Case 3
Wei is a 23-year-old patient who tested positive for SARS-CoV-2 infection approximately 2 months ago. Her early symptoms included fever and anosmia (loss of smell). Within a week, she developed a persistent cough and a few days later could not catch her breath.

Upon presentation at the emergency room, Wei’s blood oxygen saturation was 82% and a chest x-ray revealed widespread opacities that appear glass-like and signs of a secondary bacterial infection. She was admitted to the intensive care unit and placed on a ventilator. Unfortunately, the bacterial infection was resistant to the first two medications tried. Wei was placed on the ventilator for 6 weeks. She suffered irreversible damage to her lungs from the infections. Given her young age, Wei was a good candidate for a double lung transplant. The surgery went well and now she needs to be started on a medication to prevent rejection of the transplant.
Case 3

• The prescriber is considering treating with:

**Tacrolimus (Prograf)**

• Question 1: How does this drug work to prevent rejection of solid organs?

*Hint: pharmacodynamics; use [https://www.pharmgkb.org/annotatedDrugs](https://www.pharmgkb.org/annotatedDrugs)*
Case 3

• Metabolism of tacrolimus:

Tacrolimus $\xrightarrow{\text{Liver}}$ CYP3A5 $\xrightarrow{13\ O\text{-}demethyl-tacrolimus}$ Remove from the body

• Key pharmacogene for tacrolimus: CYP3A5
You recommend preemptive testing of Wei’s *CYP3A5* genotype before initiating therapy with tacrolimus. In the meantime, you have the genotypes of Wei’s parents in the electronic medical records.

Dad

*1/*6

Mom

*1/*3
Case 3

• Question 2: What genotypes and phenotypes are possible for Wei based on her mom and dad’s genotype?

<table>
<thead>
<tr>
<th>Possible Genotypes (*X/*X)</th>
<th>Phenotype (Poor/Normal/Intermediate/Ultrarapid Metabolizer)</th>
<th>Drug Therapy Recommendation (Use/Don’t Use/Change Dose)</th>
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Use This Website To Look Up Genotype-Based Dosing: https://www.pharmgkb.org/chemical/PA451578/guidelineAnnotation/PA166124619
Case 3

• Wei underwent genotyping and you have received the results from the laboratory.

  **CYP3A5: *1/*3**

• Question 3: What is Wei’s phenotype?

• Question 4: What do you recommend for their treatment? Why (better or worse benefit/toxicity)?