Name_____

By printing your name above you acknowledge that while there may have been group discussions of these problems, the work below is yours.

I want to encourage you to work together on these problems, but make sure you understand how to solve each problem on your own. Show all of your work. No credit will be given for answers without work. If a question requires you to determine a genotype show how you obtained it. Please write neatly. If I can't read it, I can't grade it. The homework is due Friday, January 28th, before class begins. If it is handed in after class has started there is a 5-point deduction and a further 5 points for each day it is late.

Answer the following questions about the information discussed in the following abstract:

Delaney *et al.,* (1996) Cystic fibrosis mice carrying the missense mutation G551D replicate human genotype-phenotype correlations. *EMBO J.* **15**: 955-63.

We have generated a mouse carrying the human G551D mutation in the cystic fibrosis transmembrane conductance regulator gene (CFTR) by a one-step gene targeting procedure. These mutant mice show cystic fibrosis pathology but have a reduced risk of fatal intestinal blockage compared with 'null' mutants, in keeping with the reduced incidence of meconium ileus in G551D patients. The G551D mutant mice show greatly reduced CFTR-related chloride transport, displaying activity intermediate between that of cftr(mlUNC) replacement ('null') and cftr(mlHGU) insertional (residual activity) mutants and equivalent to approximately 4% of wild-type CFTR activity. The long-term survival of these animals should provide an excellent model with which to study cystic fibrosis, and they illustrate the value of mouse models carrying relevant mutations for examining genotype-phenotype correlations.

What is a "null" allele of a gene? **A null allele is a loss-of-function mutation in which all protein function has been lost.**

What is a "hypomorphic" allele of a gene? **A hypomorphic allele is a loss-of-function mutation in which there is still residual protein activity/function left.**

In the spaces below list the three different CFTR mutations (G551D, mlUNC, mlHGU) in order of increasing residual protein activity. Then indicate which allele, when homozygous, would likely produce a severe CF phenotype in a patient and which allele, when homozygous, would produce the most mild form of CF in a patient.

Lowest CFTR activity ⟶ Highest CFTR activity

mlUNC (Severe) **G551D** **mlHGU (mild)**

Of the two heterozygous genotypes listed below, which would likely have the less severe form of CF? *Explain your answer*.

$cftr^{mlUNC}/cftr^{G551D}$ **$cftr^{mlHGU}/cftr^{G551D}$**

$cftr^{mlHGU}/cftr^{G551D}$ would have a less severe form of the disease since it is a combination of the most hypomorphic allele and the G551D allele. The other heterozygote has the null allele and G551D, which would produce less CFTR activity and thus have a more severe phenotype.

In tomatoes, two alleles of one gene determine the character difference of purple (P) versus green (G) stems, and two alleles of a separate, independent gene determine the character difference of "cut" (C) versus "potato" (Po) leaves. You do the following five different crosses given below, where P and G stand for purple and green **phenotypes** respectively, and C and Po stand for the "cut" and "potato" **phenotypes**. For example: P, C x P, C indicates that the two parent tomato plants have purple stems and cut leaf phenotypes, it does not indicate their genotypes.

Number of Progeny Observed

Parental **Phenotypes**	P, C	P, Po	G, C	G, Po
1. P, C x G, C	321	101	310	107
2. P, C x P, Po	219	207	64	71
3. P, C x G, C	722	231	0	0
4. P, C x G, Po	404	0	387	0
5. P, Po x G, C	70	91	86	77

Using the above data, determine which alleles for each character are dominant and which are recessive. Make sure to indicate what your allele symbols mean.

The key to this problem is to look for phenotypic ratios. In particular, the classic 3:1 dominance ratio will help you answer this section of the problem and give you a great headstart for the second part. Since they are independently assorting, you can deal with the stem color phenotype separately from the leaf phenotype.

Cross number two has two Purple parents producing 426 Purple progeny and 135 Green progeny. This is close to a 3:1 phenotypic ratio and this tells you two things. First, Purple is dominant to green and we can call the dominant Purple allele P and the recessive green allele p. Second, in order to get the 3:1 ratio both parents must he heterozygotes (Pp). Finally all green parents must be pp.

This same logic can be used with Cross 3 and the two Cut parents producing a roughly 3:1 ratio of Cut to Potato. So Cut is Dominant (C) and Potato is recessive (c). All potato parents must be cc

So now we have our dominance relationships for both genes we can finish the genotypes below.

Assign genotypes to the parents in each cross (1-5). Assume a locus is homozygous unless the data indicates otherwise. Remember that there are two alleles present for each gene. Give a **one-sentence explanation** for your answer in the space provided.

Cross 1 Genotypes: **There is a 1:1 ratio of Purple to Green and one parent was green. So the original parents were Pp and pp. A 3:1 ratio of Cut to Potato. This is created by two heterozygous Cut parents. Answer PpCc x ppCc**

Cross 2 Genotypes: **There is a 3:1 ratio of Purple to Green. This is created by two heterozygous Purple parents (Pp). There is a 1:1 ratio of Cut to Potato and one parent is Potato (cc). So the original parents were Cc and cc. Answer PpCc x Ppcc**

Cross 3 Genotypes: **All purple plants from a Purple and a Green plant. The Purple parents must by PP. A 3:1 ratio of Cut to Potato. This is created by two heterozygous Cut parents. Answer: PPCc x ppCc**

Cross 4 Genotypes: **There is a 1:1 ratio of Purple to Green and one parent was green. So the original parents were Pp and pp. All Cut plants from a Cut and a Potato plant. The Cut parents must by CC. Answer: PpCC x ppcc**

Cross 5 Genotypes **There is a 1:1 ratio of Purple to Green and one parent was green. So the original parents were Pp and pp. There is a 1:1 ratio of Cut to Potato and one parent is Potato (cc). So the original parents were Cc and cc. Answer: Ppcc x ppCc**