Variant interpretation in the CDL

At the CDL, we strive to provide comprehensive and accurate variant interpretations. To adhere to professional standards, we have adopted the recently released ACMGG/AMP guidelines for variant interpretation (Richards 2015). However, in some circumstances, our experience with certain types of variants may lead to a classification that does not strictly conform to those guidelines, including but not limited to the following:

1. Novel canonical glycine substitutions in the triple helical domain of *COL1A1, COL1A2* or *COL3A1*
2. Novel null mutations in genes in which haploinsufficiency is known to be pathogenic

In circumstances in which our experience allows us to interpret a variant as pathogenic with a high degree of certainty but the available evidence does not fulfill the guideline standards for 'pathogenic variant' classification, we will still classify the variant as pathogenic. In doing so, we strive to minimize the likelihood of introducing unnecessary uncertainty that may negatively influence patient care. We will explicitly comment on our practice in any reports in which it is pertinent, to provide full disclosure to the ordering provider and patient.

At this time, CDL does not have a reliable mechanism by which we can routinely revisit variant interpretations that were previously issued. If a variant of uncertain significance was identified in your patient at CDL, we welcome requests to re-interpret the variant using the most up-to-date evidence available and applying these new guidelines. If a variant is re-classified due information not available at the time of the original interpretation, an addendum to the original report will be issued at no additional charge. Requests for re-interpretation can be submitted by telephone, email or fax.