KU Postdoctoral Research Day

Friday, February 26, 2016
School of Pharmacy, 2010 Becker Drive, West Campus

8:30 a.m.  Registration and Refreshments,
           2nd Floor Atrium

9:00 a.m.  Career Planning Workshop:
           “Putting Your Ph.D. to Work: Planning for a
           Successful Career,” with Dr. Philip Clifford,
           3020 Pharmacy

11:00 a.m. Postdoc Research Poster Presentations,
           2040 Pharmacy

Noon  Luncheon and Networking,
       2nd Floor Atrium

1 p.m.  Postdoc Research Oral Presentations,
        3020 Pharmacy

3 p.m.  Awards Presentation:  Best Talk, Best Poster,
        3020 Pharmacy

http://www.ku-postdoc-association.dept.ku.edu/
Oral Presentations

1:00 pm Vikalp Vishwakarma, KU-Lawrence, Pharmaceutical Chemistry
Type-III Secretion Proteins as a Broadly Protective Subunit Vaccine Against
Salmonella enterica serovars

1:20 pm Samik Bagchi, KU-Lawrence, Civil, Environmental and Architectural Engineering
Fate of Microplastics in Water and Resource Recovery Facilities (WRRFs) and National
Environmental Loading Estimates

1:40 pm Ranjan Preet, KUMC, Cancer Biology
The RNA Binding Protein HuR Enhances Exosome Secretion in Colorectal Cancer

2:00 pm Huili Yao, KU-Lawrence, Chemistry
The Development of Inhibitors Targeting the BfrB-Bfd Protein-Protein Interaction in
Pseudomonas aeruginosa

2:20 pm Rita-Marie McFadden, KU-Lawrence, Molecular Biosciences
Contribution of Wnt Signaling Pathway to Asymmetric Stem Cell Division in Colon Crypts

Poster Presentations

1. Ishfaq Ahmed, KUMC, Surgery
Bacterial Dysbiosis Promotes Development of Colitis Following Chronic Notch Inhibition

2. Giuseppe Caruso, KU-Lawrence, Bioanalytical Chemistry and Pharmaceutical Chemistry
Role of Carnosine in the Modulation of Nitric Oxide Production by RAW 264.7 Macrophages

3. Hemantkumar Chavan, KUMC, Pharmacology, Toxicology and Therapeutics
Role of Mitochondrial ROS in Arsenic Mediated Mitohormesis

4. Mohammad M. Hossain, Kansas State University, College of Veterinary Medicine
Discovery of Non Species Specific Antibody Capturing Reagents in Fluorescent Microsphere
Immunoassay (FMIA): A Powerful Tool for Veterinary Diagnostic Virology

5. Colin S. McCoin, KUMC, Molecular and Integrative Physiology
Time Dependence of in vivo Leupeptin Hepatic Autophagic Flux Assay Result Interpretation

6. E. Matthew Morris, KUMC, Molecular and Integrative Physiology
Intrinsic High Aerobic Capacity Is Associated with Protection of Mitochondrial Respiratory
Capacity and Decreased Inflammation Following Chronic High-Fat/High-Cholesterol Diet

7. Jenifer K. Settle, KU-Lawrence, Bioengineering Research Center, Chemistry
Ellipsometric Investigations of Mechanism of MMP-8 Inhibition by Metal Abstraction Peptide

8. Linyong Song, KU-Lawrence, Bioengineering Research Center
How to Modulate the Long-term Behavior of Methacrylate-based Dental Adhesive?

9. Pradip K. Maity, KU-Lawrence, Chemistry
Applications of ROMP-derived Oligomeric Silica and Co/C-Reagents for small molecule
Synthesis
Type-III Secretion Proteins as a Broadly Protective Subunit Vaccine Against *Salmonella enterica* serovars

Vikalp Vishwakarma¹, Francisco J. Martinez-Becerra¹, Prashant Kumar¹, Olivia Arizmendi², Melissa M. Pressnall¹, William D. Picking¹,³, Wendy L. Picking¹*

