

Public Abstract

Despite great progress in genetics, little is known about the majority of genetic and environmental causes of complex diseases. One limitation is the great genetic complexity of the human population, in which many variations of many genes can be associated with disease. Another limitation is that it has not yet been possible to study groups of individuals over time, collecting standardized clinical, environmental, and molecular or genetic data. In humans, this has not been possible largely due to cost and ethics. Here we propose that dogs are the ideal mammal in which to identify genetic and environmental contributions to disease. Military Working Dogs (MWD) offer an unparalleled advantage in understanding the genetic mechanisms that contribute to the development of naturally occurring complex diseases. Genetic complexity in dog breeds is very dramatically reduced compared to humans, and each breed is predisposed to a different limited group of disorders. Nearly 400 inherited diseases, including diverse cancers, are well characterized in dogs. Almost all are similar to human disorders and, where known, involve the same biochemical pathways. Other major strengths of dog models is that they share an environment with humans, they also receive a high level of health care, but age five times as fast. Studies on pets share the limitations of bias that occur in the human population. MWD however have extensive clinical, behavioral, and environmental records. By using these records in combination with molecular and genetic characterizations we hope to identify environmental effects that alter heritable traits. Specifically we will integrate different kinds of information and conduct statistical analysis to identify exactly which gene variations and environmental effects are associated with increased cancer incidence or worse outcomes. We propose this would be the most powerful study of its kind to date. The successful completion of this work will yield information about genetic and environmental contributions to cancer. This information will not only be relevant to human cancers, but is likely to reveal completely novel understanding of gene-environment interactions. The ultimate applicability of this work will be the identification of genetic pathways that are affected in cancer risk and disease progression. Importantly, the development of new treatments based on our findings will be vastly accelerated in clinical studies of pet dogs with cancer. For example, if drugs targeting the biochemical pathways implicated are already in human use or in development, those could be used in dogs without requirements for clinical studies that typically take six or more years in humans. Thus our proposal has the potential to quickly identify novel genetic and environmental contributions to cancer, and to result in the rapid development of new treatments.