMORS AND NEURAL REPAIR** This group’s current research interests include, a) cancer stem cells--they were one of the laboratories to discover cancer stem cells in brain tumors and are now investigating therapeutic approaches targeting these cells. B) Molecular and cell biology of CNS stem cells: Using both gene discovery and candidate gene approaches, they are determining the mechanisms regulating stem cell self-renewal in vitro and in vivo. c) Brain and spinal cord repair: They are investigating factors that enhance or diminish the efficacy of neural stem cell transplantation in stroke and spinal cord injury. These studies include the use of human embryonic stem cells and derivatives of human induced pluripotent stem cells. In addition to these projects, the Kornblum lab participates in several collaborative studies centered around stem cells with numerous Faculty members within and outside his primary Department.
KURDISTANI, SIAVASH K	ASSOCIATE PROFESSOR	BIOLOGICAL CHEMISTRY (ACCESS PROGRAM,	MENTOR	**Scientific Interest(s):** Dr. Siavash Kurdistani's research focuses on genomic studies of

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
		BIOINFORMATICS, MOLECULAR BIOLOGY, PATHOLOGY DEPARTMENT ADMINISTRATION, PATHOLOGY DEPARTMENT ADMINISTRATION)		chromatin biology. Research Overview: Chromatin is a highly condensed complex of nucleic acid and basic proteins whose fundamental subunit, the nucleosome, has the same type of design in all eukaryotes. The nucleosome contains 147 bp of DNA wrapped around an octamer of histones consisting of two copies of each histone H2A, H2B, H3 and H4. All histones are modified by covalent linkage of extra chemical moieties to the free groups of certain amino acids. Examples include acetylation and methylation of lysines, methylation of arginines and phosphorylation of serines. These modifications are reversible and able to change the functional properties of the chromatin fiber, thereby affecting all cellular processes that are based on DNA such as transcription. The overall goal of our laboratory is to understand the dynamics, establishment and maintenance mechanisms of histone modifications. We use the model organism, Saccharomyces cerevisiae, to understand the basic biology of histone modifications and apply the learned lessons to higher eukaryotes including murine embryonic stem cells, cancer cell lines, and primary human cancer tissues. Chromatin Studies in Yeast: We use the budding yeast Saccharomyces cerevisiae as a model organism and combine standard molecular biology approaches with high throughput techniques such as DNA microarrays to simultaneously assay multiple histone modifications throughout the genome. Evidence from our genomewide studies suggests that there are global principles that govern the levels of acetylation of various residues in histones, generating combinatorial patterns of histone modifications. The histone acetylation patterns can define groups of biologically related genes in an unbiased fashion, indicating the feasibility of developing a predictive model of chromatin biology. We also exploit the powerful genetic tools in yeast to dissect the regulatory pathways that control the activity and specificity of histone modifying enzymes for histone subtypes and their modified residues. Epigenetics in Cancer: Cancer is a disease of genetic and epigenetic alterations. Epigenetics include the interrelated processes of DNA methylation, genomic imprinting and histone modifications. Up until recently, cancer epigenetics has been by and large focused on DNA methylation. However, aberrations in histone modifications are also being increasingly identified in human cancer. These aberrations may occur locally at promoters by inappropriate

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				targeting of histone modifying enzymes, leading to improper expression or repression of individual genes that play important roles in tumorigenesis. In addition to gene-gene differences, we have shown that histone modifications also show aberrations at the levels of whole nuclei, generating cell-cell differences in a given tissue. Importantly, this cellular heterogeneity in total levels of specific histone modifications occur in a stereotypical pattern which can be used to predict prognosis. Our work indicate for the first time that cellular epigenetic heterogeneity may underlie the varied clinical behavior of cancer patients and can be used to predict cancer prognosis.
