

## **Center for Drug Delivery Research Annual Report 2007-08**

The Center for Drug Delivery Research is co-directed by Drs Banga and D'Souza and has a mission to promote a strong multidisciplinary team based approach to drug delivery, embracing a variety of activities in the broad area of drug formulation and delivery. The Center membership includes the following faculty:

Dr. Ajay Banga (Co-Director)  
Dr. Martin D'Souza (Co-Director)  
Dr. Lynetta Jobe  
Dean Matthews (Advisor)  
Dr. Ravi Palaniappan  
Dr. Chalet Tan  
Dr. Hailing Zhang

The advisory board members are listed below:

Dr. Steve Bell, Vice President – Research/Clinical Development, Biosante  
Dr. Bradley A. Clark – Director, Pharm. Development, Solvay  
Dr. Mark R. Prausnitz, Assoc Professor, GA Tech  
Dr. Gurvinder Singh Rekhi, Director, R&D, Elan

The center currently consists of the following laboratories:

- Microsphere/Nanotechnology Laboratory
- Proteomics/Vaccine Delivery Laboratory
- Transdermal Delivery Laboratory
- Drug Delivery Laboratory
- Protein Formulation Laboratory
- Research Vivarium

### **Center Accomplishments 2007-08**

#### **SUMMARY**

The Center now consists of 6 faculty, and Dean Matthews serves as advisor to the Center. A new member, Dr. Chalet Tan joined the Center in 2007-08. The center looks forward to a new research area that Dr. Tan will bring to the Center.

Center faculty received new funding for research programs of \$ 482,000 during the year. A number of organizations supported the research of the department, including the Georgia Research Alliance, 2 different pharmaceutical/medical companies and the University. Center faculty and graduate students produced 9 original research articles in scholarly journals and 1 review article. Students and center faculty made 35 contributed presentations at regional, national, and international scientific meetings.

Six students associated with the Center faculty completed the requirements of the PhD Program and received their degree during Commencement held on May 3, 2008.

<b>Student</b>	<b>Dissertation Title</b>	<b>Advisor</b>
Nima Akhavein	Albumin Microspheres as Delivery Vehicles for Nuclear Factor-Kappa B Antisense Oligonucleotides	D'Souza
Sanjay G. Gayakwad	Formulation, Development and Optimization Studies for the Delivery of Oligonucleotides and Small Molecules	D'Souza
Purna Chandar Kasha	Topical and Transdermal Iontophoretic Delivery of Therapeutic Agents using Self-contained Patches	Banga
Sameer Gajanan Late	Development and Optimization of a Novel Fast Disintegrating Tablet Formulation using $\beta$ Cyclodextrin as a Diluent	Banga
Viswatej Vemulapalli	Transdermal Delivery of Small and Large Molecules using Iontophoresis and Microneedles	Banga
George Kwame Yeboah	Evaluation of Albumin Microspheres as Potential Delivery Vehicles for Oral Tuberculosis Vaccines	D'Souza

A number of graduate students working with faculty members from the Center attended local, regional and national meetings, including the Annual Graduate Research Association of Students of Pharmacy (GRASP) meeting, the annual meeting of AAPS and the Controlled Release Society. Several students received awards for presentations at scientific meetings. Of approximately 850 poster presentations at the 34th Annual Meeting of the Controlled Release Society, Sanjay Gayakwad (major advisor Dr.D'Souza) was one of 10 selected for a cash award. The awards were based on novelty, innovation, and the significance of the research work to the field of the pharmaceutical sciences. The meeting was held in Long Beach, CA in July 2007. His poster entitled "Formulation and ex-vivo evaluation of anti-sense to Nf-kB encapsulated albumin microspheres in a kidney transplant model" was authored by Sanjay Gayakwad, Nima Akhavein, Carl Oettinger and Martin J. D'Souza.

Two of four awards for poster presentations at the 2008 GRASP meeting were received by Karyn Innes Cotta and Richard Addo. The titles of the posters were "Enhancement of immunity by probiotic containing microspheres for oral typhoid vaccine" by Karyn I. Cotta and Martin D'Souza and "Development and evaluation of microparticulate based atropine formulations for its mydriatic effect" by Richard Addo, Neil Patel, Janet Akande, Aladin Siddig, and Martin D'Souza. Dr. D'Souza is advisor to both students.