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*Salmonella enterica* is an important foodborne pathogen. Infection of livestock is common and a threat to the food animal industry. Non-typhoidal *S. enterica* is the leading cause of hospitalization and death resulting from contaminated food in the US. Currently, no broadly protective vaccine is available against the many *S. enterica* serovars. We have genetically fused SPI-1 and SPI-2 tip and first translocator proteins, SipB/SipC and, SseB/SseC, respectively, to produce recombinant fusion proteins S1F and S2F, respectively, for immunization of mice. S1F and S2F, alone or together, were administered intramuscularly with monophosphoryl lipid-A (MPL) and Alhydrogel as adjuvant system. Both fusions elicited a high serum IgG response alone and together. Antibody secreting cells (ASC) isolated from bone marrow of immunized mice showed moderate to high frequencies IgG ASCs against the proteins of S1F, high frequencies to proteins in S2F, while the highest frequencies were detected in the S1S2 vaccinated group. Similarly, unique cytokine secretion patterns were detected in S1S2 vaccinated mice. When mice were challenged with *S. Typhimurium* or *S. Enteritidis*, the S1S2 vaccine formulation elicited the highest protection against death as well as prevention from cecal inflammation. These results demonstrate the proof of concept in a small animal model that the Type-III secretion protein fusion S1S2 can be used as subunit vaccine with broad coverage to protect against all *S. enterica* serovars which may be transformative to the livestock industry and improve human health.
Fate of Microplastics in Water and Resource Recovery Facilities (WRRFs) and National Environmental Loading Estimates

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Microplastics (<5 mm) have become a major and growing global pollution problem. Water and resource recovery facilities (WRRFs) have been described as a point of source for microplastics, but very little attention has been given about the fate of microplastic inside WRRFs. In this study, we have investigated the fate of microplastics through four full-scale WRRFs. All of our extracted samples were positively identified as polyethylene or poly (vinyl stearate) based on FTIR spectra. Our results suggest that activated sludge accumulate much of the plastic load. Monte Carlo analysis showed that only 0.02-0.3% of the microplastic entering into the WRRFs will eventually end up in effluent and thus discharge into waterbodies. Mass majority of environmental release of microplastics from WRRFs will occur through land application of stabilized biosolids. However, even 0.02-0.3% of the total microplastic load or an average of 16 plastic particle per liter in effluent would have severe consequences for waterbodies since WRRFs in the United States are collectively capable of treating >160 trillion liters of wastewater per day. Plastic particles also act as a carrier of invasive species. By SEM, we have observed bacterial biofilm on the plastic surface. Striking similarity was observed between activated sludge bacterial community and microplastic associated biofilm by 16s rRNA gene sequencing. This indicate the colonization of native bacteria from WRRFs on the microplastic surface that can be transported into the waterbodies. Transfer of WRRF microbial community using microplastic as a carrier material can be hazardous for the environment as the invasive species mitigate rapidly among marine habitat, potentially changing the natural ranges. Overall, this paper contributes substantially to our current understanding of WRRFs as a point of source of microplastic and the environmental fate in effluent water and beneficial biosolids.
Enhanced secretion of exosomes by cancer cells is recognized as a means of transferring oncogenic information within the tumor microenvironment. Through their ability to carry specific RNA and protein cargo, tumor-derived exosomes are effective cancer biomarkers. In cells, oncogenic mRNA transcripts are targeted for post-transcriptional regulation through 3'UTR AU-rich elements (AREs) that are bound by RNA-binding proteins. These same mRNAs are within tumor-derived exosomes, suggesting a role for RNA-binding proteins. Here, we examined the ability of HuR to influence exosome production and mRNA cargo. To test this, Tet-regulated HuR-inducible HeLa cells were used to demonstrate that cytoplasmic HuR overexpression promoted a 4-fold increase in exosomes produced. Furthermore, HuR was detected in exosomes produced only from HuR-overexpressing cells. To test if these effects were seen in CRC cells that endogenously overexpress HuR, exosome levels from CRC cells were compared to normal primary human intestinal epithelial and myofibroblast cells. The CRC cells secrete ~3-fold greater exosome levels than normal cells and enhanced exosome production was dependent upon HuR. Knockdown of HuR in CRC cells directly impacted exosome secretion to levels observed in normal cells. Using an inducible model of RasV12-mediated transformation of intestinal epithelial cells, endogenous HuR overexpression was observed concomitant with 4-fold greater levels of exosomes containing HuR as cargo. The GI-tumor bearing APCMin/+ mice produced ~3-fold more serum exosomes, with HuR as exosomal cargo in APCMin/+ mice. This work has identified a novel connection between HuR-mediated post-transcriptional regulation and tumor-derived exosome production, along with identifying exosomal HuR as a serum-based CRC biomarker.
The Development of Inhibitors Targeting the BfrB-Bfd Protein-Protein Interaction in
*Pseudomonas aeruginosa*