LANE, TIMOTHY F, PhD	ASSOCIATE PROFESSOR	OBSTETRICS & GYNECOLOGY (ACCESS PROGRAM, BIOLOGICAL CHEMISTRY, MOLECULAR BIOLOGY)	CO-PI, TRAINING COMMITTE E, MENTOR	**RESEARCH AREA** • Role of wnt genes in maintenance of stem cell microenvironments in bone. • Genetic regulation of Cancer Progression, - Role of Stem cells and microenvironment on Breast cancer progression - Stem cell identity in epithelial progenitors • Origin of tumor microvascular cells and role of circulating endothelial precursors (endothelial stem cells) in the progression of breast and ovarian cancer. • Health Disparities.
LO, ROGER. MD, PhD	ASSISTANT PROFESSOR	MEDICINE DERMATOLOGY	MENTOR	Specialty: Dermatology Clinical Interest Melanoma Research Interest Genetic underpinning of human melanoma, with an emphasis on malignant initiation in the skin Affiliation(s): Physician, Department of Medicine, Dermatology Clinical Instructor, Department of Medicine, Dermatology Member, JCCC Cancer Cell Biology Program Area Hospital Affiliation(s): Santa Monica-UCLA Medical Center and Orthopaedic Hospital Ronald Reagan UCLA Medical Center
LOWRY, WILLIAM. PhD	ASSISTANT PROFESSOR	MOLECULAR, CELL, & DEVELOPMENTAL BIOLOGY	MENTOR	**Research**: **Mechanisms of Ectodermal Development**

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				Cell fate specification in human ectodermal development Our current working knowledge of human embryonic development is limited to extrapolations of data generated in the mouse. Unfortunately, data from different species are frequently not congruent, even in the rare occasions where comparisons can be made. With recent advances in Human Embryonic Stem Cell (HESC) technology, a more serious effort to take advantage of hESC technology to model phenomena that would be impossible to study otherwise is now possible. We are using hESCs to study the process by which embryonic ectoderm bifurcates down two lineages of seemingly distinct cell types, namely neural and epidermal. **Generation of pluripotent cells from human somatic tissue** A great deal of the excitement surrounding stem cell biology is predicated on the ability of these cells to be clinically relevant in regenerative medicine, but technical and ethical hurdles are impeding progress towards the use of HESCs in a therapeutic setting. The generation of patient-specific stem cells would remove most of these hurdles, and allow for autologous transplant of cells derived from a patient's own tissue. Our most recent work and that of others demonstrated that these hurdles might be overcome through the use of reprogramming of adult somatic cells to generate cells that are seemingly indistinguishable from embryonic stem cells. We feel that the knowledge gained from our exploration of ectodermal development will be insightful for these neural and epidermal differentiation efforts from HESCs and human iPS. **Adult Stem Cell Self-Renewal and Differentiation** **Quiescence and activation of epidermal stem cells** An enormous effort has recently been devoted to understanding the mechanisms that regulate stem cell self-renewal and differentiation in the adult epidermis, but the sum of data accumulated on the role of various signaling pathways does not adequately explain the behavior of these adult stem cells. Shortly after the generation of the hair follicle, a group of epidermal stem cells becomes distinguishable and is localized to the bulge region. These adult stem cells were first identified on the basis of their slow-cycling nature and their ability to give rise to all the cells of the epidermis upon transplantation. Identifying of some of the signaling pathways that regulate stem cells in order to maintain epidermal homeostasis has still left a gaping hole in our understanding of the mechanisms behind self-renewal and differentiation in this system because we do not know how the activity of these pathways

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				intersects inside the stem cells. As a continuation of our interest in the methods by which cells receive and interpret the variety of signals into a coherent response, we are designing strategies to study the activity of various signaling pathways in epidermal stem cell self-renewal and differentiation.
