Narrative of Research and Leadership: Prabhas Moghe, PhD.

1.0 Overview of Research Accomplishments and Academic Leadership

Dr. Moghe’s research has been focused on the areas of cell-biomaterial interactions and nanomedicine, where he is now recognized as a global leader for his work on (a) parsing the metrology of cell-material interactions and assembling imaging-based tools of the emergent field of “biomateriomics”; (b) advancing nanoscale polymer designs (called nanolipoblockers) as polymer therapeutics and cell-interactive biointerfaces; (c) elucidating biomaterial microstructures that reprogram or preserve tissue functions and fates (stem cell bioengineering).

Dr. Moghe has also led a unique interdisciplinary research-inspired model for doctoral education in the U.S., exemplified through two recognized NSF-funded IGERT programs on biointerfacial engineering and integrated stem cell science and engineering at Rutgers. These programs have shaped the science, intellectual property, and professional development of over 60 PhD scholars in bioengineering and life and physical sciences.
Selected highlights of Dr. Moghe’s research activities are described further below.

1.1 High Dimensional Biology Profiling of Cell-Material Interactions

Dr. Moghe has proposed a novel approach to elucidate emergent cellular phenotypes and profile cell functional states using high content imaging of the intracellular organization of signaling protein reporters. This approach can be applied to a wide range of cell culture niches and a broad spectrum of cell types. Of particular interest is the ability of such imaging-based profiling to parse difficult to distinguish cell phenotypes (for example, in a population of heterogeneous cultures); forecast ultimate cell lineages (for example, for stem cells) and track the kinetics of cell organizational signatures as cells commit to specific lineage fates (see Fig. 1). A landmark paper by Moghe’s lab published in PNAS 2010 [1] presents a novel approach to classify stem cell emergent phenotypes using high dimensional biological organization. This approach has since been adopted by other investigators to parse oncogenic progression, in J. Cell Science 2012 [2] and to elucidate differentiation behaviors of stem cells on nanotopographies, in Biomaterials 2012 [3]. Other papers by Moghe and coworkers in J. Biomolecular Screening [4], Cell Cycle [5], and Combinatorial Chemistry and High Throughput Screening [6] apply this approach to different microenvironmental conditions and relate the forecasting tools to different stem cell lineages and sources.

Fig. 1: The Moghe lab has proposed high content imaging of cells to generate cellular descriptors that can be used to parse heterogeneous cell cultures and track stem cell lineage fates. This study was first published in Proceedings of the National Academy of Sciences in 2010 [1].
1.2 Biomaterial Paradigms for Stem Cell Regeneration

Dr. Moghe’s lab has advanced 3-D microscale scaffolds for efficient preservation or conversion of reprogrammed stem cells for applications in tissue engineering or developmental biology.

Dr. Moghe’s group has published findings on the role of critical geometric features of three-dimensional substrates that can promote the survival and self-renewal of human, pluripotent stem cells (Carlson et al., *FASEB J.*, 2012) [7]. Such features are exhibited on fibrous, textured scaffolds that mimic the extracellular matrix microorganization but cannot be recapitulated within conventional scaffolds fabricated as macroporous foams or sponges. The mechanism for the stem cell survival and self-renewal, as reported in the FASEB J. paper, is due to endogenous, extracellular matrix deposition and colony niche organization at the microscale. Using appropriately scaled 3-D constructs, prototypes of stem cell cultures with high expansion potential can be designed. Using soluble growth factors, the cell phenotypes can be rapidly switched to any of the major lineages. The most recent advances in the Moghe lab (Carlson et al., in preparation) relate to the success of obtaining highly pure neuronal populations in three-dimensional, humanized microscaffolds, starting from reprogramming induction of pluripotent stem cells (iPSCs) or somatic cells such as fibroblasts (Fig. 2).

