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Nanoscale Bioengineering of Bone-inspired, All-natural Bionanocomposite Scaffolds for Bone Substitutes and Tissue Regeneration

Throughout my entire NURF, I have continuously read and written reviews of current nanotechnology enabled bone scaffolding techniques. This has allowed me to become very knowledgeable in this medical and mechanical field, and it has also helped me develop successful research techniques and a higher writing level. Through our reviews of others' work, I have acquired a sense for critical reading and writing. With the knowledge I had gained from reading papers, I was able to better understand the bone scaffolding process and how our project relates to it. Making all-natural nanoscale bioscaffolds for bone tissue engineering in the lab really advanced my progress as a researcher and gave me great experience working with bone scaffolds.

The applications of medical nanotechnology provide exciting advances to the development of biomechanical bone scaffolds for bone tissue engineering. For example, bionanocomposites used for bone grafting present a biocompatible and biodegradable solution to current bone tissue engineering methods. Nanotechnology researchers have shown that bionanocomposites are a promising biocompatible and biodegradable material that can mimic bone's amazing natural structure. These nanocomposites could prove to be an effective, cost efficient bone scaffold alternative. Successful developments of bone-mimetic composite bionanomaterials and drug delivery systems and their incorporation into bone scaffolds will be the key in advancing nanotechnology-enabled bone tissue engineering.

Bone is a specialized form of connective tissue that forms the skeleton of the body and is built at the nano and microscale levels as a multi-component composite material consisting of a hard inorganic phase (minerals) in an elastic, dense organic network. Mimicking bone structure and its properties present an important frontier in the fields of nanotechnology, materials science and bone tissue engineering, given the complex morphology of this tissue. There has been a growing interest in developing artificial bone-mimetic nanomaterials with controllable mineral content, nanostructure and chemistry for bone and cartilage tissue engineering and substitutes. Current processes for bone tissue engineering and grafting consist of autografting, allografting, and xenografting. However, these processes are limited by the shortage or suitable materials for supplementing the healing of critical-sized bone fracture defects. Therefore, tissue engineered bone materials and procedures have become a major player in the clinical field. These grafts can be engineered with tremendous precision and quality due to the advancements in biomaterials, biocompatible technologies, and stem cell research. Our project goal is to develop an all-natural biocompatible nano-composite scaffold for bone substitutes and tissue regeneration in which drug delivery systems will be attached, specifically anti-cancer drugs.

Bionanocomposites are promising new bone materials that are both biocompatible and biodegradable and can be tuned to mimic natural bone structure and functionality. A simple and novel top-down drop-casting based method for controlled synthesis of all-bone-minerals in a biomimetic muticomponent bionanocomposite material for bone grafting has been successfully demonstrated. This bionanocomposite was synthesized using polymers and nanoparticles consisting of polycaprolactone (PCL) dissolved in benzyl alcohol, hydroxyapatite (HAP), calcium carbonate ($CaCO_3$), chitosan, a calcium- and sodium-based alginate, and collagen. The unique porous architecture can allow material transport properties across the bionanocomposite film. This composite also produced parallel collagen nanofibers which is similar to healthy natural bone structure and is especially important because of its enhanced mechanical properties. The spherical HAP granules that were produced in this nanocomposite can also be shown to possibly eliminate or reduce the nondesirable inflammation reactions of the body which is preferable for bone grafts and targeted drug delivery. Another scaffold sample was synthesized using the same particles as stated above, except with a polyethylene glycol (PEG) polymer in place of PCL. This allowed the sample to be alcohol-free and we did not need to heat the sample to evaporate the alcohol. This scaffold has been sent in to the University of Arkansas – Little Rock for SEM imaging and mechanical strength testing to be compared to the PCL based sample. Our first PCL based scaffolds have been sent in for further testing to the Italian Institute of Technology. There, our colleagues will attempt to attach anti-cancer drug delivery systems to the scaffolds which would be an exciting, novel breakthrough in this field. It may take several months, but we are excited to learn the results, at which point we will write manuscripts on the findings. Besides the laboratory, we have also written several articles and reviews. My lab partner Gary Blackburn and I have had two articles published in a trade magazine called Vacuum Technology and Coating. The titles of these articles are Nanotech Enabled Bone Tissue Engineering and Nanotech Enabled Bone Tumor Engineering. We have also written two large review papers, one titled Advances in Bionanomaterials for Bone Tissue Engineering, and the other titled Bionanomaterials for Bone Tumor Engineering. The former has been submitted to *Nanoscale*, and the latter to *Biomaterials*, two high-impact-factor international journals, through the Royal Society of Chemistry publishers.