MIKKOLA, HANNA., MD,. PhD	ASSISTANT PROFESSOR, MD, PhD	Mol, Cell & Dvlmt Bio Member: Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research JCCC Gene Regulation Program Area JCCC Hematopoietic Malignancies Program Area	MENTOR	Dr. Hanna Mikkola's group is interested in the development of hematopoietic stem cells (HSC). Their goal is to identify members of the transcriptional regulatory network that controls HSC development and function. As many of these regulators are involved both in normal blood cell development and in hematopoietic malignancies, understanding how these molecules work will also unravel the regulatory mechanisms that are disturbed in leukemias. Another line of their research focuses on studying the fetal hematopoietic microenvironments that nurture developing HSCs. As the main limitation hindering improvement of HSC therapies is the inability to maintain the self-renewal capacity and pluripotency of HSCs in culture, understanding how these programs develop in the embryo will be instrumental for learning how to expand cord blood or bone marrow HSCs, or even to generate HSCs from human embryonic stem cells, ultimately developing better cure for leukemia and other blood cell disorders.
MISCHEL, PAUL, MD	PROFESSOR	PATHOLOGY AND LAB MEDICINE (ACCESS PROGRAM, NEUROSCIENCE)	CO-PI	The Mischel laboratory aims to transform the care of patients with glioblastoma, the most common form of brain cancer in adults, through molecular medicine. We use quantitative molecular approaches to study and understand the signaling networks that are altered in cancer cells in culture, in relevant in vivo cancer model systems and most importantly in human cancer patients. We have developed, and continue to develop, a suite of approaches for studying glioblastoma patients in state-of-the-art, moleculary guided clinical trials, with the goal of using this information to develop more effective, less toxic therapies. Our laboratory is patient-focused and greatly values interdisciplinary collaboration. Our main areas of interest are: 1) Signal Transduction in glioblastoma. In cancer, response to targeted inhibitors is determined not only be the presence of the key mutant targets, but also by other critical changes in the molecular circuitry of cancer cells; e.g. such as loss of key tumor suppressor proteins, the selection for kinase resistant mutants and the deregulation of feedback loops. Our laboratory aims to elucidate this circuitry to develop more effective treatment strategies. We have a particular interest in the EGFR/PI3K/Akt/mTOR signaling network. The Mischel laboratory works very closely with Dr. Timothy Cloughesy (http://www.neurooncology.ucla.edu/) and with several research laboratories across the US and internationally.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				2) Studying the impact of molecularly targeted agents in patients. Traditional pathologic methods are not sufficient for guiding molecularly targeted therapies. Our lab aims to develop quantitative molecular diagnostic to guide more effective, personalized cancer treatment. This includes new approaches for measuring signaling networks in complex heterogeneous tumor microvenvironments, including in cancer stem cells. This work leverages new nanotechnologies and physical science approaches developed in collaboration with the Heath laboratory at CalTech through the CalTech/UCLA/Institute of Systems Biology NanoSystems Biology Cancer Center (http://www.caltechcancer.org/). 3) Oncogenic signaling and altered cellular metabolism. Understanding how oncogenic signaling in cancer regulates tumor cell metabolism and developing more effective strategies for targeting it.
NELSON, STANLEY F., MD, PhD	PROFESSOR	HUMAN GENETICS, NEUROPSYCHIATRIC INSTITUTE (ACCESS PROGRAM, BIOINFORMATICS, MOLECULAR BIOLOGY, NEUROSCIENCE, NEUROSCIENCE)	MENTOR	**Complex Genetic Trait Analysis** The Nelson Lab uses genomic approaches towards the study of complex human diseases. We have several research programs to discover genetic variants that underly Attention Deficit and Hyperactivity Disorder, Autism, and Vertigo. These projects use linkage, linkage disequilibrium and association approaches in hundreds of affected sibling pair families. The laboratory also studies the genetic causes of glioblastoma, the most common and lethal form of primary brain cancer, using large scale gene expression analysis, alternative splicing analysis and chromosomal loss information, and is developing bioinformatic approaches to use this information to identify and prioritize novel therapeutic targets. We are also developing novel technologies based on shape encoding to allow highly multiplexed cellular and molecular assays. All of these projects require a host of integrated bioinformatics approaches which rely on a large and growing repository of gene expression information from human and mouse tissues.
