

The PSF Research Grant Awards

Unearthing growth factor-free bone regeneration

Editor's note: The following is part of series highlighting The PSF Research Grant Award winners, and the research they're conducting to improve patient safety and develop new technologies for plastic surgeons.

THE RESEARCHER

Justine Lee, MD, PhD
Title: Assistant professor, Pediatric Cleft and Craniofacial Surgery, Division of Plastic and Reconstructive Surgery, UCLA Medical Center



Award: The PSF Pilot Research Grant
Project: Osteoclast Mediated Resorption of Engineered Human Bone

PSN: What is your approach to the study of engineered human bone?

Dr. Lee: Our work involves utilizing custom nanoparticulate mineralized collagen glycosaminoglycan scaffolds for the purposes of human bone regeneration. We have also incorporated the concept of inhibition of resorption in the host microenvironment in promoting osteogenic differentiation. Our proposed work is a pilot study developing the *in vitro* system to study the interactions between mineralized scaffolds and osteoclasts.

PSN: What have you found so far in your investigation of these interactions?

Dr. Lee: We've completed our characterization of osteogenic differentiation on our custom scaffolds using adult primary mesenchymal stem cells in two different species. In both humans and rabbits, we've found that mineralized collagen scaffolds induce efficient osteogenic differentiation in comparison to nonmineralized scaffolds. When we looked at the signaling pathway that was responsible for this increased efficiency, we found that activation of molecules downstream of the bone morphogenetic protein receptor was constitutively present. In other words, we found that this biomaterial can induce osteogenic differentiation independent of addition of growth factors.

PSN: What are the possible practical applications of this osteogenic differentiation for treating patients?

Dr. Lee: Currently, there are two FDA-approved growth factors that are in clinical



Justine Lee, MD, PhD, in the O.R. at the UCLA Medical Center; Dr. Lee with two of her pediatric patients (right).



use, BMP-2 and BMP-7. However, growth factors are not necessarily benign molecules. They are usually added in supraphysiologic concentrations and may cause untoward clinical side effects such as diminished maxillary growth in children, ectopic bone formation, osteolysis and an elevated risk of cancer. Thus, there's a significant need to pursue alternative growth factor independent methods for stimulating osteogenesis, potentially through biomaterial science or a temporary inhibition of resorption by the host microenvironment.

PSN: At this early stage, have you found anything unexpected that could change the course of your research?

Dr. Lee: The unexpected finding in our research is that we were able to induce growth factor independent osteogenic differentiation with our scaffold. We were also able to describe the molecular mechanisms responsible for this finding.

PSN: Who has helped guide your career as a surgeon-scientist?

Dr. Lee: I've had many clinical and scientific mentors throughout the years who have been incredibly important to my develop-

ment. Scientifically, one of the best scientists that I know is Marcus Peter, MD. As my former thesis advisor in graduate school, he set the example of how to do good science and how to do it efficiently. Clinically, Larry Zachary, MD; Russell Reid, MD; Larry Gottlieb, MD; Jim Bradley, MD; and Henry Kawamoto, MD; have made the most significant impact.

Dr. Zachary introduced me to plastic surgery in medical school and made me fall in love with surgery. I credit Dr. Reid for helping me find craniofacial surgery as a career path and letting me do a run-through of life as a surgeon/basic scientist during residency. Dr. Gottlieb taught me how to operate and how to think about surgery, and he showed me what it means to be a great doctor. Dr. Bradley and Dr. Kawamoto taught me everything I know about craniofacial surgery – and they continue to inspire me on a daily basis to always push the boundaries of the possible.

Professionally, I could not have done any of this without the mentorship of David Song, MD; Tim Miller, MD; George Rudkin,

MD; and Andy Da Lio, MD. I'll never forget the day (almost nine years ago!) that Dr. Song told me as a medical student that I had to do plastic surgery, as that decision changed my life forever – not to mention matching me to the University of Chicago plastic surgery residency, which will always be six of the best years of my life. Tim, George and Andy hired me, supported me, mentored me in my early academic career, and I can't thank them enough.