The abstract by two of Dr. Palaniappan's students, Dilip Devineni and Daniel Ezekwudo, received the Graduate Symposium Award in Biotechnology from AAPS. The award is designed to recognize excellence in graduate education in the field of pharmaceutical biotechnology. The paper entitled "Application of zeta potential as a preformulation tool in optimizing buffer conditions of pH and salts in protein solutions" was presented at the AAPS National Biotechnology Conference in Toronto during June 2008.

## PUBLICATIONS

### Research Publications

A.V. Badkar, A.M. Smith, J.A. Eppstein and A.K. Banga. Transdermal delivery of interferon alpha-2B using microporation and iontophoresis in hairless rats. *Pharmaceutical Research*. 2007; 24:1389-1395.

A. Basarkar, D. Devineni, R. Palaniappan and J. Singh. Preparation, characterization, cytotoxicity and transfection efficiency of poly(dl-lactide-co-glycolide) and poly(dl-lactic acid) cationic nanoparticles for controlled delivery of plasmid DNA. *International Journal of Pharmaceutics*. 2007; 343:247-254.

N.K. Bejugam, M. Sou, A.N. Uddin, S.G. Gayakwad and M.J. D'Souza. Effect of chitosans and other excipients on the permeation of ketotifen, FITC-dextran, and rhodamine 123 through Caco-2 cells. *Journal of Bioactive and Compatible Polymers*. 2008; 23:187-202.

C. Kolli and A. Banga. Characterization of solid maltose microneedles and their use for transdermal delivery using microporation and iontophoresis in hairless rats. *Pharmaceutical Research*. 2008; 25:104-113.

Y.H. Lai and M.J. D'Souza. Microparticle transport in the human intestinal M cell model. *Journal of Drug Targeting*. 2008; 16:36-42.

H. Nettey, D. Haswani, M.J. D'Souza and C.W. Oettinger. In vitro antimicrobial effect of encapsulated vancomycin on internalized Staphylococcus aureus within endothelial cells. *Drug Development and Industrial Pharmacy*. 2007; 33:133-139.

V. Vemulapalli, Y. Yang, P. Friden and A. Banga. Synergistic effect of iontophoresis and soluble microneedles for transdermal delivery of methotrexate. *Journal of Pharmacy and Pharmacology*. 2008; 60:27-33.

K.G. Yeboah and M.J. D'Souza. Evaluation of albumin microspheres as oral delivery system for Mycobacterium tuberculosis vaccines. *Journal of Microencapsulation*. 2008; (1):1-14.

J. Zhaowei, M.J. D'Souza and C.W. Oettinger. Reversal of LPS induced endothelial cell TNF synthesis and increased permeability with microencapsulated antisense oligomers to NF-kappa B. *Journal of Microencapsulation*. 2007; 24:596-607.

### Review Article

P. Kasha and A. Banga. A review of patent literature for iontophoretic delivery and devices. *Recent Patents on Drug Delivery & Formulation*. 2008; 2:41-50.

## RESEARCH PRESENTATIONS

R. Addo, A. Siddig and M.J. D'Souza. Evaluation of tetracaine microsphere formulations. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

R. Addo, N. Patel, J. Akande, A. Siddig and M. D'Souza. Development and evaluation of microparticulate based atropine formulations for its mydriatic effect. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

J.M. Akande, A.A. Siddig, R.T. Addo, N. Akhavein, C. Oettinger and M. D'Souza. Evaluation of the effect of microencapsulated anti-sense oligonucleotides to NF-kB on tumor development and progression. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

J.M. Akande, A.A. Siddig, R.T. Addo, N. Akhavein, C. Oettinger and M. D'Souza. Evaluation of the effect of microencapsulated antisense oligonucleotides to NF-kB on tumor development and progression. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

K.I. Cotta, J.M. Akande and M.J. D'Souza. Formulation of chemically crosslinked albumin-chitosan mixed matrix microparticulate systems. Annual Meeting and Exposition of the Controlled Release Society, Long Beach CA, July 7-11, 2007.

K.I. Cotta and M.J. D'Souza. Formulation and evaluation of the efficiency of probiotic microspheres. Georgia Life Sciences Summit 2007, Atlanta GA, October 3, 2007.

