Some Discussion points first class:

**1. Do you think it is more important to have a ‘hybrid’ genomic sequence or the sequence of a single individual? (e.g. the sequence of the human genome first announced by the HGP in 2002 versus the sequence of Jim Watson’s genome in 2008, see attached papers). You might want to have a look at publication that describes the “Completion” of the Human Genome Sequencing Project.**

> Initial genome haploid, each genomic region represented by one BAC clone subsampled n=1 from n= N (=50?). Rare variants co-localized with mutations in a new individual led to issues with short read alignment, later on.

> GRCh39 graphbased instead of fastq!

**2. What are the key principles that were learned about the spectrum of human genetic variation from the “1000 Genomes Project” (you will need to carefully read the 2015 Nature paper and come prepared to class to discuss the figures)?**

**3. If you had the resources to sequence 1000 human genome equivalents today, what organisms/individuals would you sequence?**

^ sequencing all different sorts of dog breeds

**4. Should Canada launch a program to sequence the genomes of all Canadian citizens?**

^ From the insurance perspective – in the Canadian health system, how would genomic awareness play out (think versus American!)

**5. Ng, Bamshad et al. (attached Nature Genetics paper) were able to identify a causative mutation by sequencing only 4 affected individuals (from three independent kindreds). Does this make sense?**

**6. a) Assuming there are 6 billion people on the face of the planet (each as “clones” of ~ 60 trillion cells derived from a single fertilized egg cell) and 6 billion base pairs in the human genome, what is the frequency of “new” germline sequence variants per genome?**

In the tens….error rate {2 x 10^-8} \* 6 billion

**b) What is the frequency of somatic mutation (post fertilization during somatic development) in an individual?**

60 trillion / (1 x 10^-8)

**c) Would you expect different frequencies of somatic mutation in different tissues and/or in different regions of the genome?**

**d) Is nature providing saturation mutagenesis of the human genome?**