

# Division of Interdisciplinary Medicine and Biotechnology



Vikas P. Sukhatme, MD, PhD, Chief



Ary L. Goldberger, MD, Associate Director

## ● Overview

The Division of Interdisciplinary Medicine and Biotechnology (IMBIO) is a newly formed division, perhaps the first of its type to be housed within a clinical department. IMBIO is organized under the leadership of Dr. Sukhatme, as Division Director, and Dr. Goldberger, as the Associate Director. Dr. Sukhatme will continue as Division Chief while also taking on responsibilities as the Chief Academic Officer for BIDMC. He also heads the novel clinical and translational methodologies section of the newly funded NIH initiative: the Harvard-wide Clinical Translational Science Award (CTSA).

IMBIO has both research and educational missions at BIDMC, at Harvard Medical School and its affiliated hospitals and with Harvard University, especially the Allston initiative. It anticipates many interfaces with other institutions both locally (such as MIT) and nationally.

IMBIO believes that we are at a unique time in medical history. The deciphering of the human genome affords an unprecedented platform for basic science discoveries in biology. This “genomics revolution” coupled to the information technology revolution and certain technological advances (such as robotic methods for high-throughput screening, developments in mass spectrometry, novel imaging modalities, etc) will make medicine an information-rich discipline in which health and disease will be assessed increasingly by multi-parameter data that will be easy to gather, transmit and mine.

Such information – if properly extracted and analyzed – will inexorably shift healthcare from a “one size fits all” paradigm to “individualized care.” Additionally, there will be more emphasis on preventative and predictive care and less on “symptomatic” care. In turn, biomarkers will streamline the drug development process and a

subset of them will be linked to the pathophysiology of a disease process, thus providing novel therapeutic targets. Finally, the ability to view disease as a “systems problem” will lead to new insights with diagnostic and therapeutic implications. Thus the “hardware” to elicit and detect “signals” from biological systems including humans (“translational technologies”) both *in vivo* and *ex vivo* and the analysis with sophisticated computational methods of the data obtained will lead to novel insights into disease pathophysiology – a central goal in IMBIO.

Moreover, IMBIO’s mission is to initiate and facilitate linkage from BIDMC to university departments in engineering, computational sciences, physics and chemistry. Insights from public health, law, and business will also be welcome. IMBIO will also facilitate interactions within the Department of Medicine by helping identify clinical or scientific problems that may benefit from such interactions or from methodologies that cross divisional lines. As detailed below, IMBIO will build a cross-departmental think-tank of fellows and faculty to accomplish this goal.

## ● Educational Programs

The division has a journal club every two weeks where speakers from the community discuss their research projects – the common thread is that they have an interdisciplinary approach to them. This seminar series is attended by several residents and fellows from the Department of Medicine. In addition, Dr. Sukhatme as Chief Academic Officer at BIDMC and as IMBIO Chief will inaugurate a “young faculty think-tank” seminar series later this year, directed at instructors and assistant professors who are engaged in scientific investigation throughout BIDMC. This offering will highlight research methodologies and problems that might benefit from interdisciplinary approaches and will also serve to mentor young faculty. A course for

MIT graduate students (Translational Medicine Seminars) initiated by Dr. Sukhatme under the Harvard-MIT Health Sciences and Technology (HST) Program and now in its second year will continue on under other leadership. Plans are underway for a one week “crash course” in medicine for those in other disciplines, to be offered in July 2009. Drs. S. Parikh and D. Friedman are assisting Dr. Sukhatme in the planning of this course. Dr. Griffin Weber plays a major role in the bioinformatics section of the above-mentioned Harvard CTSA.

● *Research Activities*

<i>Research Funding • AY'07</i>	
<b>Federal Direct</b> .....	<b>1,921,356</b>
<b>Federal Indirect</b> .....	<b>697,564</b>
<b>Other Direct</b> .....	<b>1,519,994</b>
<b>Other Indirect</b> .....	<b>135,053</b>

Dr. Sukhatme’s primary research interests are in vascular biology and in cancer, with projects that extend from laboratory research to clinical trials. His major focus is on integrative approaches to cancer. A major emphasis is on tumor metabolism. Strategies that alter the way in which tumors generate energy are being investigated as novel therapies using both RNAi and pharmacologic inhibitors. Other studies focus on ways to inhibit fatty acid and cholesterol biosynthesis. New ideas in breaking immune tolerance towards tumors are also being investigated. Drs. Junichi Hanai, Mohini Lutchman and Pankaj Seth work closely with him in these areas. Dr. Seth continues his studies in renal cancer. Dr. Barden Chan is probing the function of a vascular specific receptor known as Tie-1. Dr. Sukhatme and he have discovered that activation of this molecule initiates a pro-atherogenic program.

Drs. Ary Goldberger, Chung-Kang Peng and Madalena Costa focus on understanding non-linear dynamics and fundamental mechanisms of complex systems. They have developed quantitative algorithms to probe some of the generic features of such systems and applied

them to such diverse areas as heart rhythms health and disease, forecasting drug toxicity, complexity analysis of coding and non-coding human DNA sequences, and gait stability.