PSN: What do you like to with your time away from the lab?

Dr. Lee: I live a few blocks from the beach in Santa Monica; it's amazing.

PSN: Have you always been interested in a career in medicine?

Dr. Lee: I've always wanted to be a doctor, but I thought I would be a pediatrician because I love kids. It wasn't until my third year of medical school that I realized surgery is just so much fun, as well as a better match for my personality.

PSN: Outside of your current PSF-funded research, what has been your most successful project.

Dr. Lee: Outside of my current work, my favorite project was my dissertation work on apoptosis signaling with a protein called DEDD – believe it or not.

PSN: What sounds are most regularly heard in your O.R.?

Dr. Lee: Michael Jackson, Joao Gilberto, Astrud Gilberto, Antonio Jobim, Stan Getz, Pink Martini and Madeleine Peyroux. But usually, the residents and Fellows just put on whatever they want. ☺

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could be gravely affected. The real or perceived notion that we aren't available will effectively marginalize our specialty.

With continued marginalization, there will be significant erosion of patient volumes. When this occurs, the effect could be profound, as all plastic surgeons may begin competing with multiple other specialties.

Keep skills 'portfolio' updated

So what's the answer? It's unlikely that most of us have placed our financial future in a limited portfolio. Similar to financial diversification, practice diversification must be maintained. The degree of such diversification will have many influences – for instance, despite good training and experience, microsurgery will likely not be practiced by a majority of plastic surgeons. However, it's likely safe to say that every well-trained plastic surgeon can do a gluteal flap, and patients who need such services deserve good care close to home.

For the sake of our patients, our referring physicians, our practices, our communities and our specialty, I encourage each of us to remain true to ourselves and plastic surgery by remaining committed to our expertise and training. That will not only help those in our communities, but it likely will help preserve our specialty as well. ☺

Congress holds hearing on medical device tax

Medical device industry representatives and patient witnesses were invited before the Senate Finance Subcommittee on Health Care to testify on the economic and personal impact of the 2.3 percent tax on medical device companies that was put in place to pay for \$30 billion of the total cost associated with the ACA.

The bill to repeal the controversial tax (S.149/H.R.160) currently holds strong bipartisan support in both chambers. The House bill was introduced by Reps. Erik Paulsen (R-Minn.) and Ron Kind (D-Wis.) and enjoys the bipartisan support of more than 60 percent of the House. The Senate bill was introduced by Finance Committee Chairman Orrin Hatch (R-Utah) and Sen. Amy Klobuchar (D-Minn.). More than one-third of the Senate has cosponsored the bill.

During the hearing, Subcommittee Chairman Pat Toomey (R-Pa.) asked if the

expansion of insurance rolls after the implementation of the ACA has created the amount of business that would result in windfall profits for the industry, offsetting the losses from the tax. Industry representatives said that no new patient population has emerged, and the presumed profits are absent.

Ranking member Debbie Stabenow (D-Mich.), the lone Democrat to provide remarks during the hearing, focused on the positive benefits that the ACA has provided to Americans. Sen. Stabenow emphasized the story of a testifying patient from Maine who concluded that the technology provided by her medical device is irrelevant if she can't afford to pay for the device. The senator admitted that the tax is an issue that needs to be closely reviewed, but stressed that the industry as a whole is paying fewer taxes than overseas competitors and is still a strong and growing sector of the economy.

Republicans on the subcommittee noted that an excise tax – such as the medical device tax – should be reserved for products that pose risks to consumers, such as alcohol or tobacco. In practice, witnesses said that the tax results in an average loss of 29 percent in industry profits overall. This ultimately depletes or eliminates budgets for research and development, and slows the rate at which innovative technologies can be provided to patients.

Both the witnesses and the senators discussed the growing number of companies in the industry that have made drastic decisions in order to keep their businesses in the black. This includes moving to offshore manufacturing facilities, cutting benefits and salaries to current employees, and in some cases, executing layoffs. Most experts believe that the tax would ultimately be passed on to patients, increasing the cost of their health care. ☺