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Relatively high cellular iron levels are necessary for bacterial survival and iron is highly regulated. The protein-protein interaction (PPI) between BfrB (bacterioferritin) and Bfd (bacterioferritin-associated ferredoxin) in *Pseudomonas aeruginosa* plays an essential role for bacterial iron hemostasis. The valuable insights obtained from the *P. aeruginosa* BfrB-Bfd complex X-ray crystal structure and further characterization of the hot-spot residues make the PPI a feasible target for disrupting bacterial iron homeostasis for inhibiting iron mobilization from BfrB. Therefore, inhibition of the BfrB-Bfd interaction can be a novel target for antibiotic development. The inhibitor discovery was initiated with the screening of a hand-picked 220 fragment library using STD-NMR (saturation transfer difference–NMR) and SPR (surface plasma resonance). Six hits were found among the fragment library. Fragment 1-BfrB co-crystal structure was solved and SPR measurement showed that fragment 1 binding affinity ($K_d$) was 1.2 mM. Furthermore, more than 60 derivatives of fragment 1 were designed, synthesized, and characterized using *in silico* methods, *in vitro* iron release function assay, co-crystallization, SPR, bacterial cell killing *in vivo*, and FP (fluorescence polarization) methods. Up to now, the binding affinity of the lead compound is at 30 µM ($K_d$). In addition, a new method was developed to detect disruption of iron homeostasis by measuring premature secretion of siderophores. This new approach is being used to complement the *in vitro* assays by assessing the efficacy of the new compounds to penetrate bacterial cells and bind BfrB in *P. aeruginosa* cells.
Contribution of Wnt Signaling Pathway to Asymmetric Stem Cell Division in Colon Crypts

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Background: The ability of a stem cell to renew itself, as well as to create a daughter cell that differentiates to a specialized cell is critical for tissue homeostasis. Loss of this asymmetric cell division (ACD) can lead to cancer. Over 80% of colonic tumors have mutations in the Adenomatous Polyposis Coli (APC) gene. APC protein is necessary for a Wnt-inhibited beta-catenin destruction complex (BCD). Our research demonstrates that components of the BCD may contribute to asymmetric cell division. Methods: We exposed rat intestinal epithelial cells grown in culture to Wnt3a-ligated beads to provide a localized Wnt signal. Cells were stained with antibodies specific to BCD components Adenomatous Plyposis Coli (Apc), Glycogen synthase kinase 3 beta (GSK-3β), Axin, and Casein kinase 1 alpha (CK1-α) as well as to Numb. We evaluated ACD in colon tissues from mice with a mutation in the Apc gene, resulting in compromised nuclear APC localization (Apc¹mNLS/mNLS) as well as Apc⁺/+ littermate controls. Longitudinally Oriented Basal Asymmetry (LOBA) was assessed to identify specific cell curving orientation characteristic of ACD. Stem cells were identified using in situ RNA staining for Lgr5. Results: Compared to their Apc⁺/+ littermates, Apc¹mNLS/mNLS mice have fewer Lgr5-expressing cells in the crypts of the proximal colon. We also observed a pattern of lower LOBA values, suggesting less asymmetric cell division in Apc¹mNLS/mNLS, compared to Apc⁺/+ littermate control mice. BDC components APC, GSK-3β, Axin, and CK1-α showed varying degrees of Wnt-bead associated asymmetric localization in cultured intestinal epithelial cells. Conclusions: BCD components undergo ACD in response to Wnt signaling and mice with Apc-mNLS protein display alterations in stem cell numbers and features of ACD. Together, these results reveal a new molecular mechanism underlying control of stem cell division which potentially contributes to colon cancer.
**Bacterial Dysbiosis Promotes Development of Colitis Following Chronic Notch Inhibition**

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**Background.** Intestinal mucus layer disruption and gut microflora modification in conjunction with tight junction (TJ) changes can increase colonic permeability that allows bacterial dissemination and intestinal and systemic disease. *Citrobacter rodentium* (CR), a mouse infecting pathogen, is used as a model system to study the pathogenic mechanisms of enteropathogenic and enterohaemorrhagic E. coli. This study was undertaken to study the mechanism of colitis caused by CR infection combined with chronic Notch inhibition.

**Material/methods:** NIH:Swiss outbred mice were infected with CR and treated with Dibenzazepine and fed 6% Pectin diet. Mucus composition, fecal 16S rDNA analysis and components of TJ integrity were measured by standard techniques.

