

**Elliot, Sharon**

*Vascular Biology Institute  
University of Miami School of Medicine*

*2001 Program  
New Investigator (3-year project)*

**Project Title:** Chronic progressive kidney disease and exposure to cigarette smoke in the post-menopausal state

**Project Summary:** Smoking has been shown to be a major risk factor for renal disease especially in males. In fact there is evidence that the development and progression of both non-diabetic and diabetic kidney disease are associated with smoking. Although recent USRDS data suggests that women after menopause have a higher risk than men for ESRD, there is little information on the role that smoking may play. Recently, a study by Haroun et al, has shown that the risk associated with chronic kidney disease increases with smoking for both men and women. The project proposes that tobacco and estrogen deficiency represent compounding risk factors for renal injury, especially the renal disease seen in post-menopausal women. Since the number of aging women in the population is increasing, and the number of women who are smokers is also increasing, the relationship between estrogen deficiency and smoking can now be considered to be a significant health care issue

**Project Successes:** The project found that smoking accelerates the development and progression of chronic kidney disease (i.e. glomerulosclerosis) in states of estrogen deficiency and that age is a crucial determinant of the disease process. In general, female C57/Bl6 mice do not develop glomerulosclerosis in response to diabetes or unilateral nephrectomy (50% nephron reduction). These mice only develop chronic kidney disease at an advanced age (27-30 months) during anestrous (rodent menopause = estrogen deficiency). Thus, female C57/Bl6 mice are generally considered "glomerulosclerosis-resistant". In contrast, the project found that "middle-age" mice, which were ovariectomized at 15-months of age, have already established glomerulosclerosis at the age of 20 months after 5 to 6 months of "passive" smoking. The kidney lesion were characterized by the accumulation of extracellular matrix components (collagen type IV and laminin, see Figure) in the mesangium. Importantly, estrogen replacement prevented the development of glomerulosclerosis in these mice. In contrast, young ovariectomized mice (9-months old) did not develop chronic kidney disease when exposed to the same smoking protocol for 5-6 months. Thus, the increased vulnerability of the kidney to smoking-induced injury in older and estrogen-deficient individuals warrants measures to prevent teen-age smoking and smoking cessation programs at any age. The molecular mechanism(s) underlying smoking-induced kidney disease are currently studied in mesangial cells.