Dr. Libermann (as director) and Drs. Xuesong Gu, Luis Zerbini, and Manoj Bhasin Kumar run the BIDMC Genomics Center and the Dana Farber/Harvard Cancer Center Cancer Proteomics Core. Their research has a major focus in renal, prostate and ovarian cancer with strong emphasis on translational research from the bedside to the bench and back to the bedside. They focus a large part of their efforts on genomics and proteomics systems biology approaches to human diseases, applying cutting-edge technologies in genomics and proteomics combined with innovative bioinformatics analysis. Further interests are to dissect the molecular mechanisms of drug action in human cancer and the role of Ets transcription factors in cancer. Additionally, they have collaborated with a wide range of scientists locally, nationally and internationally in many other areas.

Dr. G. Weber is a medical bioinformatician with a background in biomedical engineering, computer science, and medicine. His research interests focus on ways in which biomedical informatics can improve medical education, research and patient care. Dr. Weber has established a Biomedical Research Informatics Core (BRIC), to provide informatics services to BIDMC researchers.

● *Award and Honors*

Ary L. Goldberger, MD is Program Director of the NIH-sponsored Research Resource for Complex Physiologic Signals (PhysioNet) and Ellison Senior Scholar in Aging. C.K. Peng, PhD is Associate Director, NIH-sponsored Research Resource for Complex Physiologic Signals, Faculty at Santa Fe Institute Workshop on The Foundations of Theoretical Medicine, Santa Fe, NM and Workshop on Physiologic Signals Analysis, Yuan Ze University, Chung-Li, Taiwan. Towia Libermann, PhD is a faculty member on the NIH Harvard Clinical and Translational Sciences Center 2008. Vikas P. Sukhatme, MD, PhD was named as BIDMC’s Chief Academic Officer and Harvard Faculty Dean.

## ● Selected Publications

Costa M, Goldberger AL, Peng C-K. Multiscale analysis of heart rate dynamics: entropy and time irreversibility measures. *Cardiovasc Eng* 2008; 8:88.

Peng C-K, Costa M, Goldberger AL. Adaptive data analysis of complex fluctuations in physiologic time series. *Advances in Adaptive Data Analysis* 2008 [in press].

Costa M, Ghiran I, Peng C-K, Nicholson-Weller A, Goldberger AL. Complex dynamics of human red blood cell flickering: Alterations with *in vivo* aging. *Stat Nonlin Soft Matter Phys* 2008; 78:020901.

Nikolova-Krstevski V, Bhasin M, Out HH, Libermann T, and Oettgen P. Gene expression analysis of embryonic stem cells expressing VE-cadherin (CD144) during endothelial differentiation. *BMC Genomics* 2008; 9:240.

Dusek JA, Otu HH, Wohlhueter AL, Bhasin M, Zerbini LF, Joseph MG, Benson H, and Libermann TA. Genomic Counter-Stress Changes Induced by the Relaxation Response. *PLoS ONE* 2008; 3:e257b.

Zinkin NT, Grall F, Bhaskar K, Otu HH, Spentzos D, Kalmowitz B, Wells M, Guerrero M, Asara J, Libermann TA\*, and Afdhal NH\*. Serum proteomics and biomarkers in hepatocellular carcinoma and chronic liver disease. *Clin Cancer Res* 2008; 14:470-477. \*contributed equally

Chan B, Yuan HT, Karumanchi SA, Sukhatme VP. Receptor tyrosine kinase Tie-1 overexpression in endothelial cells upregulates adhesion molecules. *Biochem Biophys Res Commun* 2008; 371:475-9.

Gallagher DC, Parikh SM, Balonov K, Miller A, Gautam S, Talmor D, Sukhatme VP. Circulating angiotensin II correlates with mortality in a surgical population with acute lung injury/adult respiratory distress syndrome. *Shock* 2007; 29:656-61.

## ● Faculty

Barden Chan, PhD	Mohini Lutchman, PhD
Madalena D. Costa, PhD	Chung-Kang Peng, PhD
Ary L. Goldberger, MD	Pankaj Seth, PhD
Xuesong Gu, PhD	Vikas P. Sukhatme, MD, PhD
Junichi Hanai, MD, PhD	Griffin Weber, MD, PhD
Manoj B. Kumar, PhD	Luiz Zerbini, PhD
Towia Libermann, PhD	

Hanai J, Cao P, Tanksale P, Imamura S, Koshimizu E, Zhao J, Kishi S, Yamashita M, Phillips PS, Sukhatme VP, Lecker SH. The muscle-specific ubiquitin ligase atrogin-1/MAFbx mediates statin-induced muscle toxicity. *J Clin Invest* 2007; 117:3940-51.

Mammoto T, Parikh SM, Mammoto A, Gallagher D, Chan B, Mostoslavsky G, Ingber DE, Sukhatme VP. Angiotensin-1 requires p190 RhoGAP to protect against vascular leakage *in vivo*. *J Biol Chem*. 2007; 282:23910-8.