**Results:** The mucus analysis revealed changed composition of O- and N-glycans in CR infected/DBZ-treated mice compared to controls. High-throughput sequencing of the bacterial 16S rDNA gene showed alterations in the microbial community structure. Indeed, mucin degrading and colitogenic bacterium, *Akkermansia muciniphila* exhibited dramatic increases in the feces of CR-infected/DBZ-treated mice. Quantitative PCR analysis revealed that colons from CR-infected/DBZ-treated mice had decreased expression of antimicrobial peptides such as Angiogenin-4, Retnlb, Intelectin-1 and Intelectin-2. Colonic crypts from CR-infected/DBZ-treated mice also exhibited significant downregulation of both TJ and adherens junction proteins, e.g., Claudin-5, ZO-2, E-Cadherin and β-catenin. To corroborate these findings in known models of colitis, both C3H/HeN mice that exhibit exaggerated response to CR infection and T- and B-cell deficient Rag-1⁻/⁻ mice following CR-infection and DBZ-treatment, exhibited exacerbation of colitis associated with dramatic increases in paracellular permeability. Chronic Notch pathway blockade depleted ISC markers Dclk1 and Lgr5 concomitant with exacerbation of colitis. 6% Pectin diet ameliorated colitis by restoring barrier integrity via recruitment of bacteria with potential anti-inflammatory functions.

**Conclusions:** 1. These studies delineate the mechanistic basis of colitis development in the aftermath of chronic Notch inhibition. 2. Our findings also caution against the use of Notch inhibitors for patients suffering from colitis-associated colon cancer.
Role of Carnosine in the Modulation of Nitric Oxide Production by RAW 264.7 Macrophages

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Carnosine (β-alanyl-L-histidine) plays an important role in a number of physiological functions related to oxidative stress. Carnosine has been shown to be involved in many cellular defense mechanisms against oxidative stress, including nitric oxide (NO) detoxification. High concentrations of NO can be produced by inducible nitric oxide synthase (iNOS) in immune cells. Excess NO production in these cells can result in the formation of dangerous reactive nitrogen species. Therefore, the protective properties of carnosine are of great interest, especially regarding its antioxidant activity against reactive oxygen and nitrogen species that are involved in oxidative stress-driven disorders. The goal of this research is to determine the role of carnosine on the production of intracellular and extracellular NO and nitrite (NO primary degradation product) by macrophages under pro-inflammatory conditions. Using the Griess assay for the detection of nitrite, we found that carnosine affects nitrite production in RAW 264.7 macrophage cells in a concentration-dependent manner without affecting cell viability. Carnosine alone does not affect the cellular nitrite production, however, one hour pre-treatment with carnosine followed by 24 or 48 h stimulation of the cells with either lipopolysaccharide (LPS) alone or LPS with interferon-γ significantly increased both nitrite production and cell differentiation. It was found that inhibitors of iNOS drastically reduced the extracellular nitrite production in macrophages. Next, cells were incubated with 4,5-diaminofluorescein diacetate (DAF-FM DA) to determine intracellular NO production and cell lysates were analyzed by microchip electrophoresis with laser-induced fluorescence (ME-LIF). These results confirmed the production of a higher amount of NO by macrophages under simulated conditions compared to control. On the other hand, pre-treatment of the cells with carnosine significantly reduced the production of NO in stimulated cells. Preliminary experiments indicate that the mechanism of NO degradation in the presence of carnosine involves a direct chemical reaction between carnosine and NO.
Role of Mitochondrial ROS in Arsenic Mediated Mitohormesis

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Inorganic arsenic is a naturally occurring metalloid that is ubiquitously present in the environment. Epidemiological studies have shown that chronic exposure of humans to inorganic arsenic is associated with liver injury, peripheral neuropathy, and an increased incidence of cancer of the skin, lung, liver, and bladder. However, there has been much controversy about the shape of the arsenic response curve, particularly at low doses. Recent epidemiological and experimental studies have shown that low dose arsenite reduces the relative risk for cancer among exposed populations and extends life-span in metazoans whereas higher concentrations increase toxicity and reduce longevity. Such biphasic response to a potentially harmful compound, commonly termed hormesis, is thought to have a significant impact on growth and longevity. In the present study we found that treatment of human and mouse primary hepatocytes with 0.01 to 100 μM arsenite produces a low dose growth promoting effect while higher dose produces cytotoxic effects. Measurement of mitochondrial bioenergetics shows that arsenite potentiates mitochondrial function at low-dose and inhibits mitochondrial function at high-dose in a manner that correlates well with the expression and activity of mitochondrial respiratory complexes. More importantly co-exposure of hepatocytes to arsenite along with ROS scavengers was able to revert the phenotype of altered mitochondrial function. Taken together these results suggest a nonlinear dose-response characteristic of arsenite in primary hepatocytes with low-dose arsenite promoting transient increase in mitochondrial function that act as transducers of arsenite induced hormesis.
Discovery of Non Species Specific Antibody Capturing Reagents in Fluorescent Microsphere Immunoassay (FMIA): A Powerful Tool for Veterinary Diagnostic Virology

