

Research Spotlight: Dr. Nancy Lane

Sex differences in musculoskeletal diseases across the lifespan

Nancy Lane, M.D., is an endowed professor of medicine and rheumatology and director of the Center for Musculoskeletal Health at the University of California, Davis, School of Medicine. Funded in part by the [Specialized Centers of Research \(SCOR\) on Sex Differences](#) program from the National Institutes of Health's Office of Research on Women's Health, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the U.S. Food and Drug Administration, Dr. Lane investigates sex differences in musculoskeletal diseases across the lifespan. Her research in osteoarthritis and osteoporosis is internationally recognized.

Q: How did you first become interested in musculoskeletal issues?

Dr. Lane: As a rheumatologist, I treated patients with inflammatory diseases with high doses of prednisone. When I saw how the prednisone caused these patients to lose bone mass and experience fractures, I became interested in different therapeutic agents to prevent or reverse this glucocorticoid-induced bone loss. Following my keen interest in the field of metabolic bone disease and osteoporosis, our research uncovered that people who were on glucocorticoids like prednisone had very fragile bones that would fracture even if they had high bone mass. We worked in our laboratory with an animal model of glucocorticoid-induced bone loss that provided vital information. We then were able to obtain NIH funding and perform a proof-of-concept clinical trial to treat patients with glucocorticoid-induced osteoporosis with a hormone called teriparatide. In that trial, we were able to reverse the glucocorticoid-induced osteoporosis. It was very exciting to go from the bedside to the bench and then back to the bedside.

Q: How does your research relate to women's health or sex differences?

Dr. Lane: Women have lower bone mass than men, and when women are treated with glucocorticoids, they also have more fractures. Women also have a higher prevalence of rheumatic and chronic inflammatory diseases.

Q: What are the challenges of using both male and female animals in research?

Dr. Lane: Many of the animal models we use in the laboratory have only been developed in one sex. Whenever possible, we try to use both male and female animals, because there can be significant differences between the sexes.

Male mice have higher bone mass than female mice, which reflects our observations in patients. Similarly, the mechanism by which male mice lose bone mass and experience increased bone fragility is different than that of female mice. By performing research in both sexes, we learn the degree of differences between the sexes. In addition, studying the differences teaches us more about the pathophysiology of diseases. This will lead to more informed treatments and better outcomes in many chronic diseases, especially musculoskeletal diseases.

Q: What should investigators consider when designing a study that uses both male and female animals?

Dr. Lane: In [our SCOR project](#) right now, we're looking at differences in peak bone mass in both sexes. One important thing is to understand the difference in male and female phenotypes. Investigators need to have enough animals to create sufficient sample sizes to test their hypotheses. There are also sex differences in response to therapies. By studying both sexes, we understand the spectrum of effects of our treatments for the disease.

Q: What advice would you give a researcher who wants to use data from both sexes in a study?

Dr. Lane: It's only worthwhile to include both sexes when you have a relevant hypothesis to test. In our situation, particularly in our SCOR grant, in one of the projects, the investigators are looking at the difference in peak bone mass between men and women. Their question is whether removing the nuclear progesterone receptor at different times in skeletal development will influence peak bone mass or acquisition of bone mass in male and female mice.

Q: How will your research improve health outcomes for both women and men?

Dr. Lane: We have four projects in our SCOR grant. One of them is preclinical, two are epidemiological, and one is a clinical trial. One project is an intervention to prevent the progression of kyphosis, which is forward-bent posture, in elderly people. We are looking to see if men and women respond to this intervention and if they respond differently. We're also looking at the epidemiology of carpal tunnel syndrome and its treatments, and we're looking to see if men and women have different responses to standard treatments. Our results may inform the clinical community not only about whether these interventions work or don't work — we're assuming they'll work — but about whether they have more of an impact in men or in women.