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*2004 Program  
New Investigator (3-year project)*

**Project Title:** Hypoxia Inhibits Bone Formation through the PI3K/AKT Signal Pathway

**Project Summary:** The age-related bone loss that occurs in both men and women in their 50s appears to be accelerated among smokers. About one in eight hip fractures in women are attributable to long-term cigarette use. Bone loss occurs rapidly in women at menopause when the bone-protective hormone estrogen decreases rapidly. Smoking both increases this process and decreases the effectiveness of hormone-replacement therapy. Cigarette smoke contains numerous harmful chemicals, such as nicotine and carbon monoxide, which decrease the amount of oxygen delivered to all tissues in the body in a process that maintains them active and healthy. This lack of oxygen is called hypoxia. Bone formation depends on the function of the bone-forming cells called osteoblasts. In humans, from very early ages, these osteoblasts are continuously being generated from progenitors found among bone marrow cells. This study will focus on the molecular mechanisms caused by hypoxia on bone formation addressing when and how cells become hypoxic (like the condition caused by cigarette smoking) and are thus inhibited from becoming mature osteoblasts.