Of particular relevance to the Moghe lab is the ability of rapidly reprogrammed stem cells to regenerate neuronal deficit that accompanies neurotrauma and neurodegenerative diseases. A recent paper from the lab in *Biointerphases* (Cherry et al., 2012) reports on the multimeric presentation of neurogenic molecule, L1, from polymer substrates to promote neuritogenesis of various primary neuronal cultures and neurogenic differentiation of human neural stem cells. A report by the Moghe lab in *Stem Cells and Development* highlights the possibility of accelerating the differentiation of human embryonic stem cells toward neuronal phenotypes using feeder cells expressing the cell adhesion molecule, E-cadherin [8].

Publications in the Moghe lab over the past decade have built up foundational work on differentiation of cellular systems in (a) 3-D microstructured scaffolds and mechanochemically tunable substrates [9-13] and (b) bioactive substrates based on the ectopic presentation of cell adhesion molecule, E-cadherin, [14-17]. In 2000-2004, the Moghe lab has reported in a series of highly cited papers in *Biotechnology and Bioengineering, Tissue Engineering, Biomaterials*, and *J. Biomedical Materials Research* that the morphogenesis and differentiation of anchorage-sensitive hepatocytes can be engineered through the interplay of substrate topography and matrix/mechanochemical stimulation. For example, a review in Science [18] cites their publication on cooperative effects on cell motility dynamics of ligand adsorption and material microstructure [19]. Using differentially compliant hydrogels, Dr. Moghe reported that increased growth factor stimulation and growth factor pulsing can be used as a dual strategy to promote differentiation or cell growth [10, 11]. This work has been in tissue engineering archival papers in *Developmental Biology* [20], reviews in *J. Appl. Physiology* [21], and in *J. Cell Science* [22].

Advancing these studies further using a new system of bioactive polyacrylamide substrates, Dr. Moghe’s laboratory showed using hydrogels of intermediate compliance that hepatocytes can be made to differentiate with highest sensitivity when exposed to increased ligand concentration [23]. This recent study was cited in a prominent review in *Science* focused on cellular engineering via rigid/compliant substrates [24] and in a 2006 review in *Nature Reviews-Molecular & Cell Biology* [25].
In the area of cellular engineering, Dr. Moghe has pioneered the approach of incorporation of adhesive and signaling cell-cell adhesion molecule, the cadherins, for controlled differentiation of hepatocytes, and more recently of embryonic and induced pluripotent stem cells. Five prominent publications from his laboratory have documented that (a) cadherin based cell-cell adhesion between liver cells and other cell types can significantly promote cell differentiation [26] (b) the mode of cadherin display can engineer the differentiation-proliferation balance [17] (c) acellular fragments of E-cadherin can used on artificial substrates to promote hepatocyte differentiation [14]; and, recently, that (d) E-cadherins can promote embryonic stem cell differentiation in conjunction with growth factor stimulation [15]. Current advances in the Moghe laboratory, using approaches utilizing microfabrication, immunocytochemistry, and DNA microarray technology, show that E-cadherin engineered embryonic stem cells can be more effectively primed to mature to differentiated hepatocyte-like cells when transplanted within liver-like environments in vitro [27]. This is the first report in the field that probes the maturation potential of ES cells in the presence of adult hepatocytes.

A recent publication from the Moghe lab in Stem Cell and Development in 2012 showed that embryonic stem cells rapidly and efficiently differentiated into neural stem cells by presenting the cell adhesion molecule, E-cadherin, to undifferentiated hESCs via E-cadherin transfected fibroblast monolayers [8]. Recent studies from the Moghe laboratory have now discovered the distinct roles of N-cadherin and L1 adhesion molecules in the retention of differentiating, reprogrammed human iPSCs and neural stem cells, particularly those converting toward neuronal phenotypes[28].