PLATH, KATHRIN, PhD	ASSISTANT PROFESSOR	BIOLOGICAL CHEMISTRY (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	Kathrin Plath joined UCLA's Biological Chemistry Department as Assistant Professor in March 2006. Born in Germany, Kathrin Plath earned her doctorate degree in cell biology from Harvard Medical School and the Humboldt University Berlin, Germany, and did her post-doctoral training at the University of California, San Francisco, and the Whitehead Institute at MIT. Her lab is particularly interested in understanding how developmental cues induce changes in chromatin structure, and how these changes regulate cell fate decisions and gene expression. For example, one specific question her lab studies is how one of the two X chromosomes in female mammalian cells is inactivated when embryonic stem cells are induced to differentiate. Dr. Plath's lab was among the first to generate induced pluripotent stem (iPS) cells from mouse and human adult cells.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				Her efforts in the reprogramming field are aimed at elucidating the mechanisms that bring adult cells back to an embryonic state and determine how the chromatin state is reset.
RADU, CAIUS, MD	ASSISTANT PROFESSOR	Mol & Medl Pharmacol/Crump Inst	MENTOR	Ovarian cancer (OvCa) is the 5th leading cause of cancer related deaths amongst women in the US. The major obstacle in treating ovarian cancer is the development of platinum resistant disease. Multiple lines of evidence implicate the existence of natural immunity against ovarian cancer. Our work aims to harnesses the ability of the adaptive immune system to control this disease. The rationale for this approach is twofold: (**1**) the presence of tumor infiltrating lymphocytes (TILs) in ovarian cancer lesions correlates with favorable prognosis; (**2**) recent studies have identified antigens, such as NY-ESO-1, expressed by the ovarian tumor epithelium and stroma (but not normal tissues) that can be targeted by CD8+ T cells. Besides developing preclinical models of the human disease, we are optimizing PET assays to monitor the adoptive cellular therapy approach, which is dynamic, occurs at distinct spatial locations and is influenced by both the nature of the tumor and the immune cells.
REITER, ROBERT E., MD	PROFESSOR	UROLOGY (ACCESS PROGRAM)	MENTOR	Clinical Interest: Benign Prostatic Hypertrophy, Bladder CA Laparoscopy, Bladder Cancer, Elevated Prostate Serum Antigen, Green light laser of prostate; Nerve Sparing Prostatectomy, Oncology, Prostate Cancer, Prostate Cancer Laparoscopy, Reconstructive, Robotic Cystectomy, Robotic Prostatectomy, Urinary Obstruction. Dr. Reiter's interest is in translational applications of molecular biology in prostate cancer. His lab's major foci and accomplishments are the following: (1) development of animal models of prostate cancer, including transgenic and knock-in models (2) discovery of cell surface target genes overexpressed or implicated in prostate cancer progression (3) development of monoclonal antibodies targeting cell surface antigens and preclinical development of these antibodies (4) prostate cancer molecular imaging, including the use of engineered antibodies for diagnosis and patient stratitication, and (5) targeting prostate cancer stem cells therapeutically. Current projects include the development of engineered antibodies targeting the prostate stem cell antigen for clinical imaging, development of a PSCA knock-in model to explore targeting of human PSCA preclinically, the exploration of epithelial to mesenchymal transition in emergence of castration resistance, and antibody targeting of EMT for prostate cancer therapy. His lab is a superb training environment for scientists with an interest in translational science of cancer.
SAKAMOTO,	PROFESSOR	PEDIATRICS-ADMINISTRATION,	MENTOR	Dr. Kathleen Sakamoto is a Pediatric Hematologist-Oncologist who

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
KATHLEEN M., MD, PhD		PEDIATRICS-HEMATOLOGY/ONCOLOGY (ACCESS PROGRAM, MOLECULAR BIOLOGY, PATHOLOGY DEPARTMENT ADMINISTRATION)		studies the molecular pathogenesis of acute myeloid leukemia (AML) and novel approaches to treat cancer. Her laboratory focuses on the role of CREB as an oncogene in leukemogenesis using mouse models, leukemia cell lines, and primary patient samples. Additional drugs that target receptor tyrosine kinases, HDAC6, and CREB are best tested for various pediatric tumors. Her laboratory is also studying the mechanism of cancer predisposition and bone marrow failure syndromes such as Diamond Blackfan Anemia. Together with collaborator, Shuo Lin, Ph.D., her laboratory has identified that p53 is upregulated in human fetal liver and zebrafish that are deficient for Ribosomal Protein Subunit 19 (RPS19). Dr. Sakamoto has also developed a novel approach to target cancer causing proteins, including the estrogen and androgen receptors, for ubiquitination and degradation. This technology is known as Protac (Proteolysis Targeting Chimeric Molecule).
