

Available research training projects for students

Supervisor: Matthew Webster (IMBIM) matthew.webster@imbim.uu.se
<http://www.anst.uu.se/maweb226/>

1) Comparative genomic analysis of the fastest evolving human gene.

We recently performed a study comparing a genome wide sample of human genes with their homologous sequences in other primates. We identified a small proportion of genes whose evolution has "accelerated" during the origin of modern humans. These genes could be important in generating adaptations that are specific to our own species. The gene with the fastest evolution in humans has accumulated 18 mutations that change its protein since we diverged from chimpanzees, whereas only one such mutation has occurred in chimpanzees. We are now interested in analyzing the evolution of this gene in other mammals using comparative genomics and bioinformatics. The aim of this project is to learn more about the function of this gene, the effect of mutations on its function, and why the gene suddenly started to evolve so much faster in humans. Skills in computer programming are essential.

2) Population genetic simulations of the human speciation event.

Ancient speciation events leave a footprint in present-day genomes, which allows us to precisely reconstruct the nature of events that lead to the formation of new species. Comparisons of human and primate genomes have suggested that the speciation event separating humans and chimpanzees was highly complex. It is possible that ancestral populations of humans and chimpanzees interbred with each other and exchanged genes after the initial split, about 6 million years ago. It is also possible that natural selection acted on certain genes, often called "speciation genes", causing humans and chimpanzees to become distinct species. The aim of this project is to analyze divergence between the human genome and other primates. We will then perform computer simulations to understand the influence of natural selection on divergence between humans and chimpanzees. Skills in computer programming are essential.

3) What genes were under selection during dog domestication?

Dog breeds exhibit more variation in size, appearance and behaviour than any other mammal. A wide variety of human genetic diseases are also common in dogs, and researchers in our department are involved in uncovering the genetic basis of these diseases with the aim of improving human health. Strong artificial selection by humans has undoubtedly had a major effect in generating the diversity of modern dogs and contributed to the diseases they

suffer from. We are interested in identifying parts of the dog genome affected by “selective sweeps” for a variety of traits. To do this we have data from more than 50,000 polymorphic sites in more than 1000 dogs generated at the genotyping platform in the Broad Institute of MIT and Harvard. The aim of this project is to use newly developed methods to scan this data for evidence for genes under selection. Skills in computer programming are essential.

4) Maintenance of a database of genome wide genotyping data in dogs.

Researchers in our department are part of a large collaborative project involving more than 20 European Universities (www.eurolupa.org). The aim of this project is to map mutations causing genetic diseases in dog, with the long-term goal of understanding the molecular basis of human disease. Huge amounts of genotyping data are being produced, mainly using Affymetrix and Illumina microarray technology. We are responsible for storing the data here in Uppsala, using a custom database system. This system is also used for performing genetic data analyses, such as whole genome disease association studies. A project is available to assist in database management and to perform genomewide scans for mutations causing disorders such as epilepsy, cancer and heart disease. Skills in computer programming are essential.