---

**Fig. 2:** The Moghe lab has advanced a new approach to generate a purified population of scaffold-cultured human neurons starting for reprogrammed fibroblasts or iPSCs for transplantation for the treatment of neurodegenerative diseases.
1.3 Nanobiomaterials and Nanobiointerfaces

In the field of nanomedicine, Dr. Moghe has built an international reputation for combining nanotechnology with biointerfacial tools that elucidate and modulate strategic cellular and tissue phenomena, which was a part of the citation for his induction as *International Fellow of Biomaterials Science and Engineering*. The Moghe lab has conceptualized and pioneered the design of macromolecular therapeutics called *Nanolipoblockers* (Fig. 3). Constructed as a library of amphiphilic sugar-derived macromolecules of varied charge, hydrophobicity, stereochemistry, and architecture, the nanolipoblockers have been envisioned to inhibit the conversion of inflammatory blood cells to fat-filled “foam cells”, the hallmark of heart disease called atherosclerosis. The Moghe lab and their collaborators at Rutgers from the Uhrich and Welsh laboratories have published several reports in leading journals on the structure-activity relations of the nanolipoblockers and the efficacy *in vitro* and *in vivo* [29-39]. A recent publication by York et al. highlights a novel approach to kinetically assemble amphiphilic macromolecules around hydrophobic sugar cores with bioactivity, thus generating highly stable and efficacious nanoparticles of nanolipoblockers [29]. By combining the nanolipoblockers with cholesterol trafficking drugs such as LXR agonists and near-infrared contrast agents, they can be used as multi-functional vehicles for drug delivery and lesion imaging [32]. This program has been continually funded by the NIH and AHA, and has received the Coulter Foundation Biomedical Engineering Translational Award.

![Diagram of nanolipoblockers](image)

**Fig. 3: Nanolipoblockers:** The Moghe lab has conceptualized a family of macromolecules termed...
February 2013

nanolipoblockers that can be used to abrogate oxidized LDL uptake and inflammation related to atherosclerosis. Using such macromolecules, novel targeted delivery of liver-X-receptor agonists was proposed to deplete cholesterol in macrophages in vitro and in vivo; Further, novel nanoparticle formulations of the NLBs were developed to exhibit improved stability in serum. Lead NLB particles show increased accumulation at atherosclerotic lesion sites in Apo-E-deficient mice.

As a part of his leadership in nanomedicine, Dr. Moghe has led a NSF-funded Nanoscale Interdisciplinary Research Team (NIRT) at Rutgers and Princeton Universities on Bioactive Nanointerfaces for Cytointernalization and Cellular Superactivation. Through these efforts, the Moghe lab advanced a new generation of cell targeted albumin-derived nanocarriers as substrates for microtemplating epithelial and mesenchymal cells [40], controlling cell adhesion and achieving extraordinary levels of endocytosis-coupled cell motility by altering ligand concentration [41]. This effort advanced a novel dynamic method to control cell motility rate by altering the endocytic kinetics through variations in nanosubstrate size and ligand concentration (Fig. 4) [42]. Another new finding was the ability of such tunable nanoscale interfaces to engineer differential levels of mesenchymal tissue contractility and extracellular matrix fibrillogenesis and deposition [43, 44], which led to new intellectual property on a method to template extracellular matrix assembly using differentially sized albumin nanoparticles [43, 44].

Fig. 4: As reported in the journal Small (2011), the Moghe lab has advanced nanobiointerfaces for dynamically modulating cell adhesion and motility. Using albumin nanocarriers of varying sizes and matrix ligand concentrations, keratinocyte polarity and motility were systematically tuned. Notably markedly higher levels motility was achieved, suggesting similar endocytically activated processes could be used for improved substrates for wound healing and re-epithelialization.
Through the NIRT program, the Moghe lab recently reported on the design of biologically tunable particles for tracking of nanoparticle cytointernalization phenomena specifically, and on a broader level, for tissue imaging and disease diagnostics. A novel design of rare earth phosphor probes with albumin nanoshells was advanced to enable upconversion-based imaging of receptor expression on cancerous cells (Fig. 5) [45].