SELIGSON, DAVID, MD	ASSOCIATE PROFEESOR	PATHOLOGY & LABORATORY MEDICINE CO-DIRECTOR AND PATHOLOGIST OF BIOMARKER INNOVATIONS LABORATORY DIRECTOR OF TISSUE ARRAY CORE FACILITY	MENTOR	**Scientific Interest(s):** Dr. David Seligson's research focuses on tissue arrays as a research platform to help link cancer gene expression directly to clinical issues in patient care. The tissue array is a dense compilation of small samplings of hundreds to thousands of solid tissues, such as human tumors. The tissues are embedded in paraffin, and therefore histologic slides may be prepared in order to do experiments examining DNA, RNA, or most typically, specific proteins of interest. Once arrays are constructed and linked to rich clinicopathologic datasets, they may be used to link the expressions of the biomolecules to various issues pertinent to both basic science and to patient care. A group of expression signatures may be used to find molecular profiles of cancer that can be used to improve patient prognostication, to help tailor treatment regimens and to find new therapeutic drug targets. Seligson and his colleagues are currently using this technique in the study of cancers of the prostate, kidney, bladder, lung, breast, uterus and brain.
SHUAI, KE, PhD	PROFESSOR	MEDICINE-DEPT ADMINISTRATION (ACCESS PROGRAM, BIOLOGICAL CHEMISTRY, MOLECULAR BIOLOGY)	MENTOR	**Scientific Interest(s):** Cell growth, differentiation, survival and apoptosis can be regulated by cytokines, growth factors and cellular stresses that trigger distinct as well as overlapping signaling pathways. Abnormal signaling is associated with human cancer. The overall research interest in Dr. Ke Shuai's laboratory is to study cellular signal transduction pathways in normal and tumor cells. These studies may provide novel therapeutic targets for cancer treatment. Shuai's work is currently centered on the role of PIAS (protein inhibitor of activated STAT) proteins in cellular signaling. In studies aimed at the

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				understanding of cytokine-activated JAK-STAT signaling pathway, Shuai's laboratory has discovered the PIAS family of proteins, which can inhibit the activity of STATs. In addition, PIAS proteins have also been shown to possess SUMO (small ubiquitin-related modifier) E3 ligase activity and can regulate a number of other transcription factors, including NF-kB and androgen receptor. Shuai and his colleagues are studying the molecular mechanism, the regulation and the biological roles of PIAS proteins in cellular signaling using a combined biochemical and genetic approach.
SLAMON, DENNIS J., MD, PhD	PROFESSOR	MEDICINE-DEPT ADMINISTRATION, MEDICINE-HEMATOLOGY-ONCOLOGY	MENTOR	Scientific Interest(s): For 12 years, Dr. Dennis Slamon and his colleagues conducted clinical and laboratory research that led to the development of the breast cancer drug Herceptin. The drug targets a specific genetic alteration found in about 30 percent of breast cancer patients. In 1998, the U.S. Food and Drug Administration approved the use of the Herceptin monoclonal antibody for treatment of advanced breast cancer. Slamon's research proved a relationship between the gene HER-2/neu, which encodes a tyrosine kinase, and a particularly aggressive form of breast cancer. He continues to place research as one of his top priorities, and is currently investigating the effectiveness of Herceptin in newly diagnosed breast cancer patients. Dr. Slamon is also working to develop new treatments for women with breast and ovarian cancers.
