

Dr. Shonni Silverberg

The central goal of this K24 renewal application is to further my development as a clinical investigator, while enhancing my opportunities and skills in the mentorship of fellows and promising young faculty interested in careers in clinical research. Patient-oriented clinical research has been the cornerstone of my medical career. My main research focus has been the investigation of asymptomatic primary hyperparathyroidism (PHPT). In recent years, my research has concentrated on the non-classical manifestations of PHPT, and the studies in this thematically related K24 program are focused in this area. My research goal is to continue to develop this program. All three themes of this renewal application were highlighted by the 3rd International Workshop on Asymptomatic PHPT (J Clin Endocrinol Metab 94:335-9, 2009) as key areas for future investigation. The themes and Specific Aims (SA's) of this research are: **Theme 1. Vitamin D deficiency in PHPT**: SA1a. To compare biochemical and skeletal features of PHPT patients with and without co-existing vitamin D deficiency. SA1b. To investigate the early effects of vitamin D repletion in PHPT on static and dynamic histomorphometric parameters of bone remodeling (by quadruple labeled bone biopsy). **Theme 2. Cardiovascular manifestations of PHPT**: SA2a. To determine whether or not abnormalities in cardiovascular structure or function in patients with asymptomatic PHPT are reversible after parathyroidectomy. SA2b. To investigate the hypothesis that some of the cardiovascular manifestations of PHPT are due to low vitamin D levels, rather than elevated calcium and PTH levels, by comparing left ventricular mass index and carotid intima medial thickness in PHPT patients with and without vitamin D deficiency. **Theme 3. Neurocognitive manifestations of PHPT** SA3a. To further investigate neurocognitive abnormalities in PHPT by assessing site-specific changes in brain metabolism after parathyroidectomy using the innovative technique of functional MRI. SA3b. To determine whether the neuropsychological abnormalities seen in hypercalcemic PHPT are present in normocalcemic PHPT. Although outside of the closely-knit theme of the K24, there are other ongoing and future opportunities for mentored research (ie theme: obesity/bariatric surgery and the skeleton: 3 mentored studies ongoing).

Importantly, the proposal will provide many opportunities to mentor junior investigators. I have had success as a mentor, with 16 current or past trainees, 10 of whom have been mentored under the current K24 award. Seven of the 10 remain in academic medicine. Of those I have mentored, 3 currently hold and 1 recently completed NIH K23 Awards, 3 completed Masters in POR (2 under my mentorship) and 2 received Endocrine Fellows Foundations grants. One mentee, who has worked with me since her fellowship began, was awarded a NIH stimulus grant. The environment at Columbia is outstanding for the development of those interested in patient oriented clinical research, with a large and supportive Endocrine Division, an excellent NIH funded Clinical Research Center and CTSA, which offers my mentees the opportunity for didactic enrichment through their Master of Science in POR program (Columbia University Mailman School of Public Health and CTSA). Both the Department of Medicine and the GCRC have made substantial commitments toward my development as a clinical investigator. The initial K24 funding period allowed me to reduce my clinical, administrative and teaching loads in order to devote more time to clinical research and to training and mentoring junior faculty and fellows. This award remains an ideal mechanism to allow me to achieve my dual goals: continued productivity in the clinical investigation of parathyroid disease, with protected time for mentoring fellows and junior colleagues interested in patient oriented clinical research as a career path.