Abstract: Canine oral melanoma (COM) is an aggressive cancer and there are no effective treatments for advanced disease. In human melanoma, the enzyme iNOS produces nitric oxide which helps the tumor grow and survive. There are now a number of drugs being developed to treat human melanoma by inhibiting iNOS expression. One of these is quercetin, a natural product from fruits and vegetables that is sold as a dietary supplement for people and dogs to prevent symptoms from allergies and arthritis. In the proposed research, we will first determine if COM produces iNOS. To accomplish this, we will examine tumor tissue from dogs with COM that has been removed by surgery. Furthermore, we will compare the survival of dogs whose tumors do and do not produce iNOS. If iNOS is important in COM, quercetin may be an effective therapy. The second part of this proposal is a study to confirm that quercetin is well-absorbed by dogs and lacking of serious side effects. We will also study two potential iNOS-associated blood markers for COM to see if they are reliable indicators of tumor burden. The results of these studies will provide us with the best dose of quercetin to use in future therapeutic trials for dogs with COM and possibly provide blood markers to assist in following the course of disease. These data will also provide rationale to offer dogs with COM other iNOS-targeted drugs as they become available.