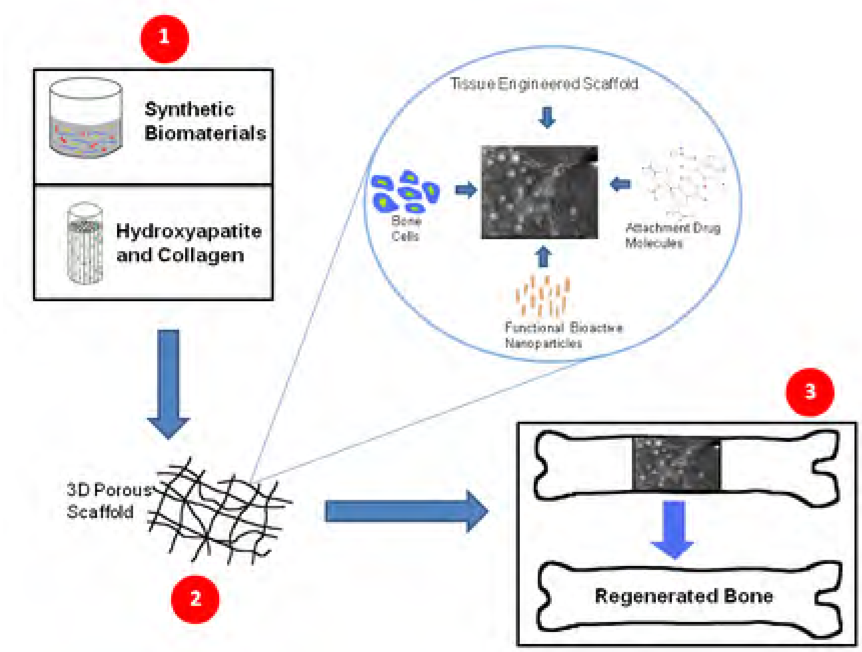

Figure 1: A schematic illustration of the bone tissue engineering process using bone cells and/or attached functional bioactive nanoparticles and drug molecules.