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Emerging virus diseases are a major threat to human and veterinary public health. Fluorescence microsphere immunoassay (FMIA) is a novel molecular diagnostic technology which can be used for the detection of emerging infectious diseases in humans and animals. Recently, FMIA has been used to detect IgM and IgG against several viruses including bovine viral diarrhea virus (BVDV), classical swine fever virus (CSFV), porcine circovirus type 2 (PCV2), porcine reproductive and respiratory syndrome virus (PRRSV), and Rift Valley fever virus (RVFV). Biotin-conjugated IgG have been commonly used as a capture antibody for the detection of IgG in traditional FMIA. The current FMIA relies on IgG as a capture antibody that may sometimes produce high backgrounds. Proteins A, G, and A/G are native recombinant proteins that bind the Fc receptors of IgG. Protein A is derived from Staphylococcus aureus (SPA), Protein G is derived from a Streptococcus species, and Protein A/G is derived from a genetically engineered recombinant form of Protein A and Protein G. However, the uses of these proteins as a capture antibody in FMIA are uncommon. The goal of this research was to develop a multiplex FMIA for the detection of antibodies to recombinant viral antigens using conjugates A, G, and A/G. For the production of recombinant antigens, viral proteins expressed in Escherichia coli were covalently bound to fluorescent polystyrene microspheres and analyzed with the Luminex xMAP® 100 instrument. Our studies showed that conjugates A, G, and A/G are suitable for screening antibodies to several newly emerged viruses such as BVDV, CSFV, PCV2, PRRSV, and RVFV.
Cellular autophagy is a tightly regulated process that controls the degradation and recycling of organelles and cellular material. In general, autophagy is activated by fasting and exercise and impaired by obesity. A number of chemical inhibitors, such as leupeptin, can be employed to study the dynamic events that encompass autophagic flux. Although these methods are established in cultured cells their use in vivo is still under development. Leupeptin, a cysteine, serine and threonine protease inhibitor, prevents lysosomal degradation and results in an accumulation of a lipidated form of the protein microtubule-associated protein 1A/B light-chain 3 (LC3-II). LC3-II is a critical autophagic protein required for autophagosome formation and induction of autophagy. In vivo leupeptin injection should lead to an accumulation of autophagosomes and LC3-II because of lysosomal inhibition, and the degree to which LC3-II accumulates is a marker of autophagic flux. We tested the effects of 4 days of wheel running or overnight fasting compared to sedentary/fed condition in C57B/6 mice (n=6) followed by a morning IP leupeptin injection with the hypothesis that exercise and fasting would increase LC3-II accumulation. Saline injected mice served as controls. Unexpectedly, sedentary/fed control mice accumulated more hepatic LC3-II than overnight fasted or wheel running mice at 4 hours post leupeptin treatment. Therefore, the timing of leupeptin administration plays a critical role in the assessment of mitophagic flux. Our next examination will determine if leupeptin injection prior to fasting or wheel running yields expected results of increased LC3II and autophagic flux.
Intrinsic High Aerobic Capacity Is Associated with Protection of Mitochondrial Respiratory Capacity and Decreased Inflammation Following Chronic High-Fat/High-Cholesterol Diet Challenge