K.I. Cotta and M.J. D'Souza. Evaluation of the efficiency of probiotic microspheres. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

K.I. Cotta and M.J. D'Souza. Formulation and characterization of chemically cross-linked albumin-chitosan mixed matrix microparticulate systems. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

K.I. Cotta and M.J. D'Souza. Enhancement of immunity by probiotic containing microspheres for oral typhoid vaccine. CDC-Georgia Research Alliance Conference, Atlanta GA, May 2008.

K.I. Cotta and M.J. D'Souza. Enhancement of immunity by probiotic containing microspheres for oral typhoid vaccine. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

B.L. D'Souza, T. Bhowmik, S. Perisamy, B. Pai, M.J. D'Souza. Nano/microparticulate delivery formulation for melanoma vaccines. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

M.J. D'Souza, P. Selvaraj, C. Oettinger, B. Pai, T. Bhowmik, B. DSouza, R. Sashidharamurthy, K. Cotta, N. Patel, S. Gayakwad and J. Akande. Novel nanotechnology platform for oral delivery of vaccines. CDC-Georgia Research Alliance Conference, Atlanta GA, May 2008.

D. Devineni, D. Ezekwudo and R. Palaniappan. Evaluation of stability of model proteins in solution using its zeta potential and osmotic second virial coefficient. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

D. Devineni, D. Ezekwudo and R. Palaniappan. Application of zeta potential as a preformulation tool in optimizing buffer conditions of pH and salts in protein solutions. AAPS National Biotechnology Conference, Toronto Canada, June 22-25, 2008.

D. Ezekwudo, D. Devineni and R. Palaniappan. Development and characterization of functionalized biodegradable hydrogel-b-PEG copolymer as drug delivery device for in-vivo targeting. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

S.G. Gayakwad, C.W. Oettinger and M.J. D'Souza. Antisense oligonucleotides to Nf-kB microspheres: Formulation, physicochemical characterization and its effect on cytokine production, inhibition of Nf-kB activation and kidney survival in a kidney transplant model. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

S.G. Gayakwad, N.J. Patel and M.J. D'Souza. Evaluation of carbohydrates as stabilizing excipients on the solid state stability of a model protein drug encapsulated into albumin nanospheres via spray drying. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

P. Kasha, Y. Yang, R. Morris, C. Anderson, W. Sembrowich and A.K. Banga. Systemic delivery of sumatriptan by iontophoresis in hairless rats. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

C. Kolli and A.K. Banga. Assessment of barrier perturbation caused by maltose microneedles. Annual Meeting and Exposition of the Controlled Release Society, Long Beach CA, July 7-11, 2007.

C. Kolli, H. Kalluri, N. Desai and A.K. Banga. DermaRoller™ as an alternative means to breach the stratum corneum barrier. Georgia Life Sciences Summit 2007, Atlanta GA, October 3, 2007.

C. Kolli, H. Kalluri, D. Farquhar and A.K. Banga. Effect of occlusion and formulation pH on pore closure in vivo following microneedle pretreatment. Georgia Life Sciences Summit 2007, Atlanta GA, October 3, 2007.

S.S.S. Lanke, C.S. Kolli, G. Li, J.G. Strom and A.K. Banga. Transdermal delivery of low molecular weight heparin using combination of microneedles and iontophoresis. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

S. Late and A.K. Banga. Influence of lubricants and moisture treatment on beta-cyclodextrin-based fast-disintegrating tablet formulation. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

N.J. Patel, S. Gayakwad, J. Johnson, J.J. Yang and M.J. D'Souza. Encapsulation and stabilization of IgG into spray-dried albumin microspheres. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

N.J. Patel, S. Gayakwad, J. Johnson, J.J. Yang and M.J. D'Souza. Stabilization of spray-dried IgG encapsulated albumin microspheres. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

S.A.A. Rizvi, F.M. Menger and M.J. D'Souza. Evaluation of novel cationic gemini surfactants for efficient gene transfer. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

S. Saluja, J. Paturi, C.S. Kolli, A.V. Badkar, S. Nema and A.K. Banga. Stability of triptorelin during transdermal transport. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