TAMANOI, FUYUHIKO, PhD.	PROFESSOR	MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC (ACCESS PROGRAM, MOLECULAR BIOLOGY)	MENTOR	**The TSC/Rheb/mTOR signaling pathway** plays critical roles in growth and proliferation of mammalian cells in response to nutrients, energy conditions and growth factors. Activation of this signaling pathway is detected in a wide range of human cancers. Genetic disorders such as tuberous sclerosis are due to the activation of the mTOR signaling. Our research focuses on the mechanism of activation of mTOR. In one line of research, we have established that Rheb G-protein acts as an activator of mTOR. Specific activation of mTOR by Rheb is reproduced in vitro using mTOR complex immunoprecipitated from cells. The mechanism of activation is being investigated. In the second line of experiments, we have identified amino acid changes in mTOR that confer hyperactivation of mTOR. This was possible by random mutagenesis approach as well as by mining human cancer genome database. Interestingly, these mutations cluster in a limited number of regions of the protein.
TEITELL, MICHAEL ALAN, MD, PhD	PROFESSOR	PATHOLOGY DEPARTMENT ADMINISTRATION (ACCESS PROGRAM, BIOMEDICAL ENGINEERING, MOLECULAR BIOLOGY, PEDIATRICS-ADMINISTRATION)	ADVISOR, TUMOR IMMUNOLOGY, MENTOR	**Teitell lab research in Tumor Cell Biology** Our lab studies mechanisms of white blood cell development and malignant transformation in humans and in unique TCL1 transgenic and OCA-B, SPRY2, and LKB1 B cell lineage-specific mouse models. These models replicate human cancer defects in cell signaling, gene regulation and epigenetics. Our group also develops new single-cell technologies for discovering basic properties common to cancerous versus normal cells.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				We co-invented a live cell interferometer that is used to monitor large populations of tumor cells, one at a time, in response to changing internal and external environments. Measured properties include dry mass accumulation or loss, changes in motion or viscoelastic properties, and cell division and death. By evaluating each cell in a population we can determine which tumor cells are the most dangerous to a patient or in our mouse models and we actively seek ways to defeat such cells. It is this new nanotechnological connection between engineering and biology that is the focus of Teitell lab efforts in cancer and cancer stem cell biology.
WITTE, OWEN N., M.D.	PROFESSOR	MICROBIOLOGY, IMMUNO & MOLECULAR GENETIC (ACCESS PROGRAM, BIOMEDICAL ENGINEERING, MOLECULAR & MEDICAL PHARMACOLOGY, MOLECULAR BIOLOGY)	MENTOR	He was named the Founding Director of the Institute of Stem Cell Biology and Medicine in 2005, recently renamed the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. He has made significant contributions to the understanding of human leukemias, immune disorders, and epithelial cancer stem cells. His work includes the discovery of tyrosine kinase activity for the ABL gene and the demonstration of the BCR-ABL oncoproteins in human leukemias, leading to the development of kinase targeted therapy as an effective treatment for these leukemias and other cancers. His work also lead to the co-discovery of Bruton's tyrosine kinase which is required for normal B-lymphocyte development, and when mutated leads to X-linked agammagloblulinemia, a form of immune deficiency. Recent work has concentrated on defining the stem cells for epithelial cancers of the prostate and other organ sites to help define new types of therapy for these diseases. Dr. Witte is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and was recently elected to the Institute of Medicine. He has received recognition for his research including the Milken Foundation Award, the Rosenthal Award of the American Association for Cancer Research, the Dameshek Prize of the American Society of Hematology, the Alpert Foundation Prize, and The Leukemia and Lymphoma Society's de Villiers International Achievement Award. Dr. Witte was the 2007 UCLA Faculty Research Lecturer. He currently serves on several editorial and advisory boards. UCLA Researchers Transform Stem Cells Found in Human Fat Into Smooth Muscle Cells ISCBM scientist Dr. Larissa V. Rodriguez and colleagues from the David Geffen School of Medicine at UCLA and the UCLA Henry Samueli School of Engineering and Applied Science today announced they have transformed adult stem cells taken from human adipose—or fat—tissue into smooth muscle cells, which help the normal function of a multitude of organs, including the intestine, bladder and arteries. The study may help

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				lead to the use of fat stem cells for smooth muscle tissue engineering and repair. Reported in the July 24 online edition of the Proceedings of the National Academy of Sciences, the study is one of the first to show that stem cells derived from adipose tissue can be changed to acquire the physical and biochemical characteristics, as well as the functionality, of smooth muscle cells.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
WU, HONG, MD, PhD	PROFESSOR	INSTITUTE FOR MOLECULAR MEDICINE, MOLECULAR & MEDICAL PHARMACOLOGY (ACCESS PROGRAM, MOLECULAR BIOLOGY, NEUROSCIENCE)	Co-PI; MENTOR	**Research Interest:** PTEN is the second most frequently deleted human tumor suppressor gene. PTEN mutation also was found to be the cause of three autosomal dominant tumor predisposition syndromes. A major focus of Dr. Hong Wu's research is to study the molecular mechanism of PTEN controlled tumorigenesis. For this, she has undertaken a combination of molecular genetics, cell biology and biochemical approaches. By analyzing cells and animals lacking the PTEN tumor suppressor, Wu and her colleagues have demonstrated that PTEN negatively regulates stem cell self-renewal, proliferation and survival. Thus, their study provides a strong link between stem cell biology and cancer biology and suggests that tumors may originate through the transformation of stem cells. They also established various animal models for human cancers, including mammary and prostate cancer models. These murine cancer models offer unique tools for both exploring the molecular mechanism underlying human cancers and for the development of new therapies. Wu's recent study demonstrated that PTEN controls p53 protein level and transcription activity, which provides a novel mechanism by which the loss of PTEN can functionally control 'two' hits in the course of tumor development by concurrently modulating p53 activity. For more detailed information, please visit the lab website.
WU, LILY. MD. PhD	ASSSOCIATE PROFESSOR	MOLECULAR & MEDICAL PHARMACOLOGY (ACCESS PROGRAM, BIOMEDICAL ENGINEERING, MOLECULAR BIOLOGY, MOLECULAR, CELLULAR & INTEGRATIVE PHYSIOLOGY, PEDIATRICS-ADMINISTRATION, UROLOGY)	MENTOR	**Research Interests:** Cancer-targeted Gene Therapy and Imaging Our laboratory is focused on development of effective gene therapy protocol from the basic molecular and virology research at the bench level to ultimately apply to treat cancer patients. Current ongoing research topics are: 1. Improving tissue- and cancer-specific gene expression at the transcriptional level. We have developed several strategies to augment the activity of tissue-specific promoters, using the prostate-specific PSA promoter as our initial model system. One of the most potent approach termed two-step transcriptional activation (TSTA) displays 1000-fold higher activity than native PSA promoter while retaining androgen regulation and cell-specificity. Besides prostate-specific promoters, cancer-specific promoters, breast-specific promoters and vascular growth factor promoters are being investigated. 2. Transcriptionally-targeted gene therapy. The approaches developed in topic 1 will be utilized in therapeutic strategies. Current cancer-directed therapeutic strategies under investigation include expression of cytotoxic genes (HSV-tk and TRAIL), anti-angiogenic genes (TSP-1 and METH-1), cell-cycle control gene (p27) and oncolytic viruses. 3. Cancer-targeted molecular imaging. Non-invasive imaging techniques such as optical charge coupled device (CCD) imaging, micro-Positron Emission Tomography (PET) and microCT are applied to monitor vector-based

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
				gene expression in vivo. These molecular imaging approaches will be coupled to gene therapy developed in topic 2. 4. Cancer metastasis and tumor vasculature. Non-invasive imaging is being applied to facilitate the monitoring of the metastatic process in living animal. Active investigation is underway to delineate the contribution tumor blood and lymphatic vessels to cancer metastasis. The goal is to develop better therapy to manage this advanced stage of cancer through a better understanding of tumor and vascular biology.