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We previously reported that the divergent aerobic capacity of the high and low capacity runner (HCR and LCR) rat model produces increased hepatic fatty acid oxidation (FAO) and maximal mitochondrial respiratory capacity in the HCR compared to LCR rats. A body of evidence suggests that a western diet results in alterations in mitochondrial function facilitating increased oxidative stress, which can produce elevated expression of pro-inflammatory genes. Herein we examined the hypothesis that increased aerobic capacity associated with increased hepatic FAO/mitochondrial respiratory capacity of the HCR rat would protect against increased liver inflammation and cell death following a chronic high-fat/high-cholesterol diet (HFHC) challenge. HCR/LCR rats were fed open source low-fat diet (LFD, 10% fat, Research Diet) prior to initiation of a 45% fat (kcal)/1% cholesterol (gram) diet (Research Diet) for 16 weeks. Both HCR and LCR rats demonstrated increased weight gain following HFHC, with only the LCR having increased fat mass gain compared to LFD. Both strains were observed to have reduced hepatic complete FAO due to HFHC; however, HCR complete FAO was greater than LCR regardless of diet. The HFHC resulted in reduced state 3 hepatic mitochondrial respiration of glutamate and pyruvate in both strains, with LCR also having reduced state 3 respiration of palmitoyl-carnitine (L-PC). However, HCR was observed to have greater hepatic mitochondrial state 3 and uncoupled respiration of glutamate, pyruvate, and L-PC compared to LCR regardless of diet. The differences in state 3 mitochondrial respiration due to diet are inversely associated with increased mRNA expression of hepatic inflammation markers (MCP-1, TLR4, TLR2, IL-b, and F4/80). However, HCR rats on HFHC demonstrate significantly lower expression of these markers compared LCR. In conclusion, HCR rats are partially protected against chronic HFHC diet induced hepatic inflammation, which is associated with greater mitochondrial respiratory capacity compared to LCR.
Ellipsometric Investigations of Mechanism of MMP-8 Inhibition by Metal Abstraction Peptide (MAP)

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Matrix metalloproteinase-8 (MMP-8) is a collagenase whose activity and dysregulation have been implicated in a number of disease states including cancer metastasis, diabetic neuropathy, and degradation of biomedical reconstructions, including dental restorations. Thus, regulation of activity of MMP-8 and other matrix metalloproteinases is a significant therapeutic target. Inhibition of MMP-8 activity has been achieved in our group via a small metal binding peptide, tether-MAP. In this work, the mechanism of this inhibition was investigated using ellipsometry to monitor interactions between tether-MAP and MMP-8. Tether-MAP was covalently bound to an amine-terminated self-assembled monolayer. Interactions of MMP-8 with this surface and control surfaces were investigated to elucidate the interactions occurring between the tether-MAP peptide and MMP-8. After MMP-8 incubation, a significant increase in thickness was observed on the peptide films but not on the control films. While incubation in zinc or nickel ions led to no significant change in height with the either surface. The results suggest a specific, long-lived binding interaction between the MAP tag on the peptide and the MMP-8 metal center as the likely mechanism of inhibition.
How to Modulate the Long-term Behavior of Methacrylate-based Dental Adhesive?

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The effort in this project is focus on how to improve the long-term performance of methacrylate-based dental adhesive. Photoacid-induced sol-gel reaction technique has been developed and two different functional methoxysilane monomers were investigated in the new-developing adhesive system. The frequency sweep tests were conducted to evaluate the thermal–mechanical properties of the control and experimental specimen response to frequency. Time-temperature superposition (TTS) was employed to generate master curves of storage modulus vs. frequency and to predict the long-term performance based on short-term experimental data. The results indicated that with increasing of the silane monomer, the storage moduli of experimental were significantly higher than that of the control at high temperature (or low frequency). Meanwhile, the functional group of methoxysilane showed limited effect on the long-term behavior of dental adhesive.
Applications of ROMP-derived Oligomeric Silica and Co/C-Reagents for Small Molecule Synthesis

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The development and application of silica-supported ROMP reagents and Nb-tagged Cobalt-graphite (Nb-Co/C) magnetic nanoparticles for the synthesis of small molecules are reported under purification-free processes. An array of high load, hybrid Si-immobilized oligomeric benzyl phosphates (Si-OBP) and triazole phosphates (Si-OTP) derivatives were successfully synthesized for the efficient benzylation and triazolation of nucleophilic species. These reagents are readily synthesized from commercially available starting materials to afford free-flowing solids on multi-gram scale in excellent yield and utilized in benzylation and triazolation reactions with a variety of nucleophiles. Additional efforts utilizing surface-initiated polymerization from Nb-tagged silica (Nb-Si) and Nb-tagged Cobalt-graphite (Nb-Co/C) magnetic nanoparticles for purification-free Intermolecular Monomer-on-Monomer (MoM) Mitsunobu protocol on sulfonamide scaffolds is also discussed.