Investigator:	**Jack Arbiser** Phone: (404) 727-5063 Email: jarbise@emory.edu
Primary Research Interest:	Dermatology
Description of Research:	Melanoma is a lethal neoplasm characterized by high rates of resistance to chemotherapy and radiation, and is notorious for metastasis. Therapeutic options for advanced melanoma are limited, with temozolomide, an alkylating agent, being the first line therapy. Temozolomide resistance is mediated by the activity of an enzyme, MGMT, which removes temozolomide adducts from DNA, and is upregulated by NF-kB. NF-kB also prevents apoptosis in melanoma through other mechanisms. It is the constitutive activation of NF-kB that underlies the resistance of melanoma to most therapies. We have demonstrated that the prime pathway mediating melanoma tumorigenesis and angiogenesis is an Akt-reactive oxygen-NF-kB signaling pathway. Thus, blockade of this pathway will likely be required to sensitize melanoma to conventional chemotherapy and radiation. We have also characterized a novel small molecule, honokiol, which downregulates Akt-reactive oxygen-NF-kB signaling. Honokiol may be a prime candidate drug for sensitizing melanoma to chemotherapy and radiation.
Relevance to VA:	Melanoma is the leading cause of death from a dermatologic condition, and is the cancer with the most rapid rise in incidence. In the United States, it is predicted that currently, 1 in 70 individuals will be diagnosed with melanoma. During the year 2008, it is predicted that over 60,000 patients will be diagnosed with melanoma, and 10,000 will eventually die of their disease. US Veterans are particularly susceptible to melanoma due to combat exposures in sun exposed areas such as the Pacific Ocean, North Africa, Vietnam, Iraq and Afghanistan, combined with an aging population of veterans of WWII, Korea, and Vietnam. Melanoma remains the leading cause of death due to a skin disorder of US Veterans.