Using a novel window of short wave infrared (SWIR) emission, the Moghe lab has leveraged the nanoscale probes to allow deeper tissue imaging as well as in vivo tracking around xenografted tissues and intraperitoneally and intravenously administered probes with molecularly targeted peptides (Fig. 6) [46]. These particles can be doped with distinct rare earth elements (e.g., ytterbium and holmium) to yield multiplexed discrimination of probes targeted to different tissues using a single source of near-infrared excitation. Additional uses of such multifunctional particles involve co-delivery of drugs to prevent cancer metastasis and co-doping with MRI contrast agents to allow for multispatial resolution of the disease anatomy along with SWIR-based optical imaging of molecular features of the disease. The Moghe lab has generated new intellectual property and is leading efforts in diagnosing different tumor phenotypes as well as atherosclerotic lesions in the vasculature triggering heart disease, both at a fundamental research scale and for translation to bring these technologies to the clinic.
Fig. 6: The Moghe lab and collaborators have developed a novel family of probes for deeper tissue imaging. Based on rare earth nanocrystal nanocomposites with albumin shells, these probes allow short wave infrared emission, which can be detected with minimal scattering and absorption in vivo, as well as improved biodistribution. These probes were deployed in an orthotopic murine melanoma model where melanoma tumors were detected post IP-injection. Multiplexed probes were designed to elicit distinct signatures of diseased tissues by exciting different rare earth dopants within the same animal. This study is currently under review at Nature Materials.
2.0 Global Recognition and Leadership Roles

The International Union of Societies for Biomaterials Science and Engineering (IUSBSE) elected Professor Prabhas Moghe as a Fellow of Biomaterials Science and Engineering (FBSE). Professor Moghe was cited for his pioneering research and educational leadership in advanced materials biology with applications to biotechnology and biomedicine. (Fig. 7) The induction ceremony took place on June 1, 2012 at the Ninth World Biomaterials Congress held in Chengdu, China. There are only 216 fellows worldwide recognized to date with this honor out of 26,000 members belonging to IUSBSE. Dr. Moghe was one of 7 new Fellows elected from the U.S. whose accomplishments were prominently recognized at the Congress in China.

Dr. Moghe was previously elected Fellow of the American Institute of Medical and Biological Engineering (AIMBE) in 2007.

In 2011, Dr. Moghe was honored as an invited scholar at the Dutch Royal Academy of Sciences as part of the first international workshop on “Materiomics”.

Through his directorship of the NSF funded IGERT programs on Biointerfaces and Integrated Science and Engineering of Stem Cells, Dr. Moghe has also led the training of over 50 PhD fellows in the US (Figs 9-10). Additionally, he has spearheaded an international network of institutes as training sites for PhD. Scholars to conduct research in emerging areas of stem cell science and engineering. A map of these sites appears below.

Fifteen different research projects have been advanced through these international partnerships, illustrated in the figure below (Fig. 8).

Dr. Moghe currently codirects a NIH funded T32 Translational Research Program on Regenerative Medicine, which offers translational fellowships to postdoctoral scientists in biomaterials science and stem cell/regenerative technologies. This program has nodes at four
key sites in the US: Rutgers/U. Pennsylvania/Princeton U.; The Harvard Hospitals; Case/Cleveland Clinic; and The Mayo Clinic.

**Fig. 9:** Dr. Moghe conceptualized and directed the research and education of over 36 PhD scholars through a NSF funded IGERT program on Integratively Engineered Biointerfaces from 2003 to 2011.

**Fig. 10:** Moghe directs a sequel IGERT program on Integrative Science and Engineering of Stem Cells awarded by the NSF from 2008-2014. NSF funded IGERT scholars at IGERT Symposium with the PI and other faculty.
3.0 Educational and Diversity Leadership

Dr. Moghe has pioneered a number of different research-centric educational initiatives at the graduate and postdoctoral level that have had transformative impacts on (a) bioengineering and biomaterials curriculum; (b) best practices in interdisciplinary research and educational PhD. training programs at the national level; and (c) approaches to foster diversity infrastructures that promote the broadened participation and leadership of minority scholars in STEM fields. Dr. Moghe is actively involved in invited talks and panel discussions organized by the National Science Foundation on promoting diversity through the NSF-funded Integrated Graduate Education and Research Traineeship (IGERT) programs and has served on the advisory board of the IGERT national forum. For his diversity leadership, Dr. Moghe received the Presidential Leadership in Diversity Award in 2007.

References