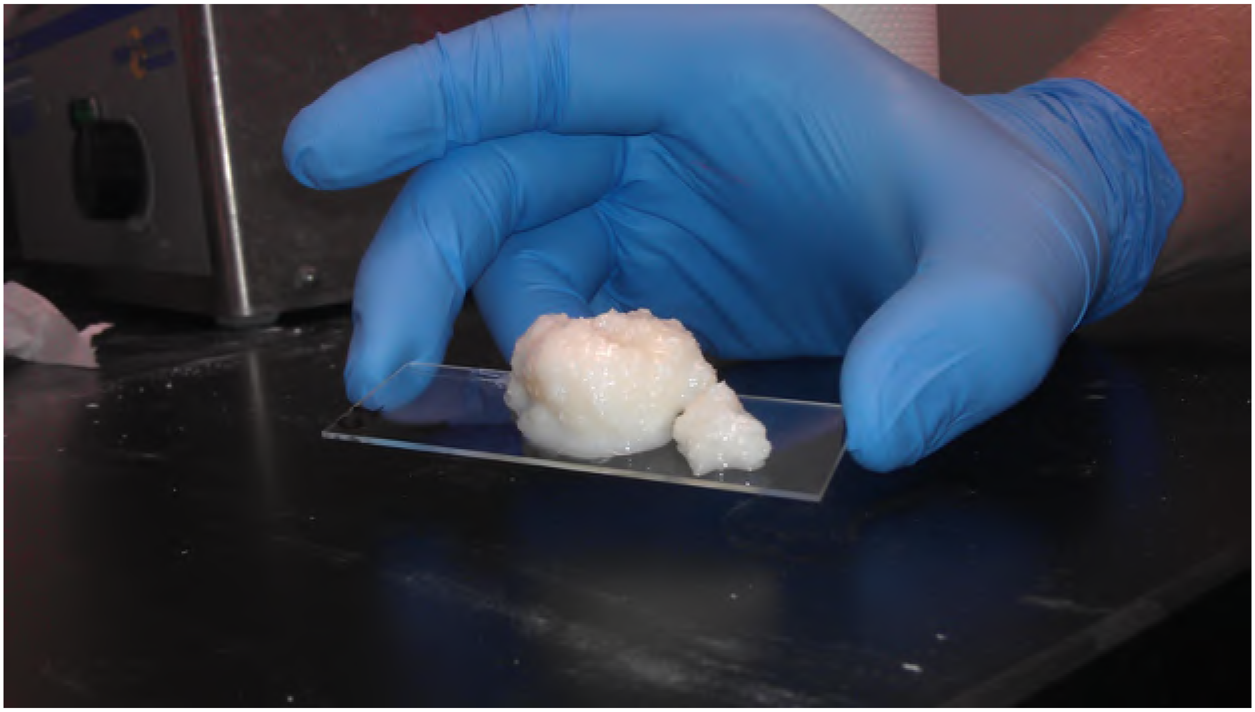

Figure 2: PCL, HAP, $CaCO_3$, chitosan, sodium alginate, calcium alginate, and collagen based bone scaffold sample placed on glass slide.

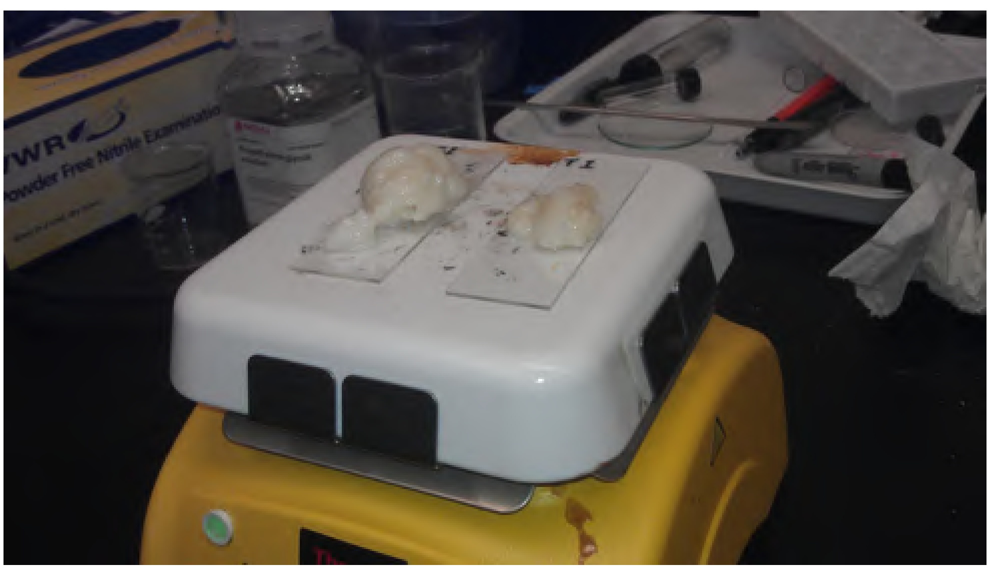

Figure 3: Samples placed on a heating pad for alcohol evaporation.

Figure 4: Scaffolds sent to the Italian Institute of Technology for anti-cancer drug attachment.

Papers published:

Vacuum Technology and Coating

- Nanotech Enabled Bone Tissue Engineering – July 2012
- Nanotech Enabled Bone Tumor Engineering – August 2012

Pending journal publications:

Nanoscale

- Advances in Bionanomaterials for Bone Tissue Engineering

Biomaterials

- Bionanomaterials for Bone Tumor Engineering

Upcoming: Nanotechnology Conference in Chicago in October