A.A. Siddig, R.T. Addo, M.J. D'Souza and C.E. Hart. In-vitro evaluation of topical microbicides for release of pre-inflammatory cytokines in human macrophages and peripheral blood mononuclear cells (PBMCS). American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

S. Siddoju, V. Vemulapalli, P.M. Friden and A.K. Banga. Lateral diffusion of drugs inside skin as determined by microdialysis. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

R.C. Siwale, A. Siddig, C. Oettinger, D. Harrison and M. D'Souza. Effect of microencapsulated catalase formulations on in-vitro pre-inflammatory effect of microencapsulated catalase formulations on in-vitro pro-inflammatory cytokine and nitrate release. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

R.C. Siwale, N. Uddin, C. Oettinger, B. Pai and M. D'Souza. Evaluation of inhibition of the vasodilatory effect of LPS in endothelial cells with antisense NF-kB and catalase microspheres. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

M.N. Uddin, D.P. Do, S.B. Pai, M.J. D'Souza. Quantification and characterization of antisense to NF-kB in bovine serum albumin microspheres. Graduate Research Association of Students in Pharmacy (GRASP) Annual Meeting, Tallahassee FL, June 6-8, 2008.

V. Vemulapalli, H. Kim, S.P. Davis, P.M. Friden and A.K. Banga. In vivo iontophoretic delivery of salmon calcitonin across microporated skin. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

V. Vemulapalli, Y. Yang, S. Siddoju, R. Conjeevaram, T. Myers, H. Teunissen and A.K. Banga. In vitro and in vivo iontophoretic delivery of SLV 318 across hairless rat skin. American

Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

G.K. Yeboah and M.J. D'Souza. Evaluation of albumin microspheres as potential delivery vehicles for oral tuberculosis vaccines. American Association of Pharmaceutical Scientists Annual Meeting, San Diego CA, November 11-15, 2007.

### **RESEARCH GRANTS/CONTRACTS AWARDED 2007-08**

A.K. Banga. Microneedles alone or in combination with other enhancement techniques for transdermal delivery of proteins. Pfizer Inc. (New York NY), \$ 250,000.

A.K. Banga. Evaluation of terbinafine and other drug cartridges for iontophoretic release and transdermal delivery. Transport Pharmaceuticals (Framingham MA), \$ 175,000.

M.J. D'Souza and R. Palaniappan. Evaluation of an oral encapsulated melanoma tumor vaccine. Georgia Research Alliance (Atlanta GA), \$50,000.

L.J. Jobe. Effect of TNF-alpha neutralizing microspheres on left ventricular remodeling. Mercer University Seed Grant (Macon GA), \$3,500.

H. Zhang. Nanoparticle drug conjugate to treat cancer with MDR. Mercer University Seed Grant (Macon GA), \$3500.

### **HONORS AND RECOGNITIONS**

Ajay K. Banga

Editorial Advisory Board

*The AAPS Journal*

*Critical Reviews in Therapeutic Drug Carrier Systems*

*Biomedical Engineering – Applications, Basis and Communications*

*Pharmaceutical Development and Technology*

*Recent Patents on Drug Delivery & Formulation*

Reviewer

*International Journal of Pharmaceutics*

*International Journal of Pharmaceutical Compounding*

*Journal of Controlled Release*

*Medical Engineering and Physics*

*Pharmaceutical Research*

Martin J. D'Souza

Award for Excellence in Research, Mercer University College of Pharmacy and Health Sciences, presented at Commencement on May 3, 2008

**MEMBERSHIP IN SCIENTIFIC AND PROFESSIONAL ORGANIZATIONS**

Ajay K. Banga	American Association of Pharmaceutical Scientists American Association of Colleges of Pharmacy Controlled Release Society, Inc. International Society for Pharmaceutical Engineering Kappa Psi Rho Chi Sigma Xi Society of Cosmetic Chemists
Martin J. D'Souza	American Association of Pharmaceutical Scientists Controlled Release Society Rho Chi Sigma Xi
Lynetta J. Jobe	American Association For Laboratory Animal Science American Heart Association American Veterinary Medical Association
Ravi Palaniappan	American Association of Pharmaceutical Scientists Controlled Release Society The Society for Mucosal Immunology
Chalet Tan	American Association of Cancer Research
Hailing Zhang	American Association of Pharmaceutical Scientists Controlled Release Society Sigma Xi