Experimental Medicine

Jerome E. Groopman, MD, Chief

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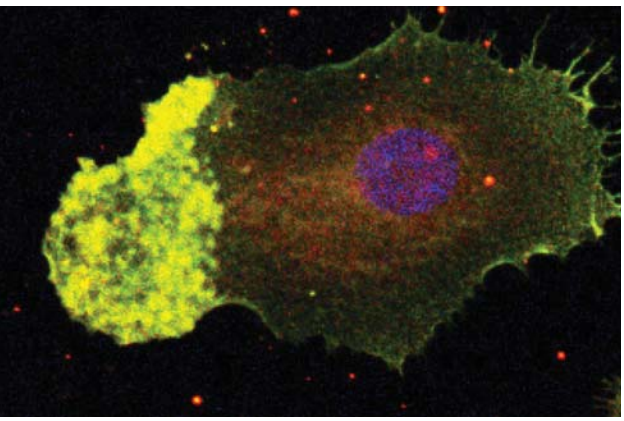
Postdoctoral Fellow

We have continued to succeed in both embarking on innovative research projects and securing extramural funding. Importantly, the Division is nurturing young scientists at the instructor level, providing mentoring on their research projects and on their efforts to secure independent support.



HIV-gp120 induces podosome formation in dendritic cells, facilitating their migration across lymphatic and vascular endothelium.

2009–2010 HIGHLIGHTS

Clinical Highlights

The research in Dr. Jerome Groopman's laboratory on a novel cyclin D1 inhibitor, ON1910, performed in collaboration with scientists at the NHLBI, moved to a pivotal phase III trial for patients with myelodysplasia that involves numerous centers in the United States and Europe. The earlier translational work demonstrated potent activity in subsets of myelodysplastic syndrome, with suppression of the neoplastic clone and emergence of normal hematopoiesis. The new clinical trial should provide data on key outcomes including survival for these patients who otherwise have failed current therapies and have a profound unmet clinical need.

Research Highlights

Dr. Gabriel Birrane, who oversees the BIDMC X-ray Crystallography Core Facility, in collaboration with Dr. Olivier Kocher, Department of Pathology, succeeded in deciphering the crystal struc-

ture of the PDZK1 protein complexed with the C-terminus of the HDL receptor scavenger class B type I (SR-BI). This work provides novel insights into the mechanism of regulation of SR-BI, an important protein involved in cholesterol transport, by the adaptor protein PDZK1.

Dr. Hava Avraham, with Dr. Shalom Avraham and the instructors Drs. Huchun Li and Seyha Seng, characterized the modulation of BRCA1 activity through heregulin binding to the ErbB-2 receptor via the PI-3 kinase/AKT pathway. This work was complemented by studies revealing that BRCA1 forms a novel complex with Nmi and c-Myc and inhibits c-Myc induced telomerase activity. This work furthers our understanding of how mutations in BRCA may result in predisposition to cancer of the breast and ovary.

Anne-Laure Dassier, Technician; **Gabriel Birrane, PhD,** Instructor; **Jerome Groopman, MD,** Chief

SELECTED PUBLICATIONS

Zhang X, Maor Y, Wang JF, Kunos G, Groopman JE. Endocannabionoid-like N-arachidonoyl serine is a novel pro-angiogenic mediator. *Br J Pharmacol* 2010; 160:1583-94.

Seng S, Avraham HK, Birrane G, Jiang S, Avraham S. Nuclear matrix protein (NRP/B) modulates the nuclear factor (Erythroid-derived 2)-related 2 (NRF2)-dependent oxidative stress response. *J Biol Chem* 2010; 285:26190-8.

Kocher O, Birrane G, Tsukamoto K, Fenske S, Yesilaltay A, Pal R, Daniels K, Ladias JAA, Krieger M. In vitro and in vivo analysis of the binding of the C terminus of the HDL receptor SR-BI to the PDZ1 domain of its adaptor protein PDZK1. *J Biol Chem* 2010; 285:34999-5010.

Tiburu EK, Bowman AL, Struppe JO, Janero DR, Avraham HK, Makriyannis A. Solid-state NMR and molecular dynamics characterization of cannabinoid receptor-1 (CB1) helix 7 conformational plasticity in model membranes. *Biochim Biophys Acta* 2009; 1788:1159-67.

Li H, Sekine M, Seng S, Avraham S, Avraham HK. BRCA1 interacts with Smad3 and regulates Smad3-mediated TGF-beta signaling during oxidative stress responses. *PLoS One* 2009; 4:e7091.

Jiang S, Lee BC, Fu Y, Avraham S, Lim B, Avraham HK. Reconstitution of mammary epithelial morphogenesis by murine embryonic stem cells undergoing hematopoietic stem cell differentiation. *PLoS One* 2010; 5:e9707.

Li H, Sekine M, Tung N, Avraham HK. Wild-type BRCA1, but not mutated BRCA1, regulates the expression of the nuclear form of catenin. *Mol Cancer Res* 2010; 8:407-20.

Hinton CV, Avraham S, Avraham HK. Role of the CXCL12 signaling axis in breast cancer metastasis to the brain. *Clin Exp Metastasis* 2010; 27:97-106.

FACULTY

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RESEARCH FUNDING

	Direct	Indirect
Federal	1,063,811	749,487
Non Federal	